REVIEW ARTICLE

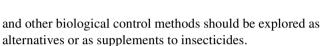
Factors enhancing the transmission of mosquito-borne arboviruses in Africa

Sandra Ateutchia Ngouanet^{1,2} · Samuel Wanji² · Anges Yadouleton³ · Maurice Demanou⁴ · Rousseau Djouaka¹ · Ferdinand Nanfack-Minkeu^{1,5}

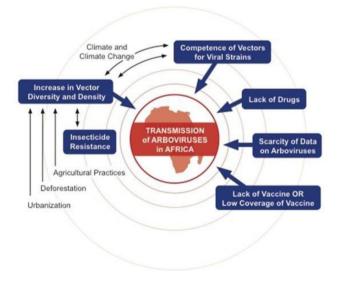
Received: 9 May 2022 / Accepted: 19 September 2022 / Published online: 18 October 2022 © The Author(s), under exclusive licence to Indian Virological Society 2022

Abstract Arthropod-borne viruses (Arboviruses) replicate in vertebrates and invertebrates and are mainly transmitted by mosquitoes. Between 2000 and 2021, several arbovirus outbreaks were recorded in African countries, including dengue, yellow fever, Chikungunya, Zika, and O'nyong nyong. Most often, the causes and factors involved in these outbreaks are unknown. We aimed to understand current knowledge regarding factors responsible for the persistent transmission and emergence of mosquito-borne arboviruses in Africa and to identify critical research gaps important for preventing future outbreaks. We used a systematic literature review between 2020 and 2021, to show that the main identified factors favoring the arbovirus outbreak in Africa are low vaccination coverage, high density and diversity of competent mosquitoes, insecticide resistance of mosquito vectors, and a scarcity of data on arboviruses. Further studies on arboviruses may include studies of competence to viral strains and the susceptibility of mosquito vectors to insecticides. Because of the detrimental effects of insecticides on human health and the environment, viral paratransgenesis

- ² Department Microbiology and Parasitology, Faculty of Science, University of Buea, P.O. BOX 63, Buea, Cameroon
- ³ Centre de Recherche Entomologique de Cotonou (CREC), Cotonou, Benin
- ⁴ Regional Yellow Fever Laboratory Coordinator World Health Organization, Inter-Country Support Team West Africa, 03 P.O. Box 7019, Ouagadougou 03, Burkina Faso
- ⁵ Department of Biology, The College of Wooster, Wooster, OH, USA



Graphical abstract Illustration of factors identified for promoting the transmission of arbovirus in Africa. The main factors are the lack of drugs and vaccines, low coverage of vaccination when a vaccine exists, competence of mosquitoes to viruses, diversity and high density of vectors. Climate change, urbanization, deforestation and agricultural practices, lead to a richness and high density of vectors.



Keywords Mosquitoes · Arboviruses · Transmission factors · Public health · Disease outbreaks · Africa



Ferdinand Nanfack-Minkeu fnanfackminkeu@yahoo.com

¹ International Institute of Tropical Agriculture (IITA), 08 Tri-Postal, P.O. Box 0932, Cotonou, Benin

Introduction

Arboviruses are viruses transmitted by arthropods and they replicate in both vertebrates and invertebrates. They are different from insect-specific viruses that replicate only in invertebrates. Arboviruses are important causes of animal and human diseases worldwide [5]. A majority of medically important arboviruses belong to viral families Flaviviridae (Dengue virus, Yellow fever virus), Togaviridae (Chikungunya virus, O'nyong nyong virus), and Phenuiviridae (Rift Valley fever Virus) [1, 5]. All viruses belonging to these families have an RNA genome that allows them to adapt/ evolve rapidly to changing host and environmental conditions. To date, most arboviruses responsible for disease outbreaks are RNA viruses. For example, approximately 200,000 cases were reported in La Réunion during an outbreak of the Chikungunya virus (CHIKV) in the Indian Ocean islands between 2004 and 2006 [63, 74]. During that outbreak, the CHIKV transmission was highly efficient by the secondary vector, Aedes albopictus due to a substitution of Alanine by Valine at position 226 of the E1 structural protein (E1-A226V), confirming point mutation (antigenic drift) as a factor responsible for arbovirus transmission [63, 74].

In Africa, most factors involved in arbovirus outbreaks are unknown and they are rarely studied. Recently, there has been an emergence and re-emergence of arbovirus outbreaks in Africa [68, 73]. In 2021, at least eight and 42 cases of yellow fever were recorded in Cameroon and Ghana respectively [78]. The overall case fatality rate was above 20% in both countries [78]. Other outbreaks include dengue in Burkina Faso, yellow fever in Angola and the Democratic Republic of Congo, and Chikungunya in Kenya, the Democratic Republic of Congo, and Sudan [2, 27, 38, 51, 57, 71]. Despite the involvement of mosquitoes in these outbreaks, the contributing factors are not well identified.

In addition to mosquitoes, other common vectors of arboviruses are ticks, midges, and sandflies [14]. Diseases spread by arthropod vectors, such as mosquitoes and ticks, are the main contributors to the global burden of infectious diseases [24]. Based on morbidity and mortality, mosquitoes are the most dangerous arthropods. In 2021, approximately 390 million annual dengue virus infections were recorded worldwide due to dengue virus transmitted by *Aedes* mosquitoes [81].

In this study, we reviewed the literature to understand current knowledge on factors responsible for the persistent transmission and emergence of mosquito-borne arboviruses in Africa and to identify critical research gaps that are important in preventing future outbreaks.

Materials and methods

Search strategy

A systematic literature search was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [40]. Peer-reviewed articles in PubMed, Web of Sciences, and LISSA databases were searched. We first screened potentially relevant records based on titles, abstracts, and keywords and then reviewed full-text articles to evaluate them according to our selection criteria. Two keyword combinations were used for searching the PubMed database on June 1st, 2020, and on September 30th, 2021. We used (1) "Arboviruses AND Africa AND Mosquitoes"; (2) (Arboviruses AND Africa AND Mosquito [Title] NOT (Tick [Title]) NOT Flies [Title]). This strategy (1) Arboviruses AND Africa AND Mosquitoes) yielded relevant results and was, therefore, also used for the other databases.

Criteria for selecting studies for this review

Studies found in these searches were considered eligible if they met any of the following criteria: (1) ecological variables that may promote virus circulation, including variables related to climate, habitat, agro-ecology, (2) the epidemiology of arboviruses including geographical location, study population, risk factors for transmission and mosquito vectors; and (3) data from Africa. Only articles in English and French were included. Review articles and studies describing only diagnostic methods or vaccine development were excluded.

Results

A total of 929 articles were searched between June 2020 and September 2021. The bibliographic search of Pub-Med, Lissa, and Web of Science produced 844 articles. The snowball technique allowed us to find 145. After removing articles that did not meet the selecting criteria, 215 were obtained, which were used in this review (Fig. 1). A review of these 215 articles showed that the factors involved in the transmission of mosquito-borne arboviruses in Africa were: the presence of mosquito vectors and competence to multiple viral strains, the mosquito resistance to insecticides, low vaccination coverage and the scarcity of data on mosquitoborne arboviruses (Table 1). Insecticide resistance was the most studied factor (28 studies) and future studies should clarify its correlation with the transmission of mosquitoborne viruses. The mosquito competence to viruses was poorly studied in Africa. The second most studied factor (20 studies) was mosquito vector density and diversity, but the

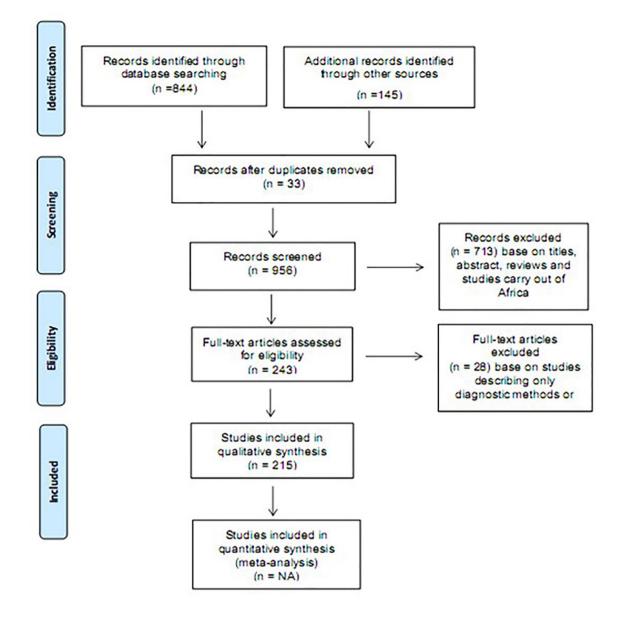


Fig. 1 The PRISMA flow diagram of our literature search to review risk factors associated with the transmission of arboviruses viruses in Africa

contribution of climate change, deforestation, urbanization, and agricultural practices were rarely studied.

High density and diversity of vectors

Africa is known to have a high number (density) and several species (diversity) of mosquito vectors. For example, in Cameroon, at least 52 *Anopheles* species have been identified and the density depends on several factors such as season, area, and collection method [46]. Unlike *Anopheles* species, ONNV vectors that are well studied, *Aedes* and *Culex* are rarely studied in Cameroon [39, 43]. However, *Ae. albopictus* and *Ae. aegypti* are the main *Aedes* species and the density of immature stages during 6 months of collection was about 646 per locality [72]. Using 1654 trap nights in South Africa, approximately 42,000 mosquitoes belonging to 10 genera, were collected between 2014 and 2017. The most abundant mosquito vectors of arboviruses were *Ae. gambiae, Coquillettidia fuscopennata, Cx. Poicilipes, Cx. pipiens* and *Ae. aegypti* [32]. The latter species is also the main abundant species in several areas of Niger, Kenya, and Tanzania [37, 47, 60]. Factors contributing to this high density and diversity are not well understood. However, climate, agriculture practices, deforestation, and urbanization are associated with the high density and diversity of mosquitoes in Africa [15]. Table 1Studies on factorscontributing to the transmissionof mosquito-borne arbovirusesin Africa

Factors	Indirect factors	Number of studies	Countries	References
Insecticides resistance	NI ^a	28	Cameroon	[4, 6, 7, 15 19, 21, 28, 32, 37, 39, 40, 43, 46, 47, 49, 52, 53, 56, 60, 61, 65, 67, 72, 83]
			Burkina Faso	
			Senegal	
			Ghana	
			Tanzania	
			Ivory Coast	
			Cape Verde	
			Democratic Republic of Congo	
			Gabon	
			Nigeria	
			Morocco	
			Benin	
Diversity and diversity	Deforestation	20	Kenya	[3, 8, 10 16, 18, 22, 29, 33–35, 45, 48, 64, 70, 75–77, 84–86]
	Climate change		Cameroon	
	Urbanization		Niger	
	Agriculture practices		Senegal	
			Democratic Republic of Congo	
			South Africa	
			Ivory Coast	
Lack of vaccination	NI	10	Cameroon	[9, 11, 23 26, 30, 50, 55, 62, 66, 80]
			Senegal	
			Morocco	
			Mali	
			Angola	
			Democratic Republic of Congo	
			Kenya	
			Burkina Faso	
			Uganda	
			Tanzania	
Competence of vectors	NI	5	The Central African Republic Senegal	[12, 25, 69
				79, 82]
			Kenya	
			Cameroon	

 $^{a}NI\!=\!unindentified$

Unlike other continents such as Europe, America, and Asia, which have a winter season where the mosquito density and diversity are almost absent because of low temperature, the climate of most countries of sub-Saharan Africa allows the presence of mosquitoes throughout the year. Indeed, most sub-Saharan African countries have a mean temperature above 15 °C and receive rainfall during 6 of the 12 months per year; these conditions are suitable for mosquito reproduction. In Sudan, Ahmed et al. [7] reported that rainfall is positively correlated with larval abundance, particularly where rain-filled containers appear to be the primary larval breeding sites. In the past, entomological studies and vector control programs were based on rainfall and seasons that were well known. Nowadays, climate change is leading to seasonal variation and thus there is a need to redefine mosquito seasons in all countries for better management of mosquito-borne diseases. Climate change is projected to increase the global surface temperature by an estimated 2.4-6.4 °C by 2100. That rise will modify the environment of mosquito vectors, which will lead to changes in the dynamics and biology of mosquito-borne diseases [4]. Indeed, temperature influences the availability of breeding sites, the longevity of mosquitoes, and their competence/ capacity to microorganisms. Since it is difficult to know the real impact of climate change, further studies should be done to estimate its impact on mosquito-borne viruses.

The abundance of mosquitoes is also influenced by agricultural practices and deforestation. Deforestation consists of the clearing of forests for timber exploitation or agricultural practices. In Cameroon, deforestation influences the density and diversity of *Culex* mosquitoes with a high number of mosquitoes collected in logged forests (900) as compared to unlogged ones (427) [39]. Cx. simpliciforceps, Cx. wigglesworthi were collected in both types of forest whereas Cx. albiventris, Cx. nebulosus and Cx. macfiei were only collected in the selected logged forest [39]. Logged forests provide adequate aeration, humidity, and temperature for the reproduction of mosquitoes leading to a rise in their density and diversity. As with deforestation, agricultural practices like irrigation, are associated with an increase in mosquito abundance and diversity. For instance, in Ethiopia, higher numbers of Anopheles mosquitoes were collected in zones that were near the irrigation sites (3 km or less) [28]. In this latter study, irrigation was used for rice cultivation after intensive deforestation. Like irrigation, the creation of fish ponds, which is becoming popular in Africa, influences the density and diversity of mosquitoes. Their impact should be studied in detail. Fish ponds are used to increase the protein consumption of the population. In Brazil, fish ponds showed a higher density of Anopheles mosquitoes than natural water bodies meaning that fish ponds increase the density of some mosquito species [19]. The impact of fish ponds on mosquito fauna and arbovirus outbreaks should be more investigated in Africa. Irrigation and fish ponds may create breeding sites for mosquitoes promoting the colonization by new species and better conditions for the existing species.

The colonization of new species is also facilitated by urbanization, which is sometimes associated with deforestation. Eastwood et al. [21] explained that rapid urbanization and alteration of natural habitats create the opportunity for new species to colonize areas previously occupied by trees leading to urban transmission of arboviruses affecting human populations. In Kenya, intact rainforests are now difficult to find as they are now frequented by local villagers and are popular for ecotourism, leading to the proliferation of certain arboreal mosquitoes [Aedes (stegomyia) spp., e.g., Aedes africanus and Ae. Vittatus] [21]. Some new mosquito species are attracted to the area after the destruction of forests. This destruction and the construction of buildings and houses leads to the arrival of anthropophilic mosquitoes and a change in the behavior of zoophilic vectors. Thus, Culex quinquefasciatus is well known as a marker of disorganized urban areas since it is abundant in polluted water of houses and buildings [56]. In addition, modeling studies showed that the Asian mosquito, An. stephensi would be more adapted to African urban cities [65]. Luckily, An. stephensi is a poor vector of arboviruses even though experimental infections have shown its competence to several viruses.

Competence of vectors to viruses

Vector competence to pathogens can be defined as the ability of vectors to allow the replication of pathogens. It is associated with the capacity of a vector to be infected and to maintain and transmit an infectious agent [61]. Competent mosquitoes, viruses, and susceptible hosts are required for an arboviral transmission or epidemic. Aedes aegypti and the invasive vector Ae. albopictus collected in Bangui, Central African Republic, are competent to transmit CHIKV suggesting a risk of an outbreak [49]. The competence of Ae. albopictus to CHIKV is modified by viral mutations suggesting that the competence of mosquitoes to all arbovirus strains should be assessed [63, 74]. CHIKV strains isolated during the Cameroon outbreak in 2006 and the Gabon outbreak in 2007 also revealed A226V mutation [52, 53]. Thus, the possession of A226V mutation in two independent outbreaks provided a selective advantage for CHIKV transmission [6].

In addition to viral strains, microbiota and immune responses also influence the competence of African mosquitoes to arboviruses [67]. In *Ae. aegypti* (Rockefeller/UGAL strain), knockdown of MYD88, a negative regulator of the Toll immune pathway, increases more than two times the DENV intensity, indicating an anti-dengue function of the Toll pathway in this arbovirus vector [83]. Carissimo et al. showed a reduction of O'nyong nyong virus replication in the African vector of malaria, *An. coluzzi* after a reduction of microbiota by antibiotic treatments, meaning a pro-viral role of microbiota in this *Anopheles* species. Viral responses of mosquitoes and other factors involved in the mosquito competence to arboviruses are under-studied in Africa because of lack of human, material and financial resources; even though, African mosquitoes are major vectors of arbovirus worldwide. Most studies in Africa incriminate the competent vectors of arboviruses but the mechanisms underpinning that competence are not deciphered.

Insecticide resistance of vectors

Insecticide resistance is the selection of an inherited trait in an insect population that results in an insect control product that no longer performs as intended. Insecticides remain the mainstay of many mosquito-borne disease control programs in Africa; so, the risk of these programs being compromised by insecticide resistance is a major concern. The development of resistance depends upon many factors that enable insects to resist insecticides. The well-studied resistance mechanisms are target site resistance and metabolic resistance. In target-site resistance, the specific binding site of an insecticide is modified, which makes the target site incompatible for activation. In the case of metabolic resistance, there is an over BNHY production/expression of detoxifying enzymes resulting in the resistance to insecticides [35]. Nevertheless, many vector species of public health importance have already developed resistance to one or more insecticides [48, 77, 84, 85]. Also, the continued use of agrochemicals in vegetable production could influence the selection of insecticide resistance in vector species [70].

Pyrethroids, carbamates, organophosphates, and organochlorines are among the four main classes of insecticides approved in public health [10]. In Ivory coast, Anopheles mosquitoes, a vector of ONNV, are resistant to all approved classes of insecticides [22]. In the Republic of Congo, after two massive outbreaks of CHIKV, the adult populations of Ae. aegypti were resistant to dichloro-diphenyl-trichloroethane (DDT) [33]. Aedes albopictus from Cameroon is also resistant to DDT, propoxur, deltamethrin, and permethrin [86]. These two latter insecticides belong to the pyrethroid class that are used to treat bed nets across Africa. Pyrethroid insecticide-treated bed nets (ITNs) help reduce the burden of mosquito-borne diseases and also increase the resistance of mosquitoes to Pyrethroid. There is, therefore, an urgent need for an alternative class of insecticide that can be used with nets to reduce selection pressure on pyrethroids. In addition to ITNs, indoor residual spraying (IRS) is also used in vector control programs in Africa but its coverage is below 50% [8,

45]. Vector control programs should increase the coverage of IRS with insecticides that do not belong to pyrethroids or organochlorine like DDT.

Lack or weak coverage of vaccination

Vaccines are one of the most powerful tools of public health. Vaccination campaigns have contributed to reduced mortality and morbidity of several infectious diseases. According to the World Health Organization (WHO), vaccination is the most effective prophylaxis against infectious disease. Vaccines are recognized as important and necessary tools to fight the advancement of diseases [16]. Despite significant advances in vaccine technologies in recent decades, some arboviruses such as O'nyong nyong, Chikungunya, and Zika still do not have an effective vaccine [76]. Vaccines are available for some arboviruses such as YFV and DENV but the coverage is weak in endemic countries. For instance, despite the availability of yellow fever (YF) vaccine, there are still outbreaks in Africa. In Senegal, YFV was detected in 2015, 2020, and 2021 [18]. From 2016 to 2017, Angola, Nigeria, and the Democratic Republic of Congo witnessed the re-emergence of YF [29, 64]. In Cameroon, YF outbreaks were reported in 1990, 2006, 2007, and 2021 [34, 75]. In Cameroon, during the 1990 YF outbreak, 125 deaths were recorded and nine confirmed cases were reported in 2021 ([70], Unpublished data) These repeated outbreaks are associated with insufficient vaccine coverage [75]. According to experts, immunization coverage of 80% or more is required to prevent outbreaks by providing 'herd immunity' [3]. In Cameroon, the average coverage for YF is around 57% and most districts do not reach 80% of immunization coverage. The weak coverage of YF vaccination is attributed to the high price of the vaccine, poor communication about the usefulness of taking a vaccine, and the absence of a cold chain in most areas.

Unlike YF for which an approved vaccine exists in most African countries, the dengue vaccine is approved in only a few countries. The dengue vaccine is marketed as Dengvaxia (CYD-TDV). It is a live attenuated virus protecting against the four dengue serotypes. Because of antibody-dependent enhancement, Dengvaxia is only recommended for dengue seropositive people meaning that there is an urgent need for an efficient vaccine for naïve people [30]. Therefore, the dengue vaccine is recommended in areas having at least 70% seroprevalence and only for people aged 9 years or older [80]. This absence of dengue vaccine in most African countries is probably the cause of multiple outbreaks observed in Burkina Faso, Gabon, Kenya, and Sudan [50, 55, 62]. Although several outbreaks of arboviruses have been reported in Africa, there are few data about those outbreaks making them difficult to understand and prevent.

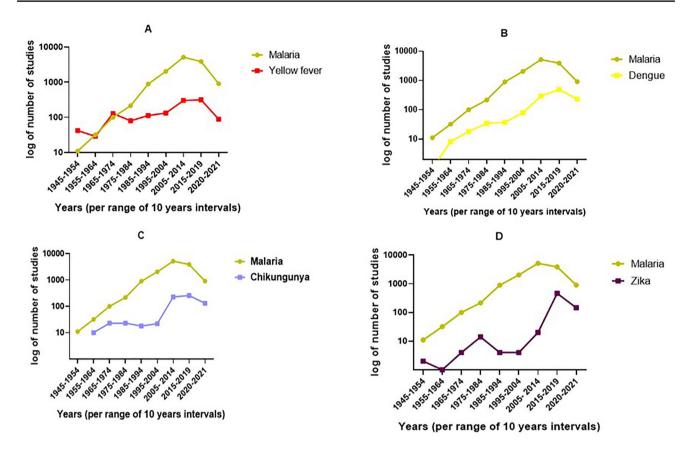


Fig. 2 Comparison of Malaria and four Arboviruses. A Malaria and Yellow fever, B Malaria and Dengue, C Malaria and Chikungunya, D Malaria and Zika

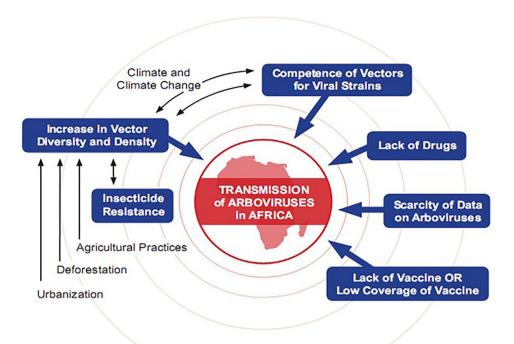
Scarcity of data on mosquito-borne arboviruses

Mosquito-borne viruses are considered neglected diseases, though around 80% of the global population is exposed to them. In Africa, most studies related to mosquito-borne diseases focus on malaria thereby neglecting studies on arboviruses [23]. Our search in PubMed shows that malaria is at least 10 times more studied as compared to YFV, DENV, CHIKV and ZIKV in Africa (Fig. 2). Arboviral infections are often misdiagnosed as malaria, due to some similar clinical symptoms and also due to the absence of good diagnostic laboratories and well-trained personnel. Health systems are totally concerned with the burden of other co-existing febrile illnesses like malaria. This latter situation leads to more than 70% of febrile illnesses being treated as presumptive malaria, without proper medical examination and laboratory diagnosis [11].

In Africa, many patients with fever are designated as having fever of unknown origin or malaria, and remain undiagnosed even if they do not respond to antimalarial drugs [9]. Under these prevailing practices, there is a real risk of ignoring arboviral diseases consequently resulting in an outbreak and potentially high morbidity and mortality [68].

Therefore, it is urgent to carry out more studies on entomological, virological, epidemiological, social, and anthropological aspects of arboviruses in Africa. These aspects are currently neglected during the outbreaks of infectious diseases, even though several studies have shown the paramount roles of social and anthropological determinants in the management of diseases [26]. Entomological and virological studies should help identify mosquito vectors and their competence to viruses. The low number of studies on mosquito competence to viruses, is due to the absence of appropriate laboratories in Africa. Indeed, most arboviruses require Biosafety Level 3 (BSL-3) laboratories, which are not available in most African countries. Epidemiological studies should provide a better overview of the severity of arboviruses in humans and animals through accurate data of their mortality and morbidity. Animals infected with arboviruses are rarely studied in Africa, even though several studies have shown the circulation of arbovirus in animals in some African countries. In Madagascar: cattle, sheep and goats, are differentially infected with RVFV and their prevalence depends on their sampling districts.

Fig. 3 Illustration of factors identified for promoting the transmission of arbovirus in Africa. The main factors are the lack of drugs and vaccines, low coverage of vaccination when a vaccine exists, competence of mosquitoes to viruses, diversity and high density of vectors. Climate change, urbanization, deforestation and agricultural practices, lead to a richness and high density of vectors



Concluding remarks and future studies

The emergence and re-emergence of viruses are a huge challenge to human health as the outbreaks they cause remain hard to predict and difficult to prevent. Better knowledge of the factors involved in the transmission of arboviruses will ease the fight against them. We show in this study that the main factors causing the outbreaks of mosquito-borne arboviruses in Africa are the presence of a high number of competent vectors, the weak coverage of vaccines or their absence, insecticide resistance of mosquitoes, and negligence of arboviruses (Fig. 3). In addition, since most arboviruses cause fever as in malaria, they are underdiagnosed and spread insidiously because of their low mortality rate in Africa. This low mortality rate of dengue in Africa as compared to Asia is an enigma. Indeed, even though dengue outbreaks were recorded in several African countries, the overall number of deaths is still low with less than 20 killed people per outbreak [55, 66]. However, the mortality rate goes up when aggravating factors such as pregnancy and other co-morbidities are present [66]. In 2018, the YF arbovirus that killed at least 70,000 people in Africa, seems the most dangerous arbovirus on this continent. However, African governments and the World health organization have adopted through an initiative called "Global strategy to eliminate yellow fever epidemics (EYE), 2017-2026 [79]", some measures to reduce its spread [25]. The three primary objectives of EYE are to protect at-risk populations, prevent the international spread of YFV, and rapidly contain YF outbreaks [82]. In addition, most African countries have created national programmes for controlling YF. The main objective of those programmes is to better coordinate the fight against YF via the identification of vectors and risk stratification of areas and people. Those programmes and experts have proved that YF outbreaks in Africa are mainly due to low vaccination coverage and the presence of competent vectors. Unlike dengue, the yellow fever vaccine is available, but few people are vaccinated. Low coverage vaccination is attributed to the high cost of vaccines and unavailability in most cities since vaccines are available most time in big cities in Africa. In addition to unvaccinated people, the circulation of competent mosquitoes also contributes to arbovirus outbreaks in Africa. The factors contributing to a high density of competent vectors are the presence of breeding sites, urbanization, insalubrity, deforestation, agricultural practices and climate change. Insecticides are mainly used to reduce the mosquito population but the resistance of mosquitoes to insecticide weakens this control. With the objective of understanding the transmission and outbreaks of mosquito borne arboviruses in Africa, we suggest the following topics for future studies:

Mosquito-borne viruses and insecticide resistance

Future studies should continue to characterize the mosquito fauna in Africa and assess their susceptibility to the major classes of insecticides used in agriculture and public health. Most studies on the resistance of mosquitoes to insecticides focus on main mosquito vectors such as *An. gambiae*, *Ae. aegypti* and *Cx. quinquefasciatus* [12, 41, 69]; secondary mosquitoes are, therefore, neglected. More efforts should be placed to identify and understand the mechanisms of insecticide resistance in all mosquito species. The insecticide resistance studies should target the four main mechanisms of resistance, namely: target site alteration, metabolism, cuticle, and behaviour. These two latter mechanisms have not been studied appropriately because of difficulties to set up protocols and standard operating procedures. Unlike cuticular and behavioural resistances, target-site and metabolic resistance are well studied, but they are not enough molecular markers for metabolic resistance. The studies on insecticide resistance should also determine any correlations between insecticide resistance and mosquito competence to viruses. Because of these multiple mechanisms of resistance, it is urgent to find alternative methods like paratransgenesis for mosquito management.

Paratransgenesis as an alternative to insecticides

Paratransgenesis in mosquitoes consists of reducing vector competence by using engineered symbiotic microorganisms. Contrary to insecticides, paratransgenesis is an environmentally friendly tool and it is more specific as compared to insecticides. Wolbachia is one of the most promising paratransgenic candidates since it reduces or impedes the transmission of several arboviruses such as dengue, Chikungunva, and Zika [17, 20]. Releases of infected Ae. aegypti with Wolbachia was efficient in blocking the transmission of dengue in Australia [58]. In addition to Wolbachia spp, some insect-specific viruses have shown interesting results. For instance, cell fusing agent virus reduces the competence of Aedes mosquitoes against Zika and dengue viruses [13]. Despite these interesting results, viral paratransgenesis is less explored as compared to bacterial paratransgenesis, and more effort should be done for characterizing insect-specific viruses, especially their interaction with other viruses [42, 44, 54]. In the absence of vaccines and specific treatments against arboviruses, viral paratransgenesis is a promising approach to complement insecticides for preventing epidemics and epizootics of arboviruses. Animal reservoirs play a significant role in arbovirus epidemics and maintenance.

Animal reservoirs of arboviruses

Infected animals with arboviruses are rarely studied in Africa, although several studies have shown epizootics of arboviruses in some African countries. In Madagascar and Cameroon: cattle, sheep and goats, are differentially infected with RVFV and their prevalence depends on their sampling locations [31, 59]. In addition, in Cameroon, the prevalence of IgG in cattle varies by season and it is higher during the dry season as compared to the rainy season [59]. The impact of animal reservoirs is not well studied in most African countries. However some studies have showed people working with animals are more infected with RVFV than those with no direct contact with them meaning that the transmission from animals to humans plays a major role during RVFV epidemics [36]. In Tanzania, RVFV is more prevalent in old people (at least 50 years old) than the young ones suggesting age as a risk factor [36]. The other risk factors should be identified for mitigating the negative impact of RVFV on human health and the economy.

Acknowledgements We thank all the team of Dr Djouaka laboratory, International Institute of Tropical Agriculture (Benin) and Dr Sirot Laura, The College of Wooster (USA), for their relevant comments and suggestions on the manuscript. We also thank Jodi Robison for designing Fig. 3.

Funding This research received funding from the welcome trust granted to RD.

Declarations

Conflict of interest The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Ethics approval and consent to participate Not applicable.

References

- Abudurexiti A, Adkins S, Alioto D, Alkhovsky SV, Avšič-Županc T, Ballinger MJ, et al. Taxonomy of the order Bunyavirales: update 2019. Arch Virol. 2019;164(7):1949–65.
- Adam A, Seidahmed OME, Weber C, Schnierle B, Schmidt-Chanasit J, Reiche S, et al. Low seroprevalence indicates vulnerability of eastern and central Sudan to infection with chikungunya virus. Vector Borne Zoonotic Dis. 2016;16(4):290–1.
- Adrien N, Hyde TB, Gacic-Dobo M, Hombach J, Krishnaswamy A, Lambach P. Differences between coverage of yellow fever vaccine and the first dose of measles-containing vaccine: a desk review of global data sources. Vaccine. 2019;37(32):4511–7.
- Afrane YA, Githeko AK, Yan G. The ecology of Anopheles mosquitoes under climate change: case studies from the effects of environmental changes in east Africa highlands. Ann N Y Acad Sci. 2012;1249:204.
- Agarwal A, Parida M, Dash PK. Impact of transmission cycles and vector competence on global expansion and emergence of arboviruses. Rev Med Virol. 2017;27(5):e1941.
- Agarwal A, Sharma AK, Sukumaran D, Parida M, Dash PK. Two novel epistatic mutations (E1:K211E and E2:V264A) in structural proteins of Chikungunya virus enhance fitness in *Aedes aegypti*. Virology. 2016;497:59–68.
- Ahmed RM, Hassan SM, Elrahman AH. Climatic factors affecting density of *Aedes aegypti* (Diptera: Culicidae) in Kassala City, Sudan 2014/2015. Asploro J Biomed Clin Case Rep. 2019;2019(2):58.
- Allcock SH, Young EH, Sandhu MS. A cross-sectional analysis of ITN and IRS coverage in Namibia in 2013. Malar J. 2018;17(1):1–13.
- Amarasinghe A, Kuritsk JN, Letson GW, Margolis HS. Dengue virus infection in Africa. Emerg Infect Dis. 2011;17(8):1349-54.

- Amelia-Yap ZH, Chen CD, Sofian-Azirun M, Low VL. Pyrethroid resistance in the dengue vector *Aedes aegypti* in Southeast Asia: present situation and prospects for management. Parasit Vectors. 2018;11(1):1–17.
- Amexo M, Tolhurst R, Barnish G, Bates I. Malaria misdiagnosis: effects on the poor and vulnerable. Lancet (London, England). 2004;364(9448):1896–8.
- Badolo A, Sombié A, Pignatelli PM, Sanon A, Yaméogo F, Wangrawa DW, et al. Insecticide resistance levels and mechanisms in *Aedes aegypti* populations in and around Ouagadougou, Burkina Faso. PLoS Negl Trop Dis. 2019;13(5):e0007439.
- Baidaliuk A, Miot EF, Lequime S, Moltini-Conclois I, Delaigue F, Dabo S, et al. Cell-fusing agent virus reduces arbovirus dissemination in *Aedes aegypti* mosquitoes in vivo. J Virol. 2019;93(18):e00705-e719.
- 14. Blitvich BJ, Magalhaes T, Laredo-Tiscareño SV, Foy BD. Sexual transmission of arboviruses: a systematic review. Viruses. 2020;12(9):933.
- Burkett-Cadena ND, McClure CJW, Estep LK, Eubanks MD. Hosts or habitats: What drives the spatial distribution of mosquitoes? Ecosphere. 2013;4(2):1–16.
- Carvalho VL, Long MT. Perspectives on new vaccines against arboviruses using insect-specific viruses as platforms. Vaccines. 2021;9(3):263.
- 17. Chouin-Carneiro T, Ant TH, Herd C, Louis F, Failloux A-B, Sinkins SP. Wolbachia strain wAlbA blocks Zika virus transmission in *Aedes aegypti*. Med Vet Entomol. 2020;34(1):116–9.
- Diagne MM, Ndione MHD, Gaye A, Barry MA, Diallo D, Diallo A, et al. Yellow fever outbreak in eastern Senegal, 2020– 2021. Viruses. 2021;13(8):1475.
- dos Reis IC, Codeço CT, Degener CM, Keppeler EC, Muniz MM, de Oliveira FGS, et al. Contribution of fish farming ponds to the production of immature *Anopheles* spp. in a malaria-endemic Amazonian town. Malar J. 2015;14(1):1–12.
- Dutra HLC, Rocha MN, Dias FBS, Mansur SB, Caragata EP, Moreira LA. Wolbachia blocks currently circulating Zika virus isolates in Brazilian *Aedes aegypti* mosquitoes. Cell Host Microbe. 2016;19(6):771–4.
- 21. Eastwood G, Sang RC, Lutomiah J, Tunge P, Weaver SC. Sylvatic mosquito diversity in Kenya—considering enzootic ecology of arboviruses in an era of deforestation. Insects. 2020;11(6):342.
- Edi CVA, Koudou BG, Jones CM, Weetman D, Ranson H. Multiple-insecticide resistance in *Anopheles gambiae* mosquitoes, Southern Côte d'Ivoire. Emerg Infect Dis. 2012;18(9):1508–11.
- Fokam EB, Levai LD, Guzman H, Amelia PA, Titanji VPK, Tesh RB, et al. Silent circulation of arboviruses in Cameroon. East Afr Med J. 2010;87(6):262–8.
- Franklinos LHV, Jones KE, Redding DW, Abubakar I. The effect of global change on mosquito-borne disease. Lancet Infect Dis. 2019;19(9):e302–12.
- 25. Gaythorpe KAM, Hamlet A, Jean K, Ramos DG, Cibrelus L, Garske T, et al. The global burden of yellow fever. Elife. 2021;10:e64670.
- Glatman-Freedman A, Nichols K. The effect of social determinants on immunization programs. Hum Vaccin Immunother. 2012;8(3):293–301.
- Grobbelaar AA, Weyer J, Moolla N, van Vuren PJ, Moises F, Paweska JT. Resurgence of yellow fever in Angola, 2015–2016. Emerg Infect Dis. 2016;22(10):1854.
- Haileselassie W, Zemene E, Lee M-C, Zhong D, Zhou G, Taye B, et al. The effect of irrigation on malaria vector bionomics and transmission intensity in western Ethiopia. Parasit Vectors. 2021;14(1):1–11.
- 29. Ingelbeen B, Weregemere NA, Noel H, Tshapenda GP, Mossoko M, Nsio J, et al. Urban yellow fever outbreak—Democratic

Republic of the Congo, 2016: towards more rapid case detection. PLoS Negl Trop Dis. 2018;12(12):e0007029.

- Izmirly AM, Alturki SO, Alturki SO, Connors J, Haddad EK. Challenges in dengue vaccines development: pre-existing infections and cross-reactivity. Front Immunol. 2020;11:1055.
- 31. Jeanmaire EM, Rabenarivahiny R, Biarmann M, Rabibisoa L, Ravaomanana F, Randriamparany T, et al. Prevalence of Rift Valley fever infection in ruminants in Madagascar after the 2008 outbreak. Vol. 11, Vector-Borne and Zoonotic Diseases. New Rochelle: Mary Ann Liebert, Inc.;2011. p. 395–402.
- 32. Johnson T, Braack L, Guarido M, Venter M, Gouveia Almeida AP. Mosquito community composition and abundance at contrasting sites in northern South Africa, 2014–2017. J Vector Ecol. 2020;45(1):104–17.
- 33. Kamgang B, Wilson-Bahun TA, Yougang AP, Lenga A, Wondji CS. Contrasting resistance patterns to type I and II pyrethroids in two major arbovirus vectors *Aedes aegypti* and *Aedes albopictus* in the Republic of the Congo, Central Africa. Infect Dis Poverty. 2020;9(1):23.
- Kebede S, Duale S, Yokouide A, Alemu W. Trends of major disease outbreaks in the African region, 2003–2007. East Afr J Public Health. 2010;7(1):22–31.
- Khan S, Uddin MN, Rizwan M, Khan W, Farooq M, Sattar Shah A, et al. Mechanism of insecticide resistance in insects/pests. Pol J Environ Stud. 2020;29(3):2023–30.
- Kumalija MS, Chilongola JO, Budodo RM, Horumpende PG, Mkumbaye SI, Vianney J-M, et al. Detection of Rift Valley Fever virus inter-epidemic activity in Kilimanjaro Region, North Eastern Tanzania. Glob Health Action. 2021;14(1):1957554.
- Labbo R, Doumma A, Mahamadou I, Arzika I, Soumana A, Kadri S, et al. Répartition, fréquence et densité d'*Aedes aegypti* au Niger. Med Sante Trop. 2019;29(1):47–54.
- Makiala-Mandanda S, Ahuka-Mundeke S, Abbate JL, Pukuta-Simbu E, Nsio-Mbeta J, Berthet N, et al. Identification of dengue and chikungunya cases among suspected cases of yellow fever in the Democratic Republic of the Congo. Vector Borne Zoonotic Dis. 2018;18(7):364–70.
- Mayi MPA, Foncha DF, Kowo C, Tchuinkam T, Brisco K, Anong DN, et al. Impact of deforestation on the abundance, diversity, and richness of *Culex* mosquitoes in a southwest Cameroon tropical rainforest. J Vector Ecol. 2019;44(2):271–81.
- Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS Med. 2009;6(7):e1000097.
- Munywoki DN, Kokwaro ED, Mwangangi JM, Muturi EJ, Mbogo CM. Insecticide resistance status in *Anopheles gambiae* (sl) in coastal Kenya. Parasit Vectors. 2021;14(1):1–10.
- 42. Nanfack Minkeu F, Vernick KD. A systematic review of the natural virome of anopheles mosquitoes. Viruses. 2018;10(5):222.
- 43. Nanfack-Minkeu F. Moustiques et maladies au Cameroun : les défis de la biologie dans la lutte antivectorielle, 1st edn. Harmattan Cameroun; 2021. ISBN 9782140194924.
- 44. Nanfack-Minkeu F, Mitri C, Bischoff E, Belda E, Casademont I, Vernick KD. Interaction of RNA viruses of the natural virome with the African malaria vector, *Anopheles coluzzii*. Sci Rep. 2019;9(1):1–10.
- 45. Nanfack-minkeu F, Zeukeng F, Tabue R. Les anophèles, vecteurs du paludisme au Cameroun-distribution, réponse anti-plasmodiale et résistance aux insecticides. In: Harmattan Cameroun, editor. Harmattan Cameroun. 2021. ISBN 9782140194924.
- 46. Nanfack-Minkeu F, Zeukeng F, Tabue R. Les anophèles, vecteurs du paludisme au Cameroun-distribution, réponse anti-plasmodiale et résistance aux insecticides. In: Moustiques et maladies au Cameroun: les défis de la biologie dans la lutte antivectorielle. L'Harmattan. 2021. ISBN 9782140194924.

487

- 47. Ndenga BA, Mutuku FM, Ngugi HN, Mbakaya JO, Aswani P, Musunzaji PS, et al. Characteristics of *Aedes aegypti* adult mosquitoes in rural and urban areas of western and coastal Kenya. PLoS ONE. 2017;12(12):e0189971.
- 48. Ngoagouni C, Kamgang B, Brengues C, Yahouedo G, Paupy C, Nakouné E, et al. Susceptibility profile and metabolic mechanisms involved in *Aedes aegypti* and *Aedes albopictus* resistant to DDT and deltamethrin in the Central African Republic. Parasit Vectors. 2016;9(1):1–13.
- 49. Ngoagouni C, Kamgang B, Kazanji M, Paupy C, Nakouné E. Potential of *Aedes aegypti* and *Aedes albopictus* populations in the Central African Republic to transmit enzootic chikungunya virus strains. Parasit Vectors. 2017;10(1):164. https://doi.org/10. 1186/s13071-017-2101-0.
- 50. Ngoi CN, Price MA, Fields B, Bonventure J, Ochieng C, Mwashigadi G, et al. Dengue and chikungunya virus infections among young febrile adults evaluated for acute HIV-1 infection in coastal Kenya. PLoS ONE. 2016;11(12):e0167508.
- Pastorino B, Muyembe-Tamfum JJ, Bessaud M, Tock F, Tolou H, Durand JP, et al. Epidemic resurgence of Chikungunya virus in democratic Republic of the Congo: identification of a new central African strain. J Med Virol. 2004;74(2):277–82.
- Peyrefitte CN, Bessaud M, Pastorino BAM, Gravier P, Plumet S, Merle OL, et al. Circulation of Chikungunya virus in Gabon, 2006–2007. J Med Virol. 2008;80(3):430–3.
- Peyrefitte CN, Rousset D, Pastorino BAM, Pouillot R, Bessaud M, Tock F, et al. Chikungunya virus, Cameroon, 2006. Emerg Infect Dis. 2007;13(5):768.
- 54. Ren X, Hoiczyk E, Rasgon JL. Viral paratransgenesis in the malaria vector *Anopheles gambiae*. PLoS Pathog. 2008;4(8):e1000135.
- 55. Ridde V, Agier I, Bonnet E, Carabali M, Dabiré KR, Fournet F, et al. Presence of three dengue serotypes in Ouagadougou (Burkina Faso): research and public health implications. Infect Dis Poverty. 2016;5:23.
- Robert V, Le Goff G, Toto J-C, Mulder L, Fondjo E, Manga L, et al. Anthropophilic mosquitoes and malaria transmission at Edea, Cameroon. Trop Med Parasitol Off organ Dtsch Tropenmedizinische Gesellschaft Dtsch Gesellschaft Tech Zusammenarbeit. 1993;44(1):14–8.
- 57. Russo G, Subissi L, Rezza G. Chikungunya fever in Africa: a systematic review. Pathog Glob Health. 2020;114(3):136–44.
- 58. Ryan PA, Turley AP, Wilson G, Hurst TP, Retzki K, Brown-Kenyon J, et al. Establishment of wMel Wolbachia in *Aedes aegypti* mosquitoes and reduction of local dengue transmission in Cairns and surrounding locations in northern Queensland, Australia. Gates open Res. 2019;3:1547.
- 59. Sado FY, Tchetgna HS, Kamgang B, Djonabaye D, Nakouné E, McCall PJ, Ndip RN, Wondji CS. Seroprevalence of Rift Valley fever virus in domestic ruminants of various origins in two markets of Yaoundé, Cameroon. PLOS Negl Trop Dis. 2022;16(8):e0010683.
- 60. Saleh F, Kitau J, Konradsen F, Kampango A, Abassi R, Schiøler KL. Epidemic risk of arboviral diseases: determining the habitats, spatial-temporal distribution, and abundance of immature *Aedes aegypti* in the urban and rural areas of Zanzibar, Tanzania. PLoS Negl Trop Dis. 2020;14(12):e0008949.
- 61. Sallum MAM, Conn JE, Bergo ES, Laporta GZ, Chaves LSM, Bickersmith SA, et al. Vector competence, vectorial capacity of *Nyssorhynchus darlingi* and the basic reproduction number of *Plasmodium vivax* in agricultural settlements in the Amazonian Region of Brazil. Malar J. 2019;18(1):1–15.
- 62. Sawadogo S, Baguiya A, Yougbare F, Bicaba BW, Nebie K, Millogo T, et al. Seroprevalence and factors associated with IgG anti-DENV positivity in blood donors in Burkina Faso during the 2016

dengue outbreak and implications for blood supply. Transfus Med. 2020;30(1):37–45.

- Schuffenecker I, Iteman I, Michault A, Murri S, Frangeul L, Vaney M-C, et al. Genome microevolution of chikungunya viruses causing the Indian Ocean outbreak. PLoS Med. 2006;3(7):e263.
- 64. Sene NM, Mavridis K, Ndiaye EH, Diagne CT, Gaye A, Ngom EHM, et al. Insecticide resistance status and mechanisms in *Aedes aegypti* populations from Senegal. PLoS Negl Trop Dis. 2021;15(5):e0009393.
- 65. Sinka ME, Pironon S, Massey NC, Longbottom J, Hemingway J, Moyes CL, 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. 2020;117(40):24900–8.
- Sondo KA, Ouattara A, Diendéré EA, Diallo I, Zoungrana J, Zémané G, et al. Dengue infection during pregnancy in Burkina Faso: a cross-sectional study. BMC Infect Dis. 2019;19(1):1–5.
- Souza-Neto JA, Powell JR, Bonizzoni M. Aedes aegypti vector competence studies: a review. Infect Genet Evol. 2019;67:191–209.
- Sow A, Loucoubar C, Diallo D, Faye O, Ndiaye Y, Senghor CS, et al. Concurrent malaria and arbovirus infections in Kedougou, southeastern Senegal. Malar J. 2016;15(1):47.
- 69. Talipouo A, Mavridis K, Nchoutpouen E, Djiappi-Tchamen B, Fotakis EA, Kopya E, et al. High insecticide resistance mediated by different mechanisms in *Culex quinquefasciatus* populations from the city of Yaoundé, Cameroon. Sci Rep. 2021;11(1):1–11.
- Talom AD, Essoung MA, Gbankoto A, Tchigossou G, Akoton R, Sahabi BBA, et al. A preliminary analysis on the effect of copper on *Anopheles coluzzii* insecticide resistance in vegetable farms in Benin. Sci Rep. 2020;10(1):6392.
- Tarnagda Z, Cissé A, Bicaba BW, Diagbouga S, Sagna T, Ilboudo AK, et al. Dengue fever in Burkina Faso, 2016. Emerg Infect Dis. 2018;24(1):170.
- 72. Tedjou AN, Kamgang B, Yougang AP, Njiokou F, Wondji CS. Update on the geographical distribution and prevalence of *Aedes aegypti* and *Aedes albopictus* (Diptera: Culicidae), two major arbovirus vectors in Cameroon. PLoS Negl Trop Dis. 2019;13(3):e0007137.
- 73. Ushijima Y, Abe H, Nguema Ondo G, Bikangui R, Massinga Loembé M, Zadeh VR, et al. Surveillance of the major pathogenic arboviruses of public health concern in Gabon, Central Africa: increased risk of West Nile virus and dengue virus infections. BMC Infect Dis. 2021;21(1):265.
- 74. Vazeille M, Moutailler S, Coudrier D, Rousseaux C, Khun H, Huerre M, et al. Two Chikungunya isolates from the outbreak of La Reunion (Indian Ocean) exhibit different patterns of infection in the mosquito, *Aedes albopictus*. PLoS ONE. 2007;2(11):e1168.
- Vicens R, Robert V, Pignon D, Zeller H, Ghipponi PM, Digoutte JP. Yellow fever epidemic in the extreme North of Cameroon in 1990: first yellow fever virus isolation in Cameroon. Bull World Health Organ. 1993;71(2):173–6.
- Weaver SC, Reisen WK. Present and future arboviral threats. Antiviral Res. 2010;85(2):328–45.
- 77. Weedall GD, Riveron JM, Hearn J, Irving H, Kamdem C, Fouet C, et al. An Africa-wide genomic evolution of insecticide resistance in the malaria vector *Anopheles funestus* involves selective sweeps, copy number variations, gene conversion and transposons. PLoS Genet. 2020;16(6):e1008822.
- 78. WHO. Yellow fever—west and central Africa. World Health Organization; 2022. Available from: https://www.who.int/emerg encies/disease-outbreak-news/item/yellow-fever---west-and-centr al-africa.
- WHO. Eliminate yellow fever epidemics (EYE) strategy 2017– 2026. Geneva: WHO; 2021.
- Wilder-Smith A, Rupali P. Estimating the dengue burden in India. Lancet Glob Heal. 2019;7(8):e988–9.

- 81. World Health O. Dengue and severe dengue. 2022. https://www. who.int/news-room/fact-sheets/detail/dengue-and-severe-dengue.
- World Health Organization. World health statistics 2018: monitoring health for the SDGs, sustainable development goals. 2018. ISBN 978–92–4–156558–5
- Xi Z, Ramirez JL, Dimopoulos G. The Aedes aegypti toll pathway controls dengue virus infection. PLoS Pathog. 2008;4(7):e1000098.
- Yared S, Gebressielasie A, Damodaran L, Bonnell V, Lopez K, Janies D, et al. Insecticide resistance in *Anopheles stephensi* in Somali Region, eastern Ethiopia. Malar J. 2020;19(1):1–7.
- 85. Yougang AP, Kamgang B, Bahun TAW, Tedjou AN, Nguiffo-Nguete D, Njiokou F, et al. First detection of F1534C knockdown resistance mutation in *Aedes aegypti* (Diptera: Culicidae) from Cameroon. Infect Dis poverty. 2020;9(1):152.
- Yougang AP, Kamgang B, Tedjou AN, Wilson-Bahun TA, Njiokou F, Wondji CS. Nationwide profiling of insecticide resistance in *Aedes albopictus* (Diptera: Culicidae) in Cameroon. PLoS ONE. 2020;15(6):e0234572.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Springer Nature or its licensor holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.