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MAJOR ARTICLE

Meeting Report on an Integrated Research Agenda for Mosquito-Borne Arboviruses

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The emergence and re-emergence of mosquito-borne arbovirus (MBV) diseases pose a rapidly expanding global health threat fueled by the convergence of multiple ecologic, economic, and social factors, including climate change, land use, poverty, deficiencies of water storage and sanitation, and limitations of vector control programs. On December 6, 2023, the Wellcome Trust and the University of Minnesota's Center for Infectious Disease Research and Policy held a meeting titled "An integrated approach to mosquito-borne arboviruses: a priority research agenda." The meeting comprised presentations, panels, and facilitated discussions aimed at describing the state of the field, highlighting recent accomplishments, identifying novel strategies, and defining priority research goals and approaches for addressing MBV disease preparedness and response. This report summarizes meeting discussions in 3 key areas: the changing epidemiology of MBV disease, current and potential transmission- and disease-monitoring strategies, and evolutionary impacts on disease burden and transmission. It concludes with a list of priority strategies for research and investment in MBV disease prevention, preparedness, and control. To prepare for future epidemics of MBV diseases, research and policy will benefit from a multipathogen approach to MBVs. Building on existing knowledge and systems, these efforts must address social and ecological factors and connect with other global health agendas.

Keywords. disease control; disease prevention; mosquito-borne arbovirus; policy; research.

Over the past 2 decades, outbreaks of arthropod-borne viruses (arboviruses), particularly mosquito-borne arboviruses (MBVs), have escalated in frequency, intensity, and geographic distribution. Rapid expansion of MBVs has been fueled by the convergence of multiple ecologic, economic, and social factors, including climate change, urbanization, global travel and trade, land use changes, poverty, deficiencies of water storage and sanitation, and insufficient vector control programs [1–4]. By exploiting travel and trade networks and adapting to urban environments, mosquito vectors are expanding their global reach and increasing the frequency and scale of outbreaks of MBV-transmitted diseases [5, 6].

Although multiple genera of mosquitoes can transmit viruses, *Aedes* (*Stegomyia*) species are of particular concern as they are the primary vectors of Dengue, chikungunya, yellow fever, and Zika viruses, among others, causing large outbreaks, which result in substantial morbidity and mortality [1, 7–12]. Additional emerging viruses could be spread by *Aedes* species, magnifying their threat to global public health. Recognizing the urgency of reducing the current and potential burden of emerging and re-emerging MBV diseases, the Wellcome Trust and the University of Minnesota's Center for Infectious Disease Research and Policy (CIDRAP) invited global experts and

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Table 1. Agenda of the Integrated Mosquito-Borne Arbovirus Strategy (December 6, 2023)

Welcome, Overview, and Objectives	
Session 1: The changing epidemiology of mosquito-borne arboviral diseases and key driving factors	
…	• Epidemiologic overview: emergence, expansion, and increasing severity of mosquito-borne arboviral diseases • Erin Staples, US Centers for Disease Control and Prevention (CDC) • Role of vectors and environmental change; Kris Murray, London School of Hygiene & Tropical Medicine (LSHTM) • World Health Organization (WHO) Global Arbovirus Initiative; Diana Rojas Alvarez, WHO • Moderated discussion; Natsuko Imai-Eaton, Wellcome
Session 2: Strategies for surveillance, early detection, and monitoring global spread	
Overview of strategies for early detection and monitoring genomic variation for emerging and re-emerging mosquito-borne viruses	• Genomic epidemiology; Nuno Faria, Imperial College London • Mathematical modeling; Henrik Salje, University of Cambridge • Vector surveillance, vector biology and emergence of mosquito-borne viruses; Rafael Maciel-de-Freitas, Fundação Oswaldo Cruz (Fiocruz) and Bernhard Nocht Institute for Tropical Medicine (BNITM) • Moderated discussion; Petra Fay, Wellcome
The role of animal reservoirs and the risk of spillover	• Animal reservoirs for mosquito-borne arboviruses; Rosemary Sang, Kenya Medical Research Institute (KEMRI), International Centre of Insect Physiology and Ecology (ICIPE) • Approaches for detection and characterization of emerging arboviruses in the Brazilian Amazon; Pedro Vasconcelos, Universidade do Estado do Pará and Instituto Evandro Chagas • Moderated discussion; Petra Fay, Wellcome
Session 3: Viral evolution and adaptation: impact on transmission and burden of disease	
Host–pathogen interactions, evolution, and environmental factors driving emergence and re-emergence	• Virus–host interactions and adaptation; Kevin Maringer, Pirbright Institute • Tracking and predicting viral adaptation; Lark Coffey, University of California, Davis • Vector control: update and future research priorities; Luke Alphey, University of York • Moderated discussion; Ana Cehovin, Wellcome
Session 4: Integrated arbovirus strategies for epidemic preparedness and response	
Panel presentations	• Building a framework for an integrated arbovirus strategy: critical needs for preparedness and response; moderator: Natsuko Imai-Eaton; Wellcome panelists: ◦ Samuel Dadzie, Noguchi Memorial Institute for Medical Research ◦ Thais dos Santos, Pan American Health Organization (PAHO) ◦ Eva Harris, University of California, Berkeley ◦ Yee-Sin Leo, National Centre for Infectious Diseases (NCID), National Healthcare Group ◦ Jean Patterson, National Institute of Allergy and Infectious Diseases (NIAID), National Institutes of Health (NIH) ◦ Steven Sinkins, MRC University of Glasgow Centre for Virus Research ◦ Jurai Wongsawat, Bamrasnaradura Infectious Diseases Institute (BIDI), Department of Disease Control, Ministry of Public Health, Thailand
Wrap up, next steps, and closing	• Josephine Golding, Wellcome • Alex Pym, Wellcome

key stakeholders to develop a research agenda for MBVs, with a focus primarily on 2 main mosquito vectors, *Ae. aegypti* and *Ae. albopictus*.

This report—which is not intended as a comprehensive overview of MBV diseases—summarizes meeting discussions in 3 key areas: the changing epidemiology of MBV disease, current and potential transmission- and disease-monitoring strategies, and evolutionary impacts on disease burden and transmission. It concludes with a list of priority strategies identified by meeting participants for research and investment in MBV disease prevention, preparedness, and control.

APPROACH

On December 6, 2023, the Wellcome Trust and CIDRAP hosted a meeting titled "An Integrated Approach to Mosquito-Borne Arboviruses: A Priority Research Agenda." Global experts and key stakeholders participated in an invitational hybrid meeting, held in person and remote at the Wellcome Trust in London, UK. Attendees represented various sectors including academic and government institutions, nongovernmental organizations, multinational agencies, industry, and funding organizations.

The meeting agenda (Table 1) was prepared in advance by the meeting organizing committee through consultation with topic area experts. The meeting comprised 4 sessions: (1) the changing epidemiology of mosquito-borne arboviral diseases and key driving factors; (2) strategies for surveillance, early detection, and monitoring global spread; (3) viral evolution and adaptation: impact on transmission and burden of disease; and (4) integrated arbovirus strategies for epidemic preparedness and response. Each session incorporated presentations, panels, and moderated discussions, with the overarching goal of describing the state of the field, highlighting recent accomplishments, identifying novel strategies, and defining priority

research goals and approaches for improving epidemic preparedness and response. Through scientific presentations, panel discussions, and facilitated large group discussions, participants defined an integrated approach to mitigating MBV disease emergence and re-emergence, including crucial research strategies that emphasize commonalities in factors driving MBV expansion and that leverage and maximize synergies for surveillance, research, prevention, and control.

The meeting notes and audio and video recordings from the meeting were reviewed and summarized. Presenters and panel discussants listed as authors reviewed and approved the meeting proceedings and outcomes contained in this report.

SUMMARY

Changing Epidemiology of Mosquito-Borne Arboviral Diseases

The incidence and geographic distribution of multiple *Aedes*-borne arboviral diseases have escalated in recent decades, resulting in larger epidemics, new geographic areas, and emergence of viruses with epidemic potential. Dengue virus infections have increased substantially in recent decades; the World Health Organization (WHO) reported a 10-fold surge in reported cases worldwide from 500 000 in 2000 to 5.2 million in 2019. Global incidence has further escalated in recent years, particularly in the Americas and Asia, and Dengue infections have appeared in new, previously unaffected, areas. As of November 2024, reported Dengue cases in the region of the Americas reached nearly 12.7 million, far exceeding the prior record of 4.3 million cases in 2023 [7, 13]. Currently, an estimated half of the world's population lives in areas with endemic Dengue transmission [14].

Yellow fever outbreaks have also occurred with increased frequency and intensity and in new geographic areas. As of 2023, 34 countries in Africa and 13 countries in South America reported cases of yellow fever within their borders [15]. Despite availability of vaccine, the 2016–2018 yellow fever outbreak in Brazil, caused by 2 sylvatic species, *Haemagogus janthinomys* and *Hg. Leucocelaenus*, represented the country's largest outbreak in >80 years, extending to new areas and resulting in 2154 reported cases and 745 deaths [16]. The increasing number and size of yellow fever outbreaks have put strains on vaccine supply. Concurrent outbreaks in Angola and the Democratic Republic of the Congo in 2016 and in Brazil in 2017–2018 led to implementation of a fractional-dose vaccination approach (consisting of one-fifth of a dose) due to constraints on global vaccine supply [17]. Yellow fever virus is not endemic to the Asia-Pacific region; however, laboratory studies demonstrate that Asian *Ae. aegypti* are competent vectors for the virus. It is unknown why outbreaks have not yet occurred in the region [18, 19].

A major outbreak of chikungunya in the Eastern Hemisphere in and around the Indian Ocean in 2005–2006 eventually spread to Europe, where autochthonous transmission was established. Autochthonous mosquito-borne transmission of chikungunya was first identified in the Americas in 2013; cases there quadrupled between 2022 and 2023 [1]. Since its emergence, chikungunya has spread rapidly; >3.6 million cases have been reported in 50 countries [5].

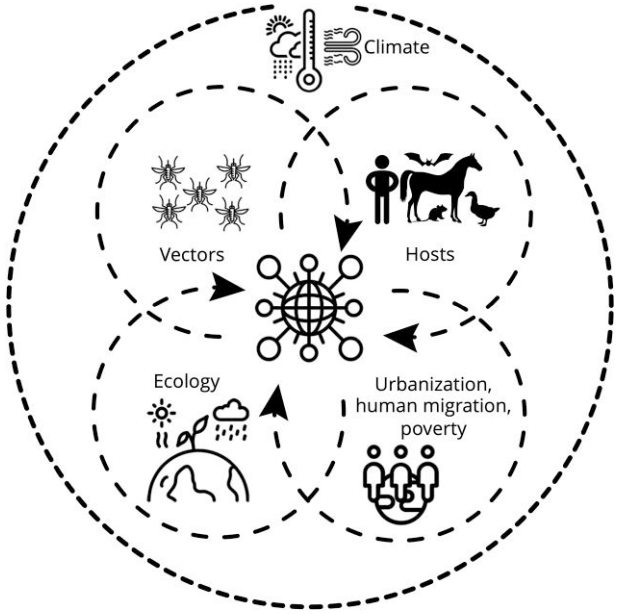

Figure 1. Mosquito-borne arboviral diseases are impacted by several interacting factors including climate; ecology; host factors; human interface and actions such as urbanization, migration, poverty, care seeking, clinical awareness, and testing; and vectors, including vector control methods. Each factor has representative illustrative icons with arrows between factors to indicate interaction.

Zika virus emerged as a pathogen of epidemic potential in 2007 in the Federated States of Micronesia, followed by additional large outbreaks in other Pacific islands, and then emerged in the Americas in 2015. Upon determining Zika virus infection as the cause of microcephaly and Guillain-Barré syndrome, the WHO declared a Public Health Emergency of International Concern (PHEIC) [20, 21]. Over 750 000 cases of Zika virus disease were reported during the outbreak, resulting in >1450 Zika-associated microcephaly cases in Brazil alone. To date, 92 countries and territories have reported evidence of autochthonous mosquito-borne Zika virus transmission [22].

Participants emphasized that the changing epidemiology of MBV diseases transmitted by *Ae. aegypti* and *Ae. albopictus* is influenced by multiple direct and indirect interacting factors, including climate, ecology, vector dynamics, and host factors including human migration, urbanization, crowding, poverty, water storage and sanitation, habitat destruction, travel, and medical care-seeking. The numerous factors that affect vector populations and viral transmission make it challenging to predict, prevent, and mitigate disease (Figure 1).

Important efforts have been made to monitor and forecast the changing geographic distribution of *Ae. aegypti* and *Ae. albopictus* and related vector-borne diseases as a result of climate change [23, 24]. Modeling scenarios predict that both *Aedes* species will expand their geographic reach in the Northern Hemisphere and contract in the Southern Hemisphere. For example, Europe is expected to become more suitable for these vectors, but regions such as the Amazon Basin, where precipitation levels are predicted to decline, will become less suitable [25]. To a given threshold, increases in temperature, precipitation, and humidity are associated with increases in suitability, but can also lead to decreases of vector species once the threshold is surpassed (eg, due to increased droughts) [26]. This complexity presents severe challenges for anticipating or preparing for climate-induced changes in arboviral diseases broadly, particularly in highly populated regions where other local factors are heavily modified (eg, built infrastructure, water resources, habitats) [27].

Participants emphasized the effects of climate not only on vector populations, but also the important impact of climate on human factors that facilitate MBV transmission and disease, including migration, urbanization, crowding, and poor water storage and sanitation. Initial outbreaks of chikungunya in coastal Kenya in 2004 were facilitated by drought conditions, during which water-holding containers were kept in close proximity to homes [28]. Similarly, in 2022, migration of nomadic populations in response to drought was associated with the first yellow fever cases in Kenya in ~30 years [29]. Environmental modifications such as deforestation, combined with elevated temperatures and rainfall, have been linked to increased incidence of MBV disease in Northern Brazil [30]. Presenters additionally provided examples of how climate has affected circulation of West Nile virus (WNV), which is transmitted by *Culex* mosquitoes. For example, early-season hurricanes were linked to increased disease rates on the northern coast of the Gulf of Mexico, while late-season El Niño–related rainfall in 2021 preceded the largest focal outbreak of WNV disease in the United States [31, 32]. Modeling has demonstrated the critical role of climate change in geographic expansion of WNV in Europe in the past century [33].

In addition to climate change, human alterations to the natural environment, such as deforestation, urban development (eg, road building, dam construction), and land use (eg, mining) have created favorable habitats for arboviral mosquito vectors, thereby encouraging emergence and re-emergence of MBVs [6]. Although anthropogenic disturbance can in some cases reduce overall abundance of mosquito vectors, it may simultaneously select for vector species tolerant of or advantaged by land use changes. For example, urbanization produced strong declines in *Aedes* and *Anopheles* species richness while simultaneously boosting *Ae. aegypti* populations [6]. Disruption of the environment can push arboviruses that normally have a localized distribution to adapt to new hosts and urban spaces.

Strategies for Monitoring Arbovirus Transmission and Disease

Multiple and complementary approaches to MBV surveillance have been developed to predict outbreak activity, detect emergence, track viral evolution, identify transmission drivers, and monitor spatiotemporal spread. Presenters emphasized the need for comprehensive, integrated surveillance to examine roles of animal reservoirs, refine vector control strategies, guide vaccine design, and develop vaccination strategies. Early detection and outbreak response require cross-sectoral collaboration, including across surveillance systems [34].

Molecular epidemiology and genomic arbovirus surveillance techniques include genomic sequencing, reconstructing evolutionary relationships using phylogenetic methods, and reconstructing viral transmission pathways using epidemiological metadata (eg, date and location of sampling, travel history, host and vector species) [35]. These methods enable early detection of outbreaks, identification of viral lineages with increased virulence, assessment of interventions, and transmission cycle characterization [36]. Participants described using genomic surveillance to enable Zika surveillance across mobility corridors [20, 37], to monitor zoonotic spillover of yellow fever and rule out vaccine reversions [38], and to improve Dengue transmission forecasting [39]. Despite its value, genomic surveillance of MBVs is underused in comparison to other pathogens; for example, Zika remains the least sequenced pathogen responsible for declaration of a PHEIC [40]. Building global capacity to monitor the genomic epidemiology of arboviral diseases will require engagement and investment of multiple stakeholders, including national governments, multilateral organizations, researchers, and public health experts.

Mathematical modeling can enhance surveillance to improve recognition of epidemic processes, disease dynamics, and transmission risk. Several examples have demonstrated the utility of mathematical models for interpreting complex information derived from multiplex serology and for analyzing highly dimensional data. Retrospective modeling and reconstruction of likely exposures among pregnant people in French Polynesia demonstrated that Zika virus infection in the first trimester of pregnancy was significantly associated with increased risk of microcephaly [41]. In combination with genomic surveillance and serosurvey data, modeling has been used to investigate duration and persistence of protective antibodies [42–44].

Integrated surveillance that combines animal surveillance, vector surveillance, human virus screening, and seroprevalence studies can reveal critical relationships between animal hosts and arboviruses and highlight transmission dynamics. Participants described how One Health approaches have been

used to detect zoonotic and vector-borne diseases, predict outbreak activity, identify spillover strains, investigate the role of animal reservoirs, and guide vector control by determining arbovirus hotspots [45–49].

Impact of Viral Evolution and Adaptation on Transmission and Burden of Disease

Most MBVs have an RNA genome with a low-fidelity, RNA-dependent RNA polymerase. Thus, MBV adaptations to different hosts are driven by evolutionary factors (eg, viral mutations, molecular virus–host interactions) as well as by ecological disturbance (eg, climate change, land use) [11, 50–52]. Meeting participants considered how factors that exert selective pressures on biodiversity, adaptation, and host interactions affect arbovirus transmission, pathogenesis, and emergence and how these factors can be addressed to better understand, prevent, and respond to MBV diseases.

In theory, significant MBV disease risk could be mitigated through vector control of *Aedes* mosquitoes, but existing vector control methods have been inadequate to reduce the burden of MBV diseases. Current nongenetic approaches—such as modification of mosquito breeding habitats, mass trapping, spatial repellents, systemic insecticides, and autodissemination of larvicide—are best implemented in combination with other vector control methods [53–57].

Genetic engineering control strategies introduce genetically modified mosquito species into areas where they mate with wild mosquitoes and produce offspring incapable of serving as viral vectors, either through vector population suppression (eg, sterile male) or modification (eg, virus resistance). These efforts include the release of sterile males using sterile insect technique/incompatible insect technique (SIT/IIT), sex–ratio distorters, release of insects carrying a dominant lethal gene, and gene drive [58–61]. These area-wide genetic control methods allow for a tailored approach based on the needs of specific communities and result in more equitable distribution and protection compared with individual-level interventions such as vaccines, drugs, and bednets [60].

An important *Aedes aegypti* control prospect hinges on the discovery that infection of mosquitoes with bacteria of the *Wolbachia* genus impedes their ability to transmit virus to humans. *Wolbachia*-carrying mosquitoes have been released in diverse global locations, including in large urban areas; promising results include reduction of Dengue and chikungunya [62–66]. Further research is needed to characterize fitness costs—and therefore the stability and invasiveness—of *Wolbachia* infection in mosquitoes and to explore whether and how *Wolbachia* affects the ecology and evolution of target viruses and nontarget microbial members of the natural microbiome [67, 68]. Most importantly, incorporation of innovative vector control strategies such as genetic engineering, SIT, or *Wolbachia* deployments must be considered under an Integrative Vector Management (IVM) approach to enhance efficacy, cost-effectiveness, and sustainability of vector control interventions by leveraging available tools and resources.

Meeting participants described techniques of arboviral experimental evolution, which involves inoculation of either a mammalian host or a mosquito with a characterized sequence of a virus. Derived virus is then sequenced intrahost and investigated with reverse genetics. These methods have been used to retrospectively identify mutations that modify infectivity, disease, and transmissibility, as well as to predict mutations with outbreak potential for diseases such as Venezuelan equine encephalitis [69], chikungunya [70–72], and Zika viruses [72].

Participants identified evolutionary factors (eg, viral mutation) and human influences (eg, climate change and land use) as drivers of viral diversity and adaptation to different reservoirs. In addition, vector control strategies themselves may contribute to viral evolution by impacting ecology in unpredictable ways. Participants emphasized the importance of reducing unintended consequences of vector control strategies; potential adverse consequences should be carefully considered and interventions designed to monitor and mitigate risk.

Ultimately, vector control will limit the amount of MBV circulating within the vector population and reduce opportunities to acquire genetic mutations that may increase viral fitness. Fewer vectors capable of transmitting viruses to animal or human hosts will also limit opportunities for evolutionary adaptation to those hosts. However, vector control strategies may have unintended effects on viral evolution that should be taken into consideration. For example, when population sizes are reduced, evolutionary forces such as genetic drift have a greater impact, which could inadvertently promote the spread of a novel variant [73]. Participants agreed that further research is needed to better understand how both genetic- and non-genetic-vector control programs may contribute to MBV evolution.

Priority Research Strategies for Arbovirus Epidemic Preparedness and Response

Systems are needed to address MBVs through systematic, integrated, multipathogen, and multihost approaches to tracking, surveillance, and resource prioritization. Presentations described integrated arbovirus strategies being undertaken by organizations including the WHO, the Pan American Health Organization/WHO Region of the Americas, and the US National Institutes of Health. Subsequent discussions identified the following actions to advance a strategic arbovirus research agenda for epidemic preparedness and response.

Establish Collaborative, Innovative Approaches to Surveillance. Collaborative surveillance across multiple sectors and geographies will strengthen early detection and rapid public health response to MBV disease outbreaks [34]. This can be accomplished through a comprehensive One Health surveillance

approach that integrates and analyzes complementary data from humans, vectors, and animal reservoirs through ongoing sampling and during outbreaks. This may be challenging considering the compartmentalized nature of most public health systems, but multiple short-term studies have successfully integrated human, animal, and vector-based WNV data; these could serve as a model for future, long-term efforts to monitor MBVs [74, 75]. An integrated, One Health surveillance approach may be more feasible in urban areas where samples can be routinely collected from human clinical cases, domestic animals, wildlife, and mosquito breeding sites. Participants emphasized that harmonizing surveillance approaches, systems, and end points is key to successful implementation of integrated surveillance.

Better approaches are needed for detecting known and emerging viruses in mosquitoes. Such surveillance, which currently requires large numbers of mosquitoes, is logistically challenging. Coordinated and standardized protocol development for integrated mosquito surveillance in locations that report frequent polymerase chain reaction–positive human and animal disease cases may increase the cost-effectiveness of vector surveillance. Collaboration among researchers working on different mosquito-borne pathogens could also improve surveillance efficiency; for example, *Aedes* mosquitoes that are currently discarded as "by-catch" from malarial vector surveillance of *Anopheles* mosquitoes could be harnessed to study both malaria and mosquito-borne arboviruses more broadly.

Animal and wildlife surveillance data could be incorporated into existing public health structures, requiring coordination in data capture, governance, and overall research framework, as well as the establishment of sentinel sites and provision of incentives for animal breeders. International partnerships between veterinary health organizations and researchers could advance information sharing and coordination of parallel surveillance systems, including those of known animal reservoirs and domestic animals in high-risk areas. Barriers to monitoring animal reservoirs include limited resources, limited funding, and lack of political will, as well as sampling challenges due to low viral prevalence.

Explore Novel Approaches to Diagnostics and Therapeutics. Antibody cross-reactivity between orthoflaviviruses such as Dengue and Zika viruses presents significant diagnostic and surveillance challenges. Plaque reduction neutralization tests (PRNTs) are used for supplementary testing for diagnosis but are labor-intensive, mostly limited to use in reference laboratories, and are not practical for use for surveillance purposes. Novel strategies are under investigation to improve the specificity of serological assays for Zika and Dengue infections, such as targeting specific antigens such as NS1 and domains I and III of the E protein.

Virus–host molecular interactions conserved across pathogens may provide the basis for developing broad-spectrum antivirals for targeting host proteins, novel vaccine approaches for both humans and livestock, and opportunities for developing refractory insects and livestock to reduce disease transmission. Previous work has been successful in developing vaccines against vector saliva that are effective at preventing tickborne disease through reducing transmission [76]. Other vaccines in development that target human arboviral disease could potentially reduce viral transmission.

Broaden Global Capacity for Genomic Surveillance. Genetic sequencing capacity built during the coronavirus disease 2019 (COVID-19) pandemic, particularly in low- and middle-income countries (LMICs), along with recent advances in metagenomics, could improve detection and response to emerging MBV diseases. For a robust public health response, rapid genomic sequencing and timely information sharing are critical. Global capacity and infrastructure for genomic sequencing created during the COVID-19 pandemic could also be leveraged to characterize the genomic diversity of mosquito-borne arboviruses. The advent of low-cost untargeted sequencing protocols offers potential for pathogen-agnostic, real-time genomic surveillance [77].

Genomic surveillance of mosquito-borne viruses is critical for assessing risks of viral variants, predicting viral emergence, and comparing the effectiveness of vaccine and *Wolbachia*-based vector control strategies. Expanding global capacity for genomic surveillance—by increasing trained staff, laboratory capacity, and supporting resources—would improve epidemiological characterization of emerging lineages in hot spots of transmission, identify drivers of transmission, and enable monitoring of spatiotemporal spread at different geographic scales and across transmission cycles. Enhanced genomic sequencing could also contribute to identification of novel drug targets, guide vaccination strategies, and refine vaccine design.

Open sharing of arbovirus genomic data is not only best practice in public health pathogen genomics, but facilitates a One Health approach by providing scientists across disciplines (eg, human, animal, entomologic, and environmental health) access to the same information. Publicly accessible platforms such as Nextstrain provide near real-time analyses of viral genomic data from different hosts and continents, accelerating the interpretation of sequence data to better inform public health responses [78]. These tools circumvent the need for individual laboratories to integrate new data sources into an existing infrastructure, which is often time- and resource-intensive, while fostering global collaboration. Therefore, in addition to enhanced genomic sequencing, efforts should be made to encourage open sharing of genomic data from MBVs to maximize public health impact.

Further Investigate the Complex Role of Climate. The role of climate change within the complex ecosystem of factors that

influence disease (ie, ecology, host availability, vector dynamics, and human behavior) remains a critical area of research. To date, attempts to predict MBV disease occurrence, frequency, and spread have been unsuccessful because of these complex dynamics [79]. Participants advocated the holistic examination of climate-sensitive viral diseases and the community of vectors relevant to their transmission in order to determine how climate interacts with other factors such as urbanization, human and animal migration, land use, water storage, sanitation, and social inequities (eg, poverty). Incorporating these interacting factors into climate change models is expected to increase their accuracy and enhance the ability to attribute changing risks to human-induced climate change specifically, a critical need for informing climate change mitigation and adaptation responses.

Further Evaluate the Impact of Vector Control Strategies. Resistance is a concern for any biocontrol method, whether genetic or nongenetic. Proposed MBV vector control strategies raise additional concerns that warrant further investigation, including the potential for unintended genetic alterations in target and nontarget species, ecological inference on population dynamics and competition, and impacts on biodiversity [80]. Conducting such investigations requires gaining community and ethical consent for field studies, as well as securing funding for laboratory research. Additional barriers include regulatory constraints, lack of resources, lack of expertise and trained personnel, and societal constraints.

Political will and public support are essential commodities to garner long-term commitment and investment at local, regional, national, and international levels to support ongoing and future work. Well-designed and -implemented studies of current and novel vector control methods will inform successful vector control policy and programs; the impact of interventions on transmission and mosquito populations must be assessed through ongoing monitoring. These studies will require sustainable approaches to surveillance, development of guidelines and standards for vector control programs, and promotion of study designs that assess ongoing improvement of vector control methods as well as novel interventions.

Build and Sustain Research Sites. Building and sustaining research sites, particularly in LMICs, for integrated human, vector, and animal research is crucial for epidemic preparedness. Sites with expert staff and laboratory capacity are needed to conduct clinical trials and observational studies, conduct vector surveillance, and inform interventions for disease prevention and vector control. Globally representative and geographically distributed research sites are critical to estimating disease incidence, identifying risk factors for transmission, collecting data critical to outbreak modeling and countermeasure development, and providing samples for diagnostic assay development. Such research sites must have access to affordable surveillance tools and diagnostic technologies (eg, cell culture models, reference genomes, and annotations), standardized protocols for sequencing and bioinformatics, and repositories to access shared resources.

Long-term, cross-sectoral investment is necessary to support research sites that have local as well as international relevance, where both infrastructure and workforce are designed to enable rapid, flexible responses to diverse epidemic threats. Capacity-building in endemic locations, development of regional reference laboratories, engagement with communities at risk, and local workforce development are needed. Such sites are costly to create and sustain. Advocacy efforts are needed to strengthen political will to support the research essential for mitigation of MBV diseases.

Investment in MBV Research and Capacity-Building. The growing global public health threat of MBVs must be met with increased investment in research, surveillance, preparedness, and response. Novel funding strategies will incentivize collaborative and coordinated research on arboviruses and across the spectrum of mosquito-borne diseases. New research and development funding models must be devised to strategically address common needs, improve efficiencies, and streamline global capacity-building.

CONCLUSIONS

The emergence and re-emergence of MBV diseases pose a rapidly expanding global health threat. Human activity and climate change dramatically affect disease occurrence in ways that currently defy prediction. Thus, the world must recognize these escalating threats and prepare for an adaptable response. Shared features and drivers of these mosquito-borne pathogens afford the opportunity to advance coordinated efforts for research, surveillance, preparedness, and response for multiple viruses with epidemic potential. To prepare for future epidemics of MBV diseases, both research and policy will benefit from a multipathogen approach to MBVs that extends beyond currently known species to include better characterization of diversity of potential pathogen communities in hosts and vectors, which may be a source of future novel arbovirus emergence into humans. Building on existing knowledge and systems, these efforts must address both social and ecological contexts and connect to other policy agendas such as the Paris Climate Accords, biodiversity targets, and Sustainable Development Goals.

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