# What sounds like *Aedes*, acts like *Aedes*, but is not *Aedes*? Lessons from dengue virus control for the management of invasive *Anopheles*

*Richard Allan, Sophie Budge, Hendrik Sauskojus*

**_Aedes_ mosquitoes are responsible for transmission of dengue, chikungunya, Zika, and yellow fever viruses. _Aedes_ mosquitoes are the pathfinders of invasive urban-living mosquitoes, and have spread into 129 countries over the past five decades. In the past 10 years _Anopheles stephensi_ has been identified within densely populated cities in Yemen and across the Horn of Africa and as far west as Nigeria. _A stephensi_'s aggressive spread is closely linked to increases in population movement due to migration, conflict, and climate change; rapid unplanned urbanisation; and resulting poor water quality, sanitation, waste container removal, and hygiene systems. As a highly invasive vector that is adept at transmitting malarial pathogens (eg, _Plasmodium vivax_ and _Plasmodium falciparum_), _A stephensi_'s spread holds huge implications for increasing malaria morbidity and mortality. Both vectors (ie, _Aedes_ species and _A stephensi_) thrive in the same urban environments, and urgent action is needed to seize the opportunity to integrate disease control resources and generate innovative vector-control tools for urban populations, to protect the many millions at risk.**

*Lancet Glob Health* 2023; 11: e165–69

Published Online November 22, 2022 https://doi.org/10.1016/S2214-109X(22)00454-5

**The MENTOR Initiative, Haywards Heath, UK** (R Allan MSc, S Budge PhD, H Sauskojus MPH)

Correspondence to: Mr Richard Allan, The MENTOR Initiative, Haywards Heath RH16 1PG, UK **richard.allan@mentor-initiative.net**

## Rapid spread of *Aedes* and *Aedes*-borne diseases

Described as the most dangerous animal in the world,[1] mosquitoes live in most parts of the globe, with *Anopheles*, *Aedes*, and *Culex* species all capable of transmitting deadly diseases to humans, posing one of the greatest threats to global health. Carrying four deadly, fast-spreading arboviruses (ie, dengue, chikungunya, Zika, and yellow fever—of which only yellow fever has a vaccine), *Aedes aegypti* is responsible for an ever-growing morbidity burden. Estimates suggest dengue virus alone infects around 390 million people annually, with 96 million (25%) displaying clinical symptoms.[2]

Prolific vectors, *A aegypti* and *Aedes albopictus* have both been very successful in establishing themselves. Their establishment often correlates with severe cases of dengue virus disease. In the 1960s, only nine countries had had severe dengue virus epidemics. Now, in 2022, around half of the world's population is at risk, with dengue virus present in 129 countries.[3] This rapid spread—even into Europe, as far as southern France—is partly due to the different climate preferences of *A aegypti* and *A albopictus*. *A albopictus* is well adapted to temperate climates and is currently spreading rampantly across the world, whereas *A aegypti* is better adapted to more tropical climates, thus allowing *Aedes* mosquitoes to thrive in almost all regions of the world.[4]

Global spread of the related arboviruses has been equally rapid, with dengue virus now the fastest growing vector-borne disease.[4] This spread has been fuelled by elements of globalisation, including rapid increases in human migration, unplanned urbanisation, global transport systems,[5] inadequate waste container removal services (which increase the number of unintentional water containers that are suitable for mosquito egg laying [eg, tin cans, coconut shells, plastic pots, and tyres]), and use of unsafe water sources and water storage practices.[4,6] As a result, *Aedes* species have thrived in urban and suburban areas, benefiting from novel alterations in the environment that have substantially affected disease transmission.[7] Given the scarcity of specific treatments and often poor supportive care, approaches to contain *Aedes*-borne viruses such as dengue virus rely on controlling the vector itself (ie, mosquitoes),[6] but these have mostly been unsuccessful in suppressing an increasing number of epidemics and the geographical expansion of endemic transmission.[2]

## *Anopheles stephensi*: a worrying newcomer

*A stephensi*, an invasive mosquito vector adept at transmitting malarial parasites *Plasmodium falciparum* and *Plasmodium vivax*, is native to south Asia, the Middle East, and southern China. Two of its three known forms (type and intermediate) are efficient vectors in rural and urban settings, making it unique among malaria vectors.[8] The first record of *A stephensi* in Africa was from Djibouti in 2012.[9] In the time since, the arrival of *A stephensi* has been associated with an increase in malaria rates to more than 30-times those reported in 2012.[10] Subsequent discoveries in 2016 in Ethiopia,[11] Sudan,[12,13] and Nigeria,[14] and more recently in 2020 in Somalia[15] (morphologically confirmed in multiple sites[16]), and in 2021, by the Mentor Initiative in southern Yemen (where it might have existed unconfirmed for decades),[17] suggest *A stephensi* is established in the region and beyond. Its introduction into the Horn of Africa (ie, Somalia and Ethiopia) has generated global concern—mainly for the potential of this invasive vector to elevate malaria in densely populated urban environments,[18,19] where transmission was considered lower than in rural communities.[20]

In a similar manner to *A aegypti and A albopictus*, *A stephensi* has adapted well to breeding in select man-made water containers associated with urban settings—preferentially in clean water, although occasionally also in turbid water.[21] The dynamic movement of populations, increasing numbers of internally displaced people (approximately 53·2 million globally in 2021),[22]

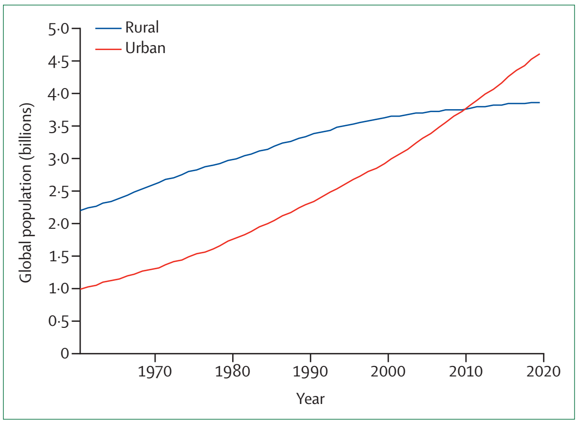


***Figure 1:*** **Proportion of the world's population in urban and rural areas, 1960–2020**
This figure was created from World Bank data on the basis of World Development Indicators.

accompanied by rapid expansion of impoverished urban settings and camps of internally displaced people (often on urban peripheries), means that a transmission surge could pose a major challenge to malaria control where urban transmission increasingly contributes to global cases.[8,19]

## The rural to urban transition

The past six decades have seen a large shift in population movement between rural and urban areas. The change in percentage split of global rural and urban populations from 1960 to 2020 is illustrated in figure 1. Although nuances in degrees of urbanisation are not captured, data estimate that in 1960, 33·6% of the global population was urban; this increased to 56·1% in 2020 and is predicted to reach 68·0% in 2050.[23] Urbanisation resulting from population movement is a complex process, involving changes in previously non-urban spaces to urban landscape, which consequently change the demographic, economic, and social make-up of rural and urban areas. Rapid urbanisation substantially increases the demand for some services, such as those relating to water, sanitation, and hygiene (WASH).[23] This type of rapid change without the necessary infrastructure also means that a quickly growing, vulnerable part of the population is left in need, particularly in peri-urban and informal settlements (including camps for internally displaced people). Additionally, in 2020, only 19·2% of rural households globally had sufficient access to WASH services, whereas 60·4% of households in urban areas had sufficient access (figure 2).

This statistic, however, hides great disparities: low-income urban households are particularly underserved, with greatly reduced access to clean drinking water.[23] This disparity bears significance for vector control. With increasing numbers of people moving to poorly resourced urban areas with unreliable piped water supply, and with global increases in internally displaced people living in temporary shelters, there is an increased dependency on man-made water storage containers—a key risk factor for increased mosquito breeding.[24]

## Expanded malaria distribution: a realistic threat

Given that, in one decade, we have detected *A stephensi* in urban settings across the Middle East, east Africa, and most recently in Nigeria in July, 2022,[14] it is not unreasonable to suggest that *A stephensi* can establish itself in urban settings, potentially even more quickly than *Aedes* species, and could increasingly contribute to global morbidity and mortality.

First, despite extensive control up to the period 1950–60, once large-scale vector-control systems (eg, community-based water storage management and larviciding) stopped or failed, the *Aedes* vector expanded rapidly. Using dengue virus as an indicator of the vector's spread, it could be determined that the rate at which dengue virus was transmitted within and across countries is in some manner rate-dependent on urbanisation.[4,7] Second, as of 2022, urbanisation has already extensively occurred and, where environmental conditions favour it, there is no limit to the speed at which *A stephensi* could spread across parts of the world. Third, unlike dengue virus infection, in which those who die usually have severe haemorrhagic disease, clinical malaria infections in young children can kill within 24 h of the primary fever. Although low-level inoculation of malaria parasites during childhood helps to gradually develop children's immune systems and prevent serious clinical outcomes, high inoculation rates can quickly overwhelm naive immune systems.

Research from 2020 suggests cities in Africa are at increased risk of malaria.[8] If transmission of malaria increases in line with the ability of *A stephensi* to multiply in Africa, this raises the potential that not only large, new populations are at risk of infection, but also a greater proportion of individuals who are immunologically susceptible given that urban residents have lower levels of previous exposure than those in rural communities.[4] People with malaria from these newly affected urban populations will be at greater risk of deterioration into severe clinical symptoms than those in previously affected populations, with a proportionately higher risk of death.

## Opportunities and challenges for control

The rapidity with which *Aedes* species have spread across the globe would suggest that few control strategies have been successful in containing them and the diseases they spread. *Aedes* control is complex: it requires standardised control measures and quality-control activities, monitoring protocols, community-based programmes, and emergency planning to mitigate the risk of epidemics.[7] Control is further complicated by increasing levels of urbanisation. Despite studies indicating a paucity of evidence for the effectiveness of dengue virus

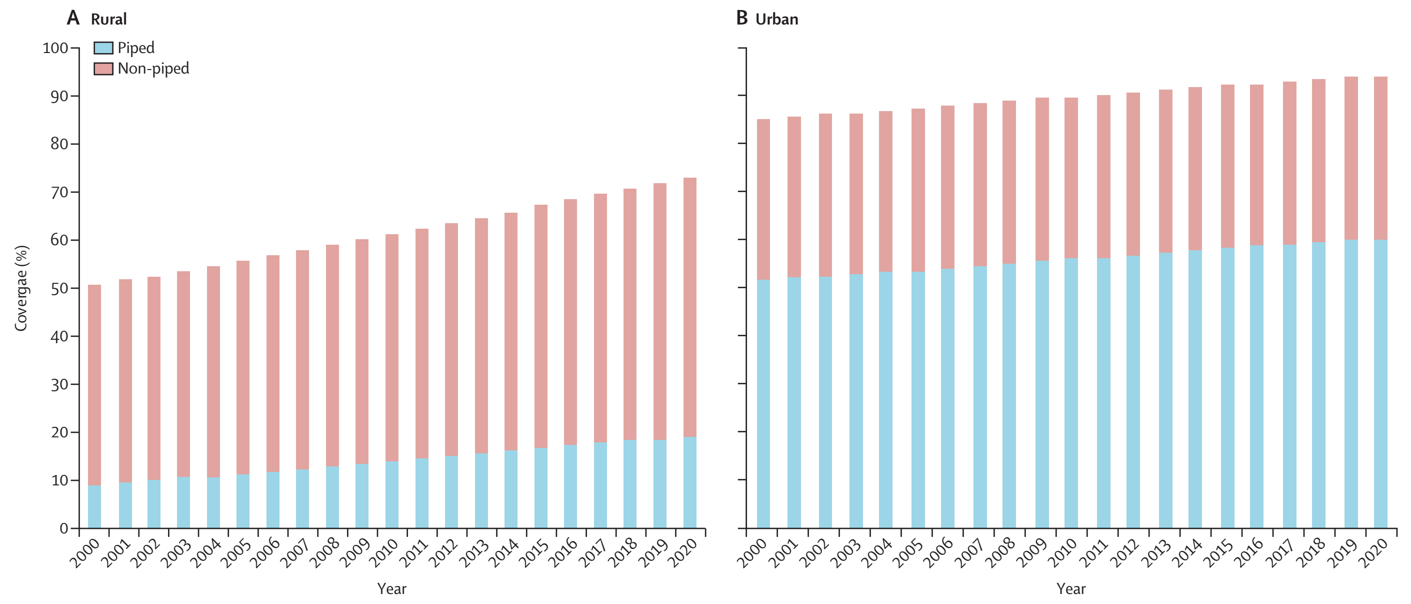


***Figure 2:* Coverage of household-level drinking water by facility type across rural and urban areas for the least developed countries, 2000–20**
Facility types are piped and non-piped. This figure was created from data from the WHO–UNICEF Joint Monitoring Programme for Water Supply, Sanitation and Hygiene.

control methods, country-level data often mask successes seen at the city level. Furthermore, although successes might be modest overall and there remains a scarcity of evidence for long-term maintenance of community programmes,[25] it is highly probable that, taken together, programmes have kept *Aedes* populations low in settings where vector populations—and related disease incidence—would otherwise have greatly increased. Previous well implemented *Aedes*-species control programmes have contained yellow fever's spread in the Americas (1900–69) and more recently dengue virus in Singapore (1970–89) and Cuba (1980–99).[26] Undoubtedly, there are lessons to be learned following decades of *Aedes* control and related diseases in urban settings.

This is not the time to wait and see. Individuals aiming to eradicate invasive *Anopheles* species must work together to take up what is known. So where are the opportunities and challenges? First, the technical challenges in controlling *A stephensi* and malaria are no more complex than those for the diseases that *Aedes* species spread. However, the fact that the two are not usually considered together highlights the divisions in current thinking. Existing vector-control programmes for *Aedes* mosquitoes in both urban and humanitarian settings offer the opportunity for combined vector-management strategies with those targeting *Anopheles*.[27] These programmes could also alleviate the burden of implementing standalone measures. Conversely, integrated vector-management strategies that target *Anopheles* breeding sites will also manage populations of *A aegypti*, *A albopictus*, and other anthropophilic *Aedes* species, and thus potentially reduce the incidence of dengue, chikungunya, Zika, and yellow fever viruses.

*A stephensi* larvae have been found coexisting in water storage containers with *A aegypti*; therefore, interventions that are already in place, as well as better management of urban infrastructure such as water management, could help control both.[8] Man-made water containers for household water storage and unmanaged waste containers are clearly key risk factors for *Anopheles* mosquitoes taking hold in urban settings. Therefore, given that internally displaced people and individuals in refugee camp settings have high dependency on household and shelter-level water storage containers, improving management of and habits around water storage and waste container disposal, and introducing piped water and control of domestic waste are essential. Vector control is integrally linked to concepts of environmental hygiene[28] and targets of the WASH sector. Integrated interventions could, therefore, be transformative in their ability to target multiple disease agents. This integration of interventions is particularly pertinent in fragile settings (ie, settings that are affected by ongoing humanitarian crises, recovering from humanitarian crises, or hosting displaced populations), where high rates of morbidity from one infectious agent are often reflected across others (eg, diarrhoea coexisting with malaria).[29] This correlation highlights the inter-related effects of environmental conditions (eg, poor sanitation leading to standing water) on disease incidence in susceptible people. Given the synergies between vectors and also between the diseases they transmit, such disconnected thinking must be overcome when it limits the ability of all actors (eg, international and national organisations involved in coordinating or ensuring delivery of essential services such as health, WASH, shelter, and education) to think creatively about how to bring disease under control. We must learn to work across different settings and outcomes.

There are clear opportunities for synergies within programming. As mentioned previously, the technical challenges in controlling *A stephensi* and malaria in African urban settings are no more complex than those used to control diseases that *Aedes* species spread. However, global malaria prevention relies on two control methods—long-lasting insecticidal nets and indoor residual spraying—neither of which are easy to use or very suitable in urban contexts (high ceilings and plaster walls can render net hanging difficult and the spraying of internal walls can be disruptive to families who must vacate during the process); therefore, the need to reimagine how we prevent malaria at scale is key. Easy-to-use innovative tools like spatial repellents and long-lasting larvicides are crucial, particularly in synergy with environmental control methods, improvements in WASH, and overall environmental hygiene. Much progress has already been made in the development of *Aedes* control in urban settings,[25] through experience with joint dengue virus and Zika virus control programmes in Latin America in 2016–17. It is probably funding, not technical capacity, that will make or break the opportunity to co-manage invasive vectors. The greater challenge will revolve around existing global and national coordination, and setup of funding mechanisms for disease control.

In 2005, the International Humanitarian and Development Coordination Architecture, working with humanitarian organisations, established a global coordination system for humanitarian responses. When this cluster system split organisations that were working in crises into 11 different skill sectors, each coordinated by a respective UN-managed or non-governmental organisation-managed cluster, it consequently created 11 or more respective funding silos. In some crisis circumstances organisations do overlap (eg, when one sector is permitted to design programmes across two or more clusters); however, this is not typically the case. Humanitarian organisations, particularly managing vector-borne disease control in a crisis, must coordinate with multiple sectors (eg, health, WASH, shelter, nutrition and education, camp coordination, and management) on a continual basis for effective operational delivery and impact. When funding is allocated in this way, it becomes fragmented. The poor cluster coordination that results can mean key areas of disease prevention are unsuccessful and are removed from cluster priority lists for donors—each placing responsibility onto another sector.

The current reality is that within the health sector, malaria, arboviruses, and other vector-borne diseases have their own separate silos of funding and structural coordination frameworks. Large organisations providing funding thus remain constricted in thinking, the effects of which can be seen in current changes in the global distribution of malaria incidence. In 2017, celebrations of malaria-related mortality reductions were tempered by the realisation that successes were largely limited to more stable, peaceful, lower-burden countries—70% of cases remain concentrated in just 11 high-burden countries.[29] Nine (82%) of these countries had long-running conflicts and large displaced, hard-to-access populations. Countries with the highest burden of deaths had received substantially less funding—per person, per year—than countries where access, security, and governance were better. In what was called "a massive wakeup call" in 2018, WHO announced a new, targeted approach to malaria control. This approach was termed high burden to high impact, and it was a country-led response intended to reignite the pace of progress in the global malaria fight.[29] Targeting proportional investment to where the disease burden is greatest might seem logical and straightforward, but silos in leadership systems, coordination mechanisms, and funding create artificial hurdles to the integrated control of multiple vectors and their diseases. Furthermore, this pushes responsibility onto already over-stretched, under-resourced, and unstable health systems and governments already struggling to meet the needs of vulnerable populations.

## Conclusion

Waiting to see if *A stephensi* takes hold in man-made urban breeding sites across Africa and the Middle East as fast and efficiently as the *Aedes* mosquito cannot be an effective control strategy. With malaria control still achieving impressive amounts of annual funding (a committed US$4·5 billion in 2022), now is the time to engage in a coordinated and integrated high-burden-to-high-impact strategy to simultaneously cut off the rapid development of urban malaria transmission and the spread of dengue virus and other *Aedes*-borne viruses. This response must escalate much faster to have a much better effect. At the same time, this situation calls on the scientific community and the private sector to innovate and create novel ways of combatting both malaria and dengue virus disease in tandem, which currently available malaria control tools are not designed for. The combined health effect of decisive, proactive, integrated control in urban settings across invasive vector species will achieve real impact for donor investment and renewed trust for the years ahead. More importantly, it would reduce morbidity and mortality from three invasive vector species that act and are controlled in largely the same way. Success would be measurable in hundreds of thousands of lives.

**Contributors**
RA led the manuscript narrative and contributed to manuscript drafting and finalisation. SB principally wrote the manuscript. HS contributed to manuscript development, drafting, and finalisation.

**Declaration of interests**
We declare no competing interests.

**Acknowledgments**
This Viewpoint received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

**References**

1 Powell JR. Mosquitoes: New contender for most lethal animal. *Nature* 2016; **540:** 525.

2 Bhatt S, Gething PW, Brady OJ, et al. The global distribution and burden of dengue. *Nature* 2013; **496:** 504–07.

3 Brady OJ, Gething PW, Bhatt S, et al. Refining the global spatial limits of dengue virus transmission by evidence-based consensus. *PLoS Negl Trop Dis* 2012; **6:** e1760.

4 Colón-González FJ, Sewe MO, Tompkins AM, et al. Projecting the risk of mosquito-borne diseases in a warmer and more populated world: a multi-model, multi-scenario intercomparison modelling study. *Lancet Planet Health* 2021; **5:** e404–14.

5 Gould E, Pettersson J, Higgs S, Charrel R, de Lamballerie X. Emerging arboviruses: why today? *One Health* 2017; **4:** 1–13.

6 WHO. Comprehensive guidelines for prevention and control of dengue and dengue haemorrhagic fever. Revised and expanded edition. 2011. https://apps.who.int/iris/bitstream/handle/10665/204894/B4751.pdf?sequence=1&isAllowed=y (accessed Oct 5, 2022).

7 Kolimenakis A, Heinz S, Wilson ML, et al. The role of urbanisation in the spread of *Aedes* mosquitoes and the diseases they transmit—a systematic review. *PLoS Negl Trop Dis* 2021; **15:** e0009631.

8 Sinka ME, Pironon S, Massey NC, et al. A new malaria vector in Africa: Predicting the expansion range of *Anopheles stephensi* and identifying the urban populations at risk. *Proc Natl Acad Sci USA* 2020; **117:** 24900–08.

9 Faulde MK, Rueda LM, Khaireh BA. First record of the Asian malaria vector *Anopheles stephensi* and its possible role in the resurgence of malaria in Djibouti, Horn of Africa. *Acta Trop* 2014; **139:** 39–43.

10 Hamlet A, Dengela D, Tongren JE, et al. The potential impact of *Anopheles stephensi* establishment on the transmission of *Plasmodium falciparum* in Ethiopia and prospective control measures. *BMC Med* 2022; **20:** 135.

11 Carter TE, Yared S, Gebresilassie A, et al. First detection of *Anopheles stephensi* Liston, 1901 (Diptera: culicidae) in Ethiopia using molecular and morphological approaches. *Acta Trop* 2018; **188:** 180–86.

12 Ahmed A, Pignatelli P, Elaagip A, Abdel Hamid MM, Alrahman OF, Weetman D. Invasive malaria vector *Anopheles stephensi* mosquitoes in Sudan, 2016–2018. *Emerg Infect Dis* 2021; **27:** 2952–54.

13 Abubakr M, Sami H, Mahdi I, et al. The phylodynamic and spread of the invasive Asian malaria vectors, *Anopheles stephensi*, in Sudan. *Biology (Basel)* 2022; **11:** 409.

14 Nigerian Institute of Medical Research. NIMR discovers new malaria vector in northern Nigeria. July 26, 2022. https://nimr.gov.ng/nimr/wp-content/uploads/2022/07/NIMR-discovers-new-malaria-vector-in-northern-Nigeria-Healthwise_-healthwise.punchng.com_.pdf (accessed Nov 9, 2022).

15 WHO. Malaria threats map: invasive vector species. 2022. https://apps.who.int/malaria/maps/threats/?theme=invasive&mapType=invasive%3A0&bounds=%5B%5B-85.52757787917207%2C-40.92847871546897%5D%2C%5B122.21751245339692%2C65.33169987498877%5D%5D&insecticideClass=PYRETHROIDS&insecticideTypes=&assayTypes=MOLECULAR_ASSAY%2CBIOCHEMICAL_ASSAY%2CSYNERGIST-INSECTICIDE_BIOASSAY&synergistTypes=&species=&vectorSpecies=&surveyTypes=&deletionType=HRP2_PROPORTION_DELETION&plasmodiumSpecies=P._FALCIPARUM&drug=DRUG_AL&mmType=1&excludeLowerPatients=false&excludeLowerSamples=false&endemicity=false&countryMode=false&storyMode=false&storyModeStep=0&filterOpen=true&filtersMode=filters&years=1985%2C2022 (accessed Oct 5, 2022).

16 Ali S, Samake JN, Spear J, Carter TE. Morphological identification and genetic characterization of *Anopheles stephensi* in Somaliland. *Parasit Vectors* 2022; **15:** 247.

17 Allan R, Weetman D, Sauskojus H, et al. Confirmation of the presence of *Anopheles stephensi* among a conflict-affected host community in Aden City, Yemen. *Res Sq* 2022; published online Aug 19. https://doi.org/10.21203/rs.3.rs-1977582/v1 (preprint).

18 Robert V, Macintyre K, Keating J, et al. Malaria transmission in urban sub-Saharan Africa. *Am J Trop Med Hyg* 2003; **68:** 169–76.

19 Takken W, Lindsay S. Increased threat of urban Malaria from *Anopheles stephensi* mosquitoes, Africa. *Emerg Infect Dis* 2019; **25:** 1431–33.

20 Fazeli-Dinan M, Azarnoosh M, Özgökçe MS, et al. Global water quality changes posing threat of increasing infectious diseases, a case study on malaria vector *Anopheles stephensi* coping with the water pollutants using age-stage, two-sex life table method. *Malar J* 2022; **21:** 178.

21 Ahmed A, Irish SR, Zohdy S, Yoshimizu M, Tadesse FG. Strategies for conducting *Anopheles stephensi* surveys in non-endemic areas. *Acta Trop* 2022; **236:** 106671.

22 UN High Commissioner for Refugees. Global trends: forced displacement in 2021. 2022. https://www.unhcr.org/62a9d1494/global-trends-report-2021 (accessed Oct 5, 2022).

23 OECD, European Commission. Cities in the world: a new perspective on urbanisation. June 16, 2020. https://www.oecd-ilibrary.org/urban-rural-and-regional-development/cities-in-the-world_d0efcbda-en (accessed Oct 5, 2022).

24 Nguyen AP, Clements ACA, Jeffery JAL, et al. Abundance and prevalence of *Aedes aegypti* immatures and relationships with household water storage in rural areas in southern Viet Nam. *Int Health* 2011; **3:** 115–25.

25 Carvalho MS, Honorio NA, Garcia LMT, Carvalho LCS. *Aedes ægypti* control in urban areas: a systemic approach to a complex dynamic. *PLoS Negl Trop Dis* 2017; **11:** e0005632.

26 Morrison AC, Zielinski-Gutierrez E, Scott TW, Rosenberg R. Defining challenges and proposing solutions for control of the virus vector *Aedes aegypti*. *PLoS Med* 2008; **5:** e68.

27 Mnzava A, Monroe AC, Okumu F. *Anopheles stephensi* in Africa requires a more integrated response. *Malar J* 2022; **21:** 156.

28 Budge S, Ambelu A, Bartram J, Brown J, Hutchings P. Environmental sanitation and the evolution of water, sanitation and hygiene. *Bull World Health Organ* 2022; **100:** 286–88.

29 WHO. High burden to high impact—a targeted malaria response. 2019. https://apps.who.int/iris/bitstream/handle/10665/275868/WHO-CDS-GMP-2018.25-eng.pdf?sequence=1&isAllowed=y (accessed Oct 5, 2022).