Zika virus: An updated review of competent or naturally infected mosquitoes

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Abstract

Zika virus (ZIKV) is an arthropod-borne virus (arbovirus) that recently caused outbreaks in the Americas. Over the past 60 years, this virus has been observed circulating among African, Asian, and Pacific Island populations, but little attention has been paid by the scientific community until the discovery that large-scale urban ZIKV outbreaks were associated with neurological complications such as microcephaly and several other neurological malformations in fetuses and newborns. This paper is a systematic review intended to list all mosquito species studied for ZIKV infection or for their vector competence. We discuss whether studies on ZIKV vectors have brought enough evidence to formally exclude other mosquitoes than Aedes species (and particularly Aedes aegypti) to be ZIKV vectors. From 1952 to August 15, 2017, ZIKV has been studied in 53 mosquito species, including 6 Anopheles, 26 Aedes, 11 Culex, 2 Lutzia, 3 Coquillettidia, 2 Mansonia, 2 Eretmapodites, and 1 Uranotauina. Among those, ZIKV was isolated from 16 different Aedes species. The only species other than Aedes genus for which ZIKV was isolated were Anopheles coustani, Anopheles gambiae, Culex perfuscus, and Mansonia uniformis. Vector competence assays were performed on 22 different mosquito species, including 13 Aedes, 7 Culex, and 2 Anopheles species with, as a result, the discovery that A. aegypti and Aedes albopictus were competent for ZIKV, as well as some other Aedes species, and that there was a controversy surrounding Culex quinquefasciatus competence. Although Culex, Anopheles, and most of Aedes species were generally observed to be refractory to ZIKV infection, other potential vectors transmitting ZIKV should be explored.

Author summary

The first isolation of Zika virus (ZIKV) in mosquitoes was made in 1948 in Aedes aegypti. Over the next years, knowledge about ZIKV increased, with detection of the virus in primates, including humans and several other mosquito species. Most of these species were collected in Africa during arbovirus surveillance studies and belong to the genus Aedes, and today, 20 mosquito species have been identified that can be naturally infected by ZIKV. Although field studies are essential to have an overview of potential mosquito
Introduction

Zika virus (ZIKV) is an arthropod-borne virus (arbovirus) belonging to the family Flaviviridae and the genus *Flavivirus*. It is a single-stranded RNA virus that was first isolated in 1947 from a sentinel rhesus monkey in the Zika Forest in Uganda and in 1948 from *A. africanus* mosquitoes in the same forest, suggesting the mosquito-borne transmission of the virus [1]. Over the past 60 years, this virus has been observed circulating among African and Asian populations [2] but with little attention from the scientific community. The ZIKV lineage circulating in Asia has been described as distinct from the African lineage, suggesting the separate sylvatic cycles of ZIKV on those continents [3]. In 2007, the first ZIKV outbreak occurred on Yap Island of the Federal States of Micronesia [4]. Between 2013 and 2014, French Polynesia was struck by ZIKV, with, for the first time, Guillain-Barré syndrome reported in a few patients following ZIKV infection. ZIKV then spread to several islands of the Pacific Ocean [5,6]. This virus may have been subsequently introduced into Brazil, but the origin of this introduction remains uncertain, and several hypotheses have been proposed, all related to international travel. These hypotheses include the visit of the Pope, with many young Catholics from Africa and Asia visiting Brazil during World Youth Day in July 2013, the World Cup in 2014 gathering thousands of people in stadiums and in various regions of Brazil, and the canoeing championship in Rio de Janeiro in 2014, with participants from Pacific countries in which ZIKV circulated during 2014 [7]. Currently, the virus circulating across the Pacific and South America belongs to the Asian lineage [3]. There has been an increasing interest in ZIKV since the outbreak started in Brazil in 2015 and spread into most of the countries of South and Central America, as well as Florida in the United States, with evidence that infection by ZIKV is associated with neurological complications such as microcephaly and several other neurological malformations in fetuses and newborns [8–10]. Current evidence is that ZIKV is not only transmitted by the bite of an infected mosquito but also through sexual intercourse [11–13]. However, mosquito bites remain the predominant route of virus transmission, with an incubation period of about 9 days and then the onset of symptoms [11].

Presently, various facts incriminate the mosquito *A. aegypti* as the main vector of ZIKV, given that it has been shown to be competent in transmitting this virus. This species is the main vector of dengue fever virus (DENV), chikungunya virus (CHIKV), and yellow fever virus. It originated in Africa and spread to Neotropical areas in the 17th and 18th centuries. Urbanization is the main factor, which facilitates an increase in *A. aegypti* populations through the proliferation of human-made containers used to store water in and around inhabited areas, which provide the aquatic larval environment required by these mosquitoes. For this reason, *A. aegypti* appears to be predominant in the transmission and spread of the virus during the recent ZIKV outbreak. Facing the strength and spread of the South American ZIKV epidemics and the fact that *A. aegypti* is not the only mosquito species living in epidemic areas, other species have been suspected to transmit the virus. Moreover, a mosquito that would transmit ZIKV needs to feed on a viremic person and become infected, and the virus must
disseminate to the hemocoel, infect the salivary glands, and be secreted into the saliva (this is the vector competence portion of vectorial capacity). That same mosquito must then feed on one or several other person(s) to disseminate ZIKV into the population. For most species of mosquitoes other than \emph{A. aegypti} (and a few closely related species), this would be extremely unlikely because of their lower anthropophilic behavior but would need to be accounted for in determining how that species would be an important vector. This information is critical when determining whether a particular mosquito species can be a vector of epidemiological importance, and that is why studies mainly focused on \emph{A. aegypti} and \emph{C. quinquefasciatus} because they are the most abundant urban mosquitoes in South America and because they preferentially feed on humans. Moreover, \emph{Culex} mosquitoes are known to transmit several viruses from the same viral family as ZIKV, such as the West Nile virus or the Japanese encephalitis virus, and current knowledge about \emph{Culex} species needs to be examined with greater consideration. This paper is a systematic review intended to evaluate whether studies performed on ZIKV vectors have brought enough evidence to formally exclude mosquitoes other than the \emph{Aedes} species (and particularly \emph{A. aegypti}) as ZIKV vectors. To that end, we discuss the well-established and potential vector competence and capacity of various mosquito species. The relevance of looking more closely at the role played by the mosquito \emph{A. aegypti}, which was considered the main vector of Zika during the American outbreak, was highlighted. The assumption that other mosquito species could have been involved in the past or are involved in current epidemics is reviewed, focusing on vector competence and mosquitoes naturally infected by the virus.

**Methods**

This study was conducted using the electronic databases PubMed and ScienceDirect with a cutoff date of August 15, 2017. Search terms included “Zika” and one of the following search items: “vector,” “mosquito,” “Culicidae,” “Aedes,” “Culex,” and “Anopheles.” Articles reviewed for this study were exclusively in English and French, in addition to some articles obtained through classical search engines because they were not referenced in the above-mentioned databases. After screening the abstracts, titles, and keywords of the identified citations, ineligible articles that mainly focused on outbreaks and the ensuing issues for humans were discarded. Eligible articles were considered relevant if they mentioned one or more aspects of the research question (i.e., entomological studies), regardless of when or where the studies were conducted.

To incriminate a species as a pathogen vector, different criteria are merged into the term “vectorial capacity,” which describes the dynamic relationship between the vectors of infectious diseases and vertebrate hosts, including environmental parameters [14]. The primary components used in estimating the vectorial capacity of mosquitoes are vector density in relation to host density, host preference, and host feeding patterns. In addition, daily survival rates and the longevity of mosquitoes are used, as well as their extrinsic incubation period and vector competence, which is the intrinsic ability (genetic) of a species (mosquito) to be infected, multiply, and transmit a pathogen to another host [15].

Herein, the cited papers used the following parameters. The infection rate corresponds to the proportion of mosquitoes with virus-infected bodies among those tested. The dissemination rate corresponds to the proportion of mosquitoes with virus-infected legs or heads among those infected. The transmission rate corresponds to the proportion of mosquitoes with infectious saliva among those infected. Transmission efficiency corresponds to the proportion of mosquitoes with infectious saliva among those tested.
The validity of species determination was based on the “Systematic Catalog of Culicidae” provided by the Walter Reed Biosystematics Unit [16], and the abbreviations for genus follow the recommendations of Reinert [17]. Considering that there is no consensus concerning the internal classification of the Aedini tribe proposed by Reinert et al. [18], in the current revision, we decided to use the traditional classification for Aedini.

Results and discussion

Publication result overview

The Boolean search identified 562 articles for “Zika vector,” 865 for “Zika mosquito,” 398 for “Zika culicidae,” 654 for “Zika Aedes,” 73 for “Zika Culex,” and 35 for “Zika Anopheles.” Among these 2,587 records, after eliminating duplicates and irrelevant records, 127 studies were considered eligible, finally resulting in 60 considered relevant to this review (Fig 1). Among these 60 articles, 37 were related to ZIKV vector competence and 23 corresponded to mosquitoes naturally infected in the field (Fig 2). From 1952 to 2017, ZIKV has been searched in 1 tabanid species and 53 mosquito species, including 6 Anopheles, 26 Aedes, 11 Culex, 2 Lutzia, 3 Coquillettidia, 2 Mansonia, 2 Eretmapodites, and 1 Uranotaenia (Table 1). Among those,
ZIKV was isolated from 16 different *Aedes* species. The only species other than *Aedes* for which ZIKV was isolated were *A. coustani*, *A. gambiae*, *C. perfuscus*, and *M. uniformis* [19–21].

Vector competence assays were performed on 22 different mosquito species, including 13 *Aedes*, 7 *Culex*, and 2 *Anopheles* species (Fig 2 and S1 Table).

**Fig 2. Synthesis of the research related to vector species of ZIKV between 1952 and March 15, 2017.** Evolution of the number of scientific papers related to vector species of ZIKV, the number of field species tested for the presence of Zika, the number of naturally ZIKV-infected species, the number of species studied experimentally for their competence, and the number of species observed once competent for ZIKV between 1952 and March 15, 2017. ZIKV, Zika virus.

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Mosquitoes tested and naturally infected with ZIKV

**In Africa.** Historically, the first detections of ZIKV in mosquitoes were observed in species of the genus *Aedes* in studies carried out in Africa through methods of immunoassays for detection of antiviral antibodies (mostly hemagglutination inhibition test). The first isolation of ZIKV occurred in 1947 during a routine surveillance for yellow fever in the Zika Forest, Uganda, from a sentinel rhesus monkey [1]. The following year, in 1948, this virus was detected from *A. africanus*, a sylvatic mosquito, by intracerebral neutralization test in the same forest [1]. The use of defined antisera in these tests permitted differentiation of ZIKV from other known viruses such as yellow fever or DENV. Over the next 10 years, knowledge about ZIKV increased. Primates, including humans, were considered to be the main reservoirs of ZIKV, with transmission to humans primarily through mosquito vectors [1,63,76]. In the interim, several arboviruses were isolated in various mosquitoes from the Zika Forest, including *Aedes ingrami* and *Culex annulioris*, but ZIKV remained identified only in *A. africanus* (Table 1) [62,63]. The first isolation in a species other than *A. africanus* occurred in 1969 in *A. aegypti* from Malaysia [56]. In that study, *A. albopictus* was also sampled but did not exhibit
Table 1. Vector species naturally infected by ZIKV or studied experimentally for their ZIKV competence.

| Vector species | Vector competence assay | Field studies with natural ZIKV infection |
|----------------|-------------------------|------------------------------------------|
|                | Competent               | Not competent                            | Infected | Not infected |
| Culicidae: Anophelinae |                         |                                         |          |              |
| Anopheles brohieri       | [20]                    |                                         |          |              |
| Anopheles coustani       | [19,21]                 |                                         | [20,22]  |              |
| Anopheles funestus       | [20,22,23]              |                                         |          |              |
| Anopheles gambiae        | [24]                    | [21]                                    | [20,22,23,25] |              |
| Anopheles nili           | [20,22]                 |                                         |          |              |
| Anopheles rufipes        | [21,26]                 |                                         |          |              |
| Anopheles stephensi      | [24]                    |                                         |          |              |
| Culicidae: Culicinae: Aedini |                 |                                         |          |              |
| Aedes aegypti            | [27–53]                 | [54,55]                                 | [19,21,26,56–59] | [22,23,25,60,61] |
| Aedes africanus          | [1,19,21,62–67]         |                                         | [20,22,68] |              |
| Aedes albopictus         | [30,32,35,42,46–48,51,69] | [25]                              | [56,58,59] |              |
| Aedes apicoargentatus    | [65]                    |                                         |          |              |
| Aedes argenteopunctatus  |                         |                                         | [20–22,60] |              |
| Aedes camptorhynchus     | [51]                    |                                         | [22]     |              |
| Aedes circumluteolus     |                         |                                         |          |              |
| Aedes cozi               |                         |                                         | [60]     |              |
| Aedes cumminsi           |                         |                                         | [22,60]  |              |
| Aedes dalzieli           | [19–21,26,60]          |                                         | [22]     |              |
| Aedes fowleri            | [21,26]                 |                                         | [22]     |              |
| Aedes furcifer           | [19,21,22,26,57,60,67] |                                         |          |              |
| Aedes hensilli           |                         |                                         | [4,61]   |              |
| Aedes hirsutus           | [19]                    |                                         | [22]     |              |
| Aedes ingrami            |                         |                                         | [63]     |              |
| Aedes luteocephalus      | [55]                    |                                         | [19–23,26,60,67] |              |
| Aedes metallicus         | [19,21]                 |                                         | [22]     |              |
| Aedes minutus            | [21,26]                 |                                         | [20]     |              |
| Aedes neoafricanus       | [21,26]                 |                                         | [20,60]  |              |
| Aedes notoscriptus       | [51]                    | [38]                                    | [22,66,68]| [57,60]     |
| Aedes opok               |                         |                                         | [22]     |              |
| Aedes palpale*           |                         |                                         |          |              |
| Aedes polynesiensis      | [31]                    |                                         | [22]     |              |
| Aedes procax             | [38]                    |                                         | [22]     |              |
| Aedes simpsoni           |                         |                                         | [23,25]  |              |
| Aedes taeniorhynchus     | [70]                    |                                         | [22]     |              |
| Aedes tarsalis           |                         |                                         | [22]     |              |
| Aedes taylori            | [19,21,26]              |                                         | [60]     |              |
| Aedes triseriatus        | [35]                    |                                         | [22]     |              |
| Aedes unilineatus        | [55]                    | [19]                                    | [22,60]  |              |
| Aedes vexans             | [71,72]                 |                                         | [61]     |              |
| Aedes vigilax            |                         |                                         |          |              |
| Aedes vittatus           | [55]                    |                                         | [19–21,26,57] | [22,23,60] |
| Culicidae: Culicinae: Culicini |                |                                         |          |              |
| Culex annulifloris       |                         |                                         | [22,63]  |              |
| Culex annulirostris      | [38,51]                 |                                         | [22,63]  | (Continued)
ZIKV infection. However, by 2000, ZIKV was detected from 13 distinct mosquito species among the 43 species studied in several African countries (Fig 2 and Table 1). During a yellow fever outbreak in Nigeria, *Aedes luteocephalus* was shown to be infected by ZIKV. Surprisingly, in that study, neither *A. africanus* nor *A. aegypti* exhibited the presence of ZIKV [23]. However, the primary vector of ZIKV was suspected to be *A. aegypti*, first because of its urban habitats concomitant with the high prevalence observed in human populations [77] and also because its ability to transmit the virus to a new host was shown experimentally [28].
Several arbovirus surveillance studies conducted in Africa highlighted an increasing number of mosquitoes naturally infected with ZIKV. Thus, in the Central African Republic, ZIKV was isolated from *Aedes opok* and *A. africanus* [64,68]. In Senegal, *Aedes furcifer*, *Aedes taylori*, *A. luteocephalus*, *Aedes dalzieli*, *Aedes vittatus*, and *M. uniformis* were infected by ZIKV [20], as were *A. aegypti*, *A. africanus*, *Aedes neoafriicanus*, *Aedes fowleri*, *Aedes metallicus*, and *Aedes minitus* [21,26,60]. In the latter study, ZIKV was also isolated from *A. coustani*, *A. gambiae*, and *M. uniformis* [21]. In Burkina Faso and Ivory Coast, ZIKV was isolated from various *Aedes* species [22,57]. In 2014, another study conducted in Senegal revealed that several *Aedes* species were naturally infected by ZIKV, as were *C. perpiscus* and *M. uniformis*, suggesting that ZIKV was still circulating in Africa [19]. ZIKV isolated from *Culex*, *Anopheles*, or *Mansonia* species might reveal their potential role as secondary vectors in the transmission and viral maintenance of ZIKV. However, based on recent studies revealing that neither *C. quinquefasciatus* nor *Culex pipiens* can be considered competent species [73,74], it seems more plausible that this infection was caused by an undigested blood meal after a bite on animals infected with ZIKV. Some nonvector species could also develop gut-limited infections without transmitting the pathogen [78]. Vector competence studies are nevertheless not consensual concerning the ability of these 2 species to be infected and to transmit ZIKV, suggesting that *Culex* species but also other potential vectors transmitting ZIKV should be explored [37,75]. A study performed in Gabon in 2007 isolated ZIKV in *A. albopictus*, revealing a new potential threat from this invasive species in Africa but also out of Africa [25]. Although ZIKV hosts are not clearly identified, the ZIKV transmission cycle involves one or more vertebrate hosts and one or more mosquito vectors. In Africa, ZIKV is mainly maintained by a sylvatic cycle involving nonhuman primates; however, some serological studies suggest that other mammals could be reservoirs [79].

**Out of Africa.** Between the end of the 1960s and the 2000s, ZIKV dispersed to several Asian countries, as observed through seroprevalence studies [80], but few vector studies were conducted, possibly because of the clinical similarity of the symptoms of ZIKV, DENV, and CHIKV infections. In 2007, after the ZIKV outbreak reported in the Pacific Island of Yap, entomological studies mainly focused on *Aedes hensilli* because of its abundance and the presumption that it was the most likely vector of DENV. Even if 73% of Yap residents were estimated to have been recently infected by ZIKV, the virus was not isolated from the sampled *A. hensilli* or *C. quinquefasciatus* [4,61]. However, high rates of infection were found in a study in which the probable vector *A. hensilli* was experimentally infected, reinforcing the plausibility that this species served as a vector during the ZIKV outbreak [61]. *A. aegypti* nevertheless remained the suspected vector in the transmission of ZIKV in Asia.

In 2013–2014, ZIKV caused outbreaks in several Pacific Islands including French Polynesia and Easter Island in Chile, but no vector was strictly identified, although *A. aegypti* and *Aedes polynesiensis* were assumed to play a role in the transmission of the virus [81,82].

In 2015, some cases of humans infected by ZIKV were reported in Brazil, developing into an outbreak that spread throughout South America, the Caribbean islands, and Central America. Originally adapted to a zoonotic cycle in Africa, ZIKV evolved into an urban cycle involving a human reservoir and domestic mosquito vectors. In South America, *A. aegypti* and *C. quinquefasciatus* are among the most abundant species in urban areas and were first suspected to be the main vectors of ZIKV. *C. quinquefasciatus* is both a domestic and opportunistic mosquito in its feeding behavior. Because it does not have a marked trophic preference, the blood meals it takes are largely conditioned by the host populations [83]. In South American urban areas, the community of vertebrates is dominated by humans. In this case, the probability that one of these *Culex* takes 2 consecutive blood meals on a human more than 7 days apart is high and could imply a significant role of this species in the transmission of ZIKV. Consequently, at
the beginning of the outbreak in the Americas, the questions surrounding the detection of ZIKV only in *Aedes* species and not in other species remain: was this due to a lack of data, or did this reflect the reality of the situation?

**Vector competence evidence**

**A. aegypti.** The first evidence of ZIKV transmission via mosquito bites was found experimentally for an African strain of *A. aegypti* in 1956 in Nigeria; even though *A. africanus* was presumed to be the vector, the number of samples was insufficient at that time [27]. Although *A. aegypti* was not primarily suspected to be involved in the transmission of ZIKV, that study demonstrated that the virus was probably able to multiply in this species and that infected mosquitoes were capable of transmitting the virus to a susceptible host. In that study, mosquitoes infected via an artificial blood feeding on a mouse skin membrane transmitted ZIKV to a rhesus monkey up to 72 days post mosquito infection, suggesting the high persistence of the virus in the salivary glands [27]. The same year, the experimental infection of a human with ZIKV could not confirm its transmission via *A. aegypti* having blood meal on that human [54]. Only 1 study was conducted in the next 50 years, and this study confirmed the ability of *A. aegypti* to transmit the virus to a new host in experimental conditions. This observation was made during a comparison between experimental transmission of yellow fever and ZIKV and observing effects on mice previously inoculated intracerebrally with homogenates of infectious mosquitoes [28]. While methods of ZIKV titration were generally based on intracerebral inoculation of the virus in mice, after 2012, the literature describes less-invasive methods such as Vero cell line or plaque assay (S1 Table). The infectivity titers of a virus can be determined by infecting a particular cell line with increasing dilutions of the virus material and determining the highest dilution producing cytopathic effect in 50% of the inoculated cells. In this case, the 50% endpoint dilution is expressed as tissue culture infectious dose 50 (TCID 50/mL). Plaque assays remain one of the most accurate methods for the direct quantification of infectious virion through the counting of discrete plaques [84] and are the most used method in ZIKV vector competence studies (S1 Table). These methods are generally complemented with molecular techniques such as quantitative real-time (qRT)-PCR that can easily show that viral RNA is present. However, the sole use of this technique indicates the presence of RNA and does not mean that any live virus is present, and the technique needs further testing.

Since 2012, about 30 studies have evaluated *A. aegypti* competence for ZIKV transmission in experimental conditions [29–48,50–53,55,85]. Even if it is now well accepted that *A. aegypti* is the main vector of ZIKV in urban areas, experimental studies are not entirely consistent regarding the stages of infection, the spread of the virus to the salivary glands, and the incubation period in the mosquito’s body. The extrinsic incubation period for ZIKV in *A. aegypti* varies between these different studies, as do the infection rate, the dissemination rate (with first detection of the virus in the salivary glands between 6 and 14 days post infection [DPI]), and the transmission rate and efficiency. These disparities might be explained by the way these studies were conducted. Several studies have shown that feeding on a viremic animal tends to produce significantly higher infection, dissemination, and transmission rates than feeding on an artificial blood meal through a membrane [34,35,44,70]. Similarly, using nonfrozen, freshly grown virus tends to produce significantly higher infection (and dissemination and transmission) rates than feeding on an artificial blood meal made with frozen stock virus [39,47]. In addition, the origin—African or Asian—of the ZIKV strain, as well as the origin of the population of mosquitoes, may impact the infection, dissemination, and transmission rates [39,44,48]. However, even if the coupling mosquito virus strain is important, the origin of the virus is not sufficient to explain
the differences observed in the vector competence studies. Some conflicting results concerning viral transmission were also described. A study on a Senegalese *A. aegypti* population described a high transmission rate of about 88% from 7 DPI [28], but mosquitoes were inoculated with ZIKV, a method which cannot be compared with standard vector competence studies. An *A. aegypti* population from Singapore orally infected with ZIKV via an artificial blood meal resulted in salivary gland infection rates of 100% at 10 DPI [29]. High concentrations of ZIKV in the blood meal provided to *A. aegypti* mosquitoes from Mexico exhibited high transmission efficiency [47]. Brazilian, Australian, and Chinese populations of *A. aegypti* infected with ZIKV revealed high transmission efficiency, up to 90% at 14 DPI [34,36,40,46,51]. A laboratory strain of *A. aegypti* coinfectd with both ZIKV and CHIKV also showed high transmission efficiency for ZIKV [53].

Nevertheless, to our knowledge, these are the only studies providing such a high transmission efficiency for this species, contrasting with the generally low or moderate transmission efficiency observed in various strains of *A. aegypti*, even those highly susceptible to ZIKV [30–33,35,38,39,42,44,55]. The methods used in the latter competence studies are overall in agreement regarding the origin of the virus (mainly the Asian strain), the viremia of the blood meal, and the mode of administration (mainly artificial blood feeding through membrane). Methods to evaluate ZIKV transmission are generally based on detection or titration of the virus (mainly plaque or TCID assays on saliva expectorates, complemented by qRT-PCR; S1 Table). In 2017, a study highlighted another approach that may be used for “natural transmission,” with a successful transmission of ZIKV by an infectious *A. aegypti* bite to a live mouse [52]. However, the engorgement methods (mosquitoes feeding on viremic animal or with an artificial blood meal, the type of membranes), the preparation of the blood meal (virus freshly grown or from a frozen stock), the different virus primers used for detection, the microbiome, the virome, and the origin of the mosquito population are all factors that may lead to the observed conflicting results and require further investigation (S1 Table). For example, significant variation in competency for ZIKV transmission among *A. aegypti* mosquito populations from the Americas was highlighted [30,43]. Actually, the genetic diversity of different populations of *Aedes* species may largely explain those differences, as was observed for the transmission rate for several distinct populations of *A. aegypti* for DENV [86] and CHIKV [87].

*A. albopictus*. Native to Southeast Asian tropical and subtropical regions, *A. albopictus* became well adapted to temperate regions, and its distribution now includes North America and Europe [88]. In Europe, this mosquito was initially found in the area around the Mediterranean Sea, but it is unexpectedly and progressively spreading further north in Europe [89]. This quick spread of the “Asian tiger mosquito” means that tropical arboviruses are becoming a concern for populations in temperate climates. During the severe 2005–2007 CHIKV epidemic reported in the Indian Ocean, *A. aegypti* but also *A. albopictus* were described as the main vectors of this virus, as was observed on the French island of Réunion, where *A. albopictus* was the dominant species [90]. Although *A. albopictus* is not suspected to be the main vector of the most recent arbovirus outbreaks in South America, its similarity to *A. aegypti* [91], its implication in CHIKV and DENV transmission [92,93], and its distribution in the Americas, Western Europe, and South and East Asia means that this species remains the focus of much attention [94].

The vector competence of *A. albopictus* has been well established for CHIKV and DENV [87,93], but ZIKV transmission remained to be clarified at the beginning of the American outbreak because few studies had clearly demonstrated the ability of this species to transmit the virus. The first suspicion of the potential role of this species in ZIKV transmission appeared in Indonesia, where *A. albopictus* and *A. aegypti* were widely distributed close to some human ZIKV-infected patients [80]. The first evidence of *A. albopictus* competence in transmitting
ZIKV was provided in 2013 from a mosquito population in Singapore [69]. This study revealed that this species was susceptible to the Ugandan strain of ZIKV, with high dissemination rates and high transmission rates and efficiency. Seven DPI, all infected mosquitoes exhibited ZIKV in their salivary glands, contrasting with the results observed during the ensuing years, when transmission efficiency was much lower [30,32,35,42,46–48]. In these studies, populations of A. albopictus from Brazil, the US, China, or Italy infected with the Asian strain of ZIKV had overall lower infection, dissemination, and transmission rates than A. aegypti but were capable of transmitting ZIKV despite a low efficiency. However, Australian A. albopictus infected with the Asian strain of ZIKV revealed high transmission efficiency [51], which is concordant with an A. albopictus competence study from Singapore [69].

**Other Aedes species.** Although recent studies have mainly focused on the above species, other mosquito species from the genera Aedes or Culex may have the potential to be good vectors, depending on their geographical distribution. Most of the studies concerning vector competence in other species were conducted after the beginning of the outbreak in the Americas, except for some old studies conducted in the 1950s in Africa. Indeed, A. aegypti may not alone account for the extent of this epidemic, and some other species coexisting in the same urban areas might potentially be ZIKV vectors. In addition to A. aegypti and A. albopictus, 11 Aedes species, including sylvatic and urban species, have been tested experimentally for their competence (Table 1; S1 Table), showing that A. luteocephalus and A. vittatus from Senegal have the viral genome in their saliva 15 DPI and, consequently, the potential to transmit ZIKV [55]. In the same study, Aedes unilineatus had low infection and dissemination rates and was not able to transmit the virus. Similarly, laboratory colonies of Aedes triseriatus, a mosquito known to be a vector of La Crosse virus, tolerant of a wide range of temperatures and broadly distributed across North America, was able to be infected by ZIKV but exhibited dissemination and transmission rates of 0% [35]. However, in this study, samples were in too short supply, which could explain this null rate, and further investigation on A. triseriatus competence for ZIKV is required. Other Aedes species, including Aedes notoscriptus, Aedes procax, and Aedes vigilax collected in Australia were also infected by ZIKV with a prototype of the African strain. Although methods were similar to other studies performed with A. aegypti, these species did not contain virus in the saliva expectorates and, consequently, were not able to transmit ZIKV [38]. However, in another study, Australian A. notoscriptus and Aedes camptorhynchus had a low transmission efficiency, suggesting that even though they are probably unable to sustain large outbreaks, these species could trigger some secondary cases [51]. Other vector competence studies on Aedes vexans collected in the northern US revealed its capacity to transmit ZIKV [71,72]. A. vexans is one of the most abundant mosquito species in the northern US. This aggressive mosquito has a long flight range, feeds primarily on large mammals, and attacks humans both day and night [95]. Its feeding behavior, combined with its ability to transmit ZIKV, could contribute to its role as a potential vector of ZIKV in the Northern Hemisphere. No evidence of ZIKV transmission was highlighted in a population of A. polynesiensis sampled on Tahiti Island, France, without any viral particle found in the saliva [31], nor in 1 Aedes taeniorhynchus strain from the US coast of the Gulf of Mexico that was refractory to ZIKV infection [70]. A. polynesiensis was nevertheless highly suspected in transmission on the Pacific Islands because of its ability to transmit DENV, CHIKV, and the Ross River virus [96–98].

**Culex species.** Despite the lack of evidence that various other mosquito species can transmit ZIKV, the supposition that a genus other than Aedes, such as Culex, might be competent in transmitting this virus remains strong. For example, C. quinquefasciatus is one of the most abundant mosquitoes in anthropized tropical and subtropical areas, as is C. pipiens in anthropized temperate regions. These species have been studied since the beginning of the outbreak
in the Americas, and some discrepancies exist concerning their ability to transmit the virus. The absence of, or very low, infection rates, without any subsequent ZIKV transmission, was observed experimentally in C. quinquefasciatus from Brazil, the US, China, and Australia [24,36,38,39,43,46,48,49,51,70,73,74]. However, 1 study conducted in Brazil revealed that ZIKV was able to replicate in the body of the mosquito [37]. Nevertheless, this experiment is based on ZIKV RNA detection without detection of infectious virus, leading to the need for assessing their result. Meanwhile, Chinese C. quinquefasciatus was described as a competent vector for ZIKV in experimental conditions [75]. Though controversial, these studies suggest that caution should be taken with regard to the status of Culex. As suggested for Aedes species, the method by which the mosquitoes were fed, the different levels of viremia delivered to the mosquito, the virome, the microbiome, and the origin of the mosquito population may influence the experimental vector competence of this species.

Evidence for the lack of competence of other Culex species was recently provided via populations of C. pipiens from Italy, the US, Tunisia, and Germany that were experimentally exposed to ZIKV through an artificial blood meal without being infected [33,35,39,42,49,73,74]. Similarly, ZIKV infection could not be detected in Culex sitiens and Culex annulirostris from Australia [38,51] nor for Culex torrentium and Culex molestus from Germany [42].

The lack of competence of Culex species was reinforced by the absence of infection in a natural population of C. quinquefasciatus collected during an outbreak of ZIKV in Mexico [58], and in C. quinquefasciatus collected in the vicinity of suspected cases of ZIKV infection in Rio de Janeiro, Brazil, from June 2015 to May 2016 [59].

Based on their refractoriness to infection and the absence of viral particles in the saliva, it appears that the tested Culex species could possess a midgut barrier that corresponds to the site involved in the first stages of viral attachment, penetration, and replication. This was suggested by studies of the viral competence of C. quinquefasciatus and C. pipiens in which the mosquito midgut barrier was bypassed by inoculating the virus directly into the hemocoel, but neither dissemination nor transmission was observed [49,73]. On the other hand, this could reflect the general refractoriness of the mosquito species to ZIKV.

Anopheles species. Only 2 Anopheles species have been tested in vector competence studies, A. gambiae and Anopheles stephensi [24]. These 2 species were not able to be infected, suggesting that they do not play a role in ZIKV transmission to humans. Although Anopheles mosquitoes are mostly known to transmit parasites, they are also responsible for transmission of O’nyong-nyong virus, which is closely related to CHIKV [99].

There is, consequently, a need to conduct field studies to identify the largest number of species from various genera that are potential vectors of ZIKV, as well as laboratory studies to confirm the lack of competence of these species. Moreover, the distinction between vectorial capacity and vector competence must be observed with caution. Vectorial capacity refers to all of the environmental, behavioral, cellular, and biochemical factors that may have an influence on the association between a vector, the pathogen transmitted by the vector, and the vertebrate host to which the pathogen is transmitted [100]. Vectorial capacity is essentially determined by both environmental and behavioral factors. For example, a particular mosquito species might be genetically and biochemically compatible for the complete development of a particular pathogen (i.e., vector competent for this pathogen), but if this species does not coexist temporally and spatially with a vertebrate host that harbors the pathogen, or if the preferred blood source for this species does not include that vertebrate, this mosquito would not be a suitable vector for this pathogen [100]. Therefore, a mosquito species that has a high vector competence would not automatically imply that this species is a vector of epidemiological importance. For these
reasons, *A. aegypti* remains the species most likely to be responsible for the spread of the virus in the Americas.

### A. aegypti and the outbreak in the Americas

**Low vector competence but high vectorial capacity.** Even if in experimental conditions *A. aegypti* and *A. albopictus* show little vector competence, this does not reflect their potential to cause epidemics, driven not only by their vector capacity (i.e., their large populations and host feeding preferences and frequencies) but also by human parameters. Indeed, one of the hypotheses explaining the drastic spread and virulence of the outbreak concerns the origin of the virus. In the Americas, the virus has been described to belong to the Asian genotype and is closely related to the strain that circulated in French Polynesia in 2013 [101]. Moreover, vector competence assays with the strain circulating in the Americas did not show high infectivity for *A. aegypti*, suggesting that the sole origin of the virus could not explain the differences between the outbreak in the Americas and previous outbreaks [39]. The limited diagnostic capabilities in Africa and Asia (i.e., the absence of field research in areas where other arboviral infections were present), combined with a relative immune population, might partly explain why it became a threat in the Americas with a naïve human population. Increased global travel, uncontrolled urbanization associated with areas where the possibility of maintaining proper hygiene is poor, and populations with limited access to water—requiring them to store water, leading to increased mosquito breeding sites—might explain the extent of this epidemic.

*Aedes* eggs are desiccation-resistant and can consequently survive for long periods, leading to the potential persistence of arbovirus in the eggs. Like for other flaviviruses such as DENV [102] or yellow fever [103], vertical transmission of ZIKV in *A. aegypti* and *A. albopictus* was demonstrated [45,104,105]. The filial infection rate (FIR) in *A. aegypti* mosquitoes injected intrathoracically with ZIKV was 1/290 [104]. In another study, *A. aegypti* and *A. albopictus* receiving a viremic blood meal had a FIR of 1/84 [105]. This value is not entirely consistent with the previous study and appears to be high compared with the FIR observed for other flaviviruses. ZIKV seems to have a great capacity to be transmitted vertically by *A. aegypti* and *A. albopictus*, and it has been observed that this vertical transmission may be different depending on the origin of the mosquito. It seems that vertical transmission may play a role in the propagation and maintenance of ZIKV, but the impact of this transmission appears to be negligible compared with horizontal transmission [105].

Moreover, despite the absence of evidence, some studies hypothesized that a link exists between climatic events such as El Niño and the spread of ZIKV from Brazil to North America [106–109]. El Niño leads to extreme temperatures in northern South America, which might enhance the development of *A. aegypti*. Moreover, higher temperatures can increase the habitat of this tropical mosquito and might have an influence on the physiology of the mosquito through higher biting rates, lower mortality, and smaller extrinsic incubation periods. However, the link between ZIKV outbreak in the Americas and this climatic event should be taken with caution insofar as the major CHIKV outbreak in the same area, which is transmitted by the same vector—*A. aegypti*—occurred in 2014, which was not an El Niño year. Even if *A. aegypti* does not have a good vector competence, the main reason for its good vectorial capacity relies on the fact that most of the individuals mainly feed on humans with multiple bites in a single gonotrophic cycle [110], which contrasts with the behavior of other mosquito species found during the 2015 outbreak. Moreover, locally, cases of ZIKV were all acquired in areas where *A. aegypti* is present, suggesting that if other species were involved in any significant extent, then there would have been cases in other areas.
Strategies for mosquito management. The project of eradication of the *A. aegypti* mosquito began in the first half of the 20th century, after it had been established that this mosquito transmitted the urban yellow fever. Sanitation reform, in particular getting rid of stagnant water, where this mosquito lays its eggs, was the most effective way to eradicate *A. aegypti*, in combination with the use of insecticides to fight adult mosquitoes [111]. In 1934, Brazil had managed to eradicate the mosquito in several cities in its northeast, and the country launched efforts to do so nationwide. In 1942, Brazil was declared to be free of *A. aegypti*, through a combination of public education and fumigation, mainly with the organochlorine dichlorodiphenyltrichloroethane (DDT). Five years later, several South American countries, in association with the Pan American Sanitary Organization, planned on wiping out *A. aegypti* across the continent [111]. In 1962, after years of indoor residual spraying of high doses of DDT, military-grade organization, and funding to train personnel and buy equipment, the eradication of *A. aegypti* became successful in 18 countries of the Americas plus several islands of the West Indies. As these efforts succeeded, *A. aegypti* control lost political importance, and attention and funding declined [111]. The failure to maintain this success was and is still now complicated by population increase, extensive and sprawling urbanization, and the lack of municipal infrastructure such as piped water. This failure could mainly explain the regular invasions of DENV, CHIKV, and ZIKV in South America.

Today, the use of insecticides is one of the major components in the global strategy to control mosquito-associated diseases. Indeed, to fight populations of mosquitoes, the available tools include insecticide spatial spraying and reducing the production of larvae. Other methods are used around the world, depending on the legislation of the country, such as introducing *Wolbachia* intracellular bacteria into the bodies of *A. aegypti* individuals with the intent to shorten the lifespan of female mosquitoes [112]. Another method carried out in Brazil was the use of transgenic *A. aegypti*, which expresses a self-limiting transgene in order to prevent larvae from developing to adulthood [113]. In the absence of controls over these methods, which are highly controversial and also depend on the country’s legislation, the main global mosquito management strategy remains removing breeding sites and the use of insecticides. The use of insecticides always implies a delicate balance between, on the one hand, their efficacy and the resistance of the target populations and, on the other hand, the demonstrated or supposed toxicity for humans and the environment. In South America, the main target of the antivectorial fight to prevent ZIKV spread was the urban mosquito *A. aegypti*.

However, if ZIKV had a sylvatic cycle in South America, it would involve other mosquito species that would not be compatible with the current vector control. In Africa and Asia, sylvatic cycles have been described with ZIKV, involving many species of animals in which the virus or antibodies have been isolated, such as monkeys, rodents, bats, orangutans, and carabasos [114]. In the Americas, studies on ZIKV in vertebral hosts are scarce, but the remarkable diversity of Latin American wildlife species provides a potential to establish a sylvatic ZIKV cycle, along with more than 200 mosquito species, which needs to be explored and surveyed [115]. A sylvatic cycle of ZIKV would make its elimination almost impossible, and the use of insecticides remains focused on the urban mosquito *A. aegypti*. However, the widespread use of these chemical compounds around the world has led to resistant phenotypes in vector populations [116–118]. These resistant phenotypes are due to a combination of multiple and complex mechanisms, such as the greater metabolic detoxification of insecticides before they reach the nervous system [119–121] and the decreased sensitivity of the targeted proteins through mutations of the neural targets of the insecticides [121]. A question remains to be elucidated; namely, can insecticide resistance interact with pathogen transmission and particularly for ZIKV in mosquitoes? First, insecticide resistance may have a direct impact on ZIKV outbreaks by making it more difficult to satisfactorily reduce mosquito populations [122]. Secondly, the
molecular mechanisms involved in detoxification or in gene response to insecticide exposure such as immune response may interact with signaling pathways involved in response to viral infection, as observed in *A. gambiae* with the parasite *Plasmodium falciparum*, in which positive or negative interactions were observed [123–125]. The number of mosquitoes in a population and the lifespan of resistant insects may be higher in regions where insecticides are used [126,127]. Consequently, the observed high resistance rates in the *A. aegypti* population of South America may have enhanced the transmission and spread of ZIKV.

**Conclusion**

Despite several years of entomological investigations and the discovery of many mosquito species naturally infected by ZIKV, recent advances revealed that *A. aegypti* may be the major vector driving recent epidemics, while other *Aedes* species may contribute to the sylvatic transmission cycle of ZIKV. Since the beginning of the ZIKV outbreak in the Americas, the number of studies has soared, and it has been shown that the epidemic resulted from a combination of several factors, including highly anthropophilic mosquito behavior, environment parameters, and human factors such as population increase, urbanization, and the failure to provide municipal services such as piped water. Although our knowledge increases concerning the vector competence of *Aedes* and *Culex* species, there is still a need to explore which other species could be competent for ZIKV. At a time when data on sexual transmission in humans are oriented towards specific public health measures, including state recommendations on sexuality and the procreation of individuals living in an epidemic area, further research on mosquito infection and transmission is fundamental.

**Supporting information**

**S1 Table. Comparison of vector competence studies of ZIKV.** Virus titres calculated by the method of Reed and Muench are expressed as the reciprocal of the log$_{10}$ dilution, which killed 50% of the mice inoculated. The TCID$_{50}$ test quantifies the amount of virus required to produce cytopathic effect in 50% of inoculated tissue culture cell. PFU is a measure of the number of particles capable of forming plaques per unit volume. FFU is the unit of a variant of the plaque assay, the FFA based on immunostaining techniques. The infection rate corresponds to the proportion of mosquitoes with virus-infected bodies among those tested. The dissemination rate corresponds to the proportion of mosquitoes with virus-infected legs among those infected. The transmission rate corresponds to the proportion of mosquitoes with infectious saliva among those infected. The transmission efficiency corresponds to the proportion of mosquitoes with infectious saliva among those tested. In the table, high infection, dissemination, or transmission were arbitrarily chosen as values greater than 60% among the tested mosquitoes, a moderate value between 40% and 60%, and a low value less than 40%. AP-61, *Aedes pseudoscottellaris* 61; CHIKV, chikungunya virus; DPI, day post infection; FFA, focus forming assay; FFU, focus forming unit; NA, not available; PFU, plaque forming unit; TCID, tissue culture infectious dose; ZIKV, Zika virus.

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References

1. Dick GWA, Kitchen SF, Haddow AJ. Zika Virus (I). Isolations and serological specificity. Trans R Soc Trop Med Hyg. 1952; 46: 509–520. https://doi.org/10.1016/0035-9203(52)90042-4 PMID: 12995440

2. Haynes EB. Zika Virus Outside Africa. Emerg Infect Dis. 2009; 15: 1347–1350. https://doi.org/10.3201/eid1509.090442 PMID: 19788800

3. Haddow AD, Schuh AJ, Yasuda CY, Kasper MR, Heang V, Huy R, et al. Genetic characterization of Zika virus strains: geographic expansion of the Asian lineage. PLoS Negl Trop Dis. 2012; 6: e1477. https://doi.org/10.1371/journal.pntd.0001477 PMID: 22389730

4. Duffy MR, Chen T-H, Hancock WT, Powers AM, Kool JL, Lanciotti RS, et al. Zika virus outbreak on Yap Island, Federated States of Micronesia. N Engl J Med. 2009; 360: 2536–2543. https://doi.org/10.1056/NEJMoa0805715 PMID: 19516034

5. Cao-Lormeau V-M, Roche C, Teissier A, Robin E, Berry A-L, Mallet H-P, et al. Zika Virus, French Polynesia, South Pacific, 2013. Emerg Infect Dis. 2014; 20: 1085–1086. https://doi.org/10.3201/eid2006.140138 PMID: 24856001

6. Musso D, Nilles EJ, Cao-Lormeau V-M. Rapid spread of emerging Zika virus in the Pacific area. Clin Microbiol Infect. 2014; 20: O595–O596. https://doi.org/10.1111/cmi.12707 PMID: 24902088

7. De Carvalho NS, De Carvalho BF, Fugac¸a CA, Doris B, Bica ES. Zika virus infection during pregnancy and microcephaly occurrence: a review of literature and Brazilian data. Braz J Infect Dis Off Publ Braz Soc Infect Dis. 2016; 20: 282–289. https://doi.org/10.1016/j.bjid.2016.02.006 PMID: 27102780

8. McCarthy M. Zika virus was transmitted by sexual contact in Texas, health officials report. BMJ. 2016; 352: i720. https://doi.org/10.1136/bmj.i720 PMID: 26848011

9. Kramer LD, Ciota AT. Dissecting vectorial capacity for mosquito-borne viruses. Curr Opin Virol. 2015; 15: 112–118. https://doi.org/10.1016/j.coviro.2015.10.003 PMID: 26569343

10. Gaffigan TV, Wilkerson RC, Pecor JE, Stoffer JA, Anderson T. Systematic Catalog of Culicidae—I. Walter Reed Biosystematics Unit. In: Systematic Catalog of Culicidae [Internet], [cited 24 Jan 2017]. Available: http://wwww.mosquitocatalog.org/. Accessed 24 January 2017.

11. Reinitz JF. List of abbreviations for currently valid generic-level taxa in family Culicidae (Diptera). Eur Mosq Bull. 2009; 68–76.

12. Eltringham BF, Edman JD. Medical entomology. Kluwer academic publishers; 2004. p. 659.

13. Kramer LD, Ciota AT. Dissecting vectorial capacity for mosquito-borne viruses. Curr Opin Virol. 2015; 15: 112–118. https://doi.org/10.1016/j.coviro.2015.10.003 PMID: 26569343

14. Gaffigan TV, Wilkerson RC, Stoffer JA, Anderson T. Systematic Catalog of Culicidae—I. Walter Reed Biosystematics Unit. In: Systematic Catalog of Culicidae [Internet], [cited 24 Jan 2017]. Available: http://www.mosquitocatalog.org/. Accessed 24 January 2017.

15. Althouse BM, Hanley KA, Diaho M, Sall AA, Ba Y, Faye O, et al. Impact of Climate and Mosquito Vector Abundance on Syltrophic Arbovirus Circulation Dynamics in Senegal. Am J Trop Med Hyg. 2015; 92: 88–97. https://doi.org/10.4269/ajtmh.13-0617 PMID: 25404071
22. Robert V, Lhuillier M, Meunier D, Sarthou JL, Moneny N, Digoutte JP, et al. Virus amaril, dengue 2 et autres arbovirus isolés de moustiques, au Burkina Faso, de 1983 à 1986: considérations entomologiques et épidémiologiques. Bull Soc Pathol Exot. 1993; 86: 90–100.

23. Lee VH, Moore DL. Vectors of the 1969 yellow fever epidemic on the Jos Plateau, Nigeria. Bull World Health Organ. 1972; 46: 669–673. PMID: 4403105

24. Dodson BL, Rasgon JL. Vector competence of Anopheles and Culex mosquitoes for Zika virus. PeerJ. 2017; 5: e3096. https://doi.org/10.7717/peerj.3096 PMID: 28316896

25. Grard G, Caron M, Mombo IM, Nkoghe D, Mbou Ondo S, Jiolle D, et al. Zika virus in Gabon (Central Africa)—2007: a new threat from Aedes albopictus? PLoS Negl Trop Dis. 2014; 8: e2681. https://doi.org/10.1371/journal.pntd.0002681 PMID: 24516683

26. Monlun E, Zeller H, Le Guenno B, Traoré-Lamizana M, Hervy JP, Adam F, et al. [Surveillance of the circulation of arbovirus of medical interest in the region of eastern Senegal]. Bull Soc Pathol Exot 1990. 1993; 86: 21–28.

27. Boorman JPT, Porterfield JS. A simple technique for infection of mosquitoes with viruses transmission of Zika virus. Trans R Soc Trop Med Hyg. 1956; 50: 238–242. https://doi.org/10.1016/0035-9203(56)90029-3 PMID: 13337908

28. Li MI, Wong PSJ, Ng LC, Tan CH. Oral susceptibility of Singapore Aedes (Stegomyia) aegypti (Linnaeus) to Zika virus. PLoS Negl Trop Dis. 2012; 6: e1792. https://doi.org/10.1371/journal.pntd.0001792 PMID: 22953014

29. Chouin-Carneiro T, Vega-Rua A, Vazeille M, Yebakima A, Girod R, Goindin D, et al. Differential Susceptibilities of Aedes aegypti and Aedes albopictus from the Americas to Zika Virus. PLoS Negl Trop Dis. 2016; 10: e0004543. https://doi.org/10.1371/journal.pntd.0004543 PMID: 26938868

30. Richard V, Paoaafaita T, Cao-Lormeau V-M. Vector Competence of French Polynesian Aedes aegypti and Aedes polynesiensis for Zika Virus. PLoS Negl Trop Dis. 2016; 10: e0005024. https://doi.org/10.1371/journal.pntd.0005024 PMID: 27649620

31. Aliota MT, Peinado SA, Velez ID, Osorio JE. The wMel strain of Wolbachia Reduces Transmission of Zika virus by Aedes aegypti. Sci Rep. 2016; 6: 28792. https://doi.org/10.1038/srep28792 PMID: 27364935

32. Aliota MT, Peinado SA, Osorio JE, Bartholomay LC. Culex pipiens and Aedes triseriatus Mosquito Susceptibility to Zika Virus. Emerg Infect Dis. 2016; 22: 1857–1859. https://doi.org/10.3201/eid2210.161082 PMID: 27434194

33. Fernandes RS, Campos SS, Ferreira-de-Brito A, Miranda RM de, Barbosa da Silva KA, Castro MG de, et al. Culex quinquefasciatus from Rio de Janeiro Is Not Competent to Transmit the Local Zika Virus. PLoS Negl Trop Dis. 2016; 10: e0004993. https://doi.org/10.1371/journal.pntd.0004993 PMID: 27598421

34. Guedes DR, Paiva MH, Donato MM, Barbosa PP, Krokovsky L, Rocha SWDS, et al. Zika virus replication in the mosquito Culex quinquefasciatus in Brazil. Emerg Microbes Infect. 2017; 6: e69. https://doi.org/10.1038/emi.2017.59 PMID: 28790458

35. Hall-Mendelin S, Pyke AT, Moore PR, Mackay IM, McMahon JL, Ritchie SA, et al. Assessment of Local Mosquito Species Incriminates Aedes aegypti as the Potential Vector of Zika Virus in Australia. PLoS Negl Trop Dis. 2016; 10: e0004959. https://doi.org/10.1371/journal.pntd.0004959 PMID: 27643685

36. Weger-Lucarelli J, Rücker C, Chotivan N, Nguyen C, Garcia Luna SM, Fauver JR, et al. Vector Competence of American Mosquitoes for Three Strains of Zika Virus. PLoS Negl Trop Dis. 2016; 10: e0005101. https://doi.org/10.1371/journal.pntd.0005101 PMID: 27763679

37. 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: 771–774. https://doi.org/10.1016/j.chom.2016.04.021 PMID: 27156023
41. Costa-da-Silva AL, Ioshino RS, Araújo HRC de, Kojin BB, Zanotto PM de A, Oliveira DBL, et al. Laboratory strains of Aedes aegypti are competent to Brazilian Zika virus. PloS One. 2017; 12: e0171951. https://doi.org/10.1371/journal.pone.0171951 PMID: 28187183

42. Heitmann A, Jansen S, Lüthken R, Leggewie M, Badusche M, Pluskota B, et al. Experimental transmission of Zika virus by mosquitoes from central Europe. Euro Surveill Bull Eur Sur Mal Transm Eur Commun Dis Bull. 2017; 22. https://doi.org/10.2807/1560-7917.ES.2017.22.2.30437 PMID: 28106528

43. Fernandes RS, Campos SS, Ribeiro PS, Raphael LM, Bonaldo MC, Lourenço-de-Oliveira R. Culex quinquefasciatus from areas with the highest incidence of microcephaly associated with Zika virus infections in the Northeast Region of Brazil are refractory to the virus. Mem Inst Oswaldo Cruz. 2017; 112: 577–579. https://doi.org/10.1590/0074-02760170145 PMID: 28767975

44. Roundy CM, Azar SR, Rossi SL, Huang JH, Leal G, Yun R, et al. Variation in Aedes aegypti Mosquito Competence for Zika Virus Transmission. Emerg Infect Dis. 2017; 23: 625–632. https://doi.org/10.3201/eid2304.161484 PMID: 28287375

45. Li C, Guo X, Deng Y, Xing D, Sun A, Liu Q, et al. Vector competence and transovarial transmission of two Aedes aegypti strains to Zika virus. Emerg Microbes Infect. 2017; 6: e23. https://doi.org/10.1038/emi.2017.8 PMID: 28442754

46. Liu Z, Zhou T, Lai Z, Zhang Z, Jia Z, Zhou G, et al. Competence of Aedes aegypti, Ae. albopictus, and Culex quinquefasciatus Mosquitoes as Zika Virus Vectors, China. Emerg Infect Dis. 2017; 23: 1085–1091. https://doi.org/10.3201/eid2307.161528 PMID: 28430562

47. Ciota AT, Biasiosuknia SM, Zink SD, Brecher M, Ehbar DJ, Morissette MN, et al. Effects of Zika Virus Strain and Aedes Mosquito Species on Vector Competence. Emerg Infect Dis. 2017; 23: 1110–1117. https://doi.org/10.3201/eid2307.161633 PMID: 28430564

48. Pompon J, Morales-Vargas R, Manuel M, Huat Tan C, Vial T, Hao Tan J, et al. A Zika virus from America is more efficiently transmitted than an Asian virus by Aedes aegypti mosquitoes from Asia. Sci Rep. 2017; 7. https://doi.org/10.1038/s41598-017-01282-6 PMID: 28450714

49. Kenney JL, Romo H, Duggal NK, Tzeng W-P, Burkhalter KL, Brault AC, et al. Transmission Incompetence of Culex quinquefasciatus and Culex pipiens pipiens from North America for Zika Virus. Am J Trop Med Hyg. 2017; 96: 1235–1240. https://doi.org/10.4269/ajtmh.16-0865 PMID: 28500817

50. Tan CH, Wong PJ, Li M, Yang H, Ng LC, O’Neill SL. wMel limits zika and chikungunya virus infection in a Singapore Wolbachia-introggressed Ae. aegypti strain, wMel-Sg. PLoS Negl Trop Dis. 2017; 11. https://doi.org/10.1371/journal.pntd.0005496 PMID: 28542240

51. Duchemin J-B, Mee PT, Lynch SE, Vedururu R, Trinidad L, Paradkar P. Zika vector transmission risk in temperate Australia: a vector competence study. Virol J. 2017; 14: 108. https://doi.org/10.1186/s12985-017-0772-y PMID: 28599659

52. Secundino NFC, Chaves BA, Orfano AS, Silveira KRD, Rodrigues NB, Campolina TB, et al. Zika virus transmission to mouse ear by mosquito bite: a laboratory model that replicates the natural transmission process. Parasit Vectors. 2017; 10. https://doi.org/10.1186/s13071-017-2286-2 PMID: 28728607

53. Göertz GP, Vogels CBF, Geertsema C, Koenraadt CJM, Pijlman GP. Mosquito co-infection with Zika and chikungunya virus allows simultaneous transmission without affecting vector competence of Aedes aegypti. PLoS Negl Trop Dis. 2017; 11; e0005654. https://doi.org/10.1371/journal.pntd.0005654 PMID: 28506893

54. Bearcroft WG. Zika virus infection experimentally induced in a human volunteer. Trans R Soc Trop Med Hyg. 1956; 50: 442–448. PMID: 13380987

55. Diagne CT, Diallo D, Faye O, Ba Y, Faye O, Gaye A, et al. Potential of selected Senegalese Aedes spp. mosquitoes (Diptera: Culicidae) to transmit Zika virus. BMC Infect Dis. 2015; 15: 492. https://doi.org/10.1186/s12879-015-1231-2 PMID: 26527535

56. Marchette NJ, Garcia R, Rudnick A. Isolation of Zika virus from Aedes aegypti mosquitoes in Malaysia. Am J Trop Med Hyg. 1969; 18: 411–415. PMID: 497639

57. Akoua-Koffi C, Diarrassouba S, Béné V, Ngéchi JM, Bozoa T, Bosson A, et al. [Investigation surrounding a fatal case of yellow fever in Côte d’Ivoire in 1999]. Bull Soc Pathol Exot 1990. 2001; 94: 227–230.

58. Guerbois M, Fernandez-Salas I, Azar SR, Danis-Lozano R, Alpuche-Aranda CM, Leal G, et al. Outbreak of Zika Virus Infection, Chiapas State, Mexico, 2015, and First Confirmed Transmission by Aedes aegypti Mosquitoes in the Americas. J Infect Dis. 2016; 214: 1349–1356. https://doi.org/10.1093/infdis/jiw364 PMID: 27436433

59. Ferreira-de-Brito A, Ribeiro IP, de Miranda RM, Fernandes RS, Campos SS, da Silva KAB, et al. First detection of natural infection of Aedes aegypti with Zika virus in Brazil and throughout South America. Mem Inst Oswaldo Cruz. 2016; 111: 655–658. https://doi.org/10.1590/0074-02760160332 PMID: 27706382
60. Traore-Lamizana M, Zeller H, Monlun E, Mondo M, Hervy JP, Adam F, et al. Dengue 2 outbreak in southeastern Senegal during 1990: virus isolations from mosquitoes (Diptera: Culicidae). J Med Entomol. 1994; 31: 623–627. PMID: 7932611

61. Ledermann JP, Guillaumot L, Yuy L, Saweyog SC, Tided M, Machieng P, et al. Aedes hensilli as a potential vector of Chikungunya and Zika viruses. PLoS Negl Trop Dis. 2014; 8: e3188. https://doi.org/10.1371/journal.pntd.0003188 PMID: 25299181

62. Weinbren MP, Williams MC. Zika virus: further isolations in the Zika area, and some studies on the strains isolated. Trans R Soc Trop Med Hyg. 1958; 52: 263–268. PMID: 13556872

63. Haddow AJ, Williams MC, Woodall JP, Simpson DI, Goma LK. TWELVE ISOLATIONS OF ZIKA VIRUS FROM ADEES (STEGOMYIA) AFRICANUS (THEOBALD) TAKEN IN AND ABOVE A UGANDA FOREST. Bull World Health Organ. 1964; 31: 57–69. PMID: 14230895

64. Saluzzo JF, Herve J-P, Germain M, Geoffray B, Huard M, Fabre J, et al. Seconde série d’isolement du virus de la fièvre jaune, à partir d’Aedes africanus (Theobald), dans une galerie forestière des savanes semi-humides du Sud de l’Empire Centraficain. Cah ORSTOMSérie Entomol Médicale Parasitol. 1979; 17: 19–24.

65. McCrae AW, Kirya BG. Yellow fever and Zika virus epizootics and enzootics in Uganda. Trans R Soc Trop Med Hyg. 1982; 76: 552–562. PMID: 6304948

66. Berthet N, Nakoune E, Kamgang B, Selekon B, Descorps-Décére S, Gessain A, et al. Molecular characterization of three Zika flaviviruses obtained from sylvatic mosquitoes in the Central African Republic. Vector Borne Zoonotic Dis Larchmt N. 2014; 14: 862–865. https://doi.org/10.1089/vbz.2014.1607 PMID: 25514122

67. Faye O, Faye O, Diallo D, Diallo M, Weidmann M, Sall AA. Quantitative real-time PCR detection of Zika virus and evaluation with field-caught mosquitoes. Virol J. 2013; 10: 311. https://doi.org/10.1186/1743-422X-10-311 PMID: 24148652

68. Germain M, Sureau P, Hervé J-P, Fabre J, Mouchet J, Robin Y, et al. Isolements du virus de la fièvre jaune à partir d’Aedes du groupe A. africanus (Theobald) en République Centrafricaine: importance des savanes humides et semi-humides en tant que zone d’émergence du virus amari. Cah ORSTOMSérie Entomol Médicale Parasitol. 1976; 14: 125–139.

69. Wong P-SJ, Li MI, Chong C-S, Ng L-C, Tan C-H. Aedes (Stegomyia) albopictus (Skuse): a potential vector of Zika virus in Singapore. PLoS Negl Trop Dis. 2013; 7: e2348. https://doi.org/10.1371/journal.pntd.0002348 PMID: 23936579

70. Hart CE, Roundy CM, Azar SR, Huang JH, Yun R, Reynolds E, et al. Zika Virus Vector Competency of Mosquitoes, Gulf Coast, United States. Emerg Infect Dis. 2017; 23. https://doi.org/10.3201/eid2303.161636 PMID: 28005002

71. Gendemalik A, Weger-Lucarelli J, Garcia Luna SM, Fauer JR, Rückert C, Murrieta RA, et al. American Aedes vexans Mosquitoes are Competent Vectors of Zika Virus. Am J Trop Med Hyg. 2017; 96: 1338–1340. https://doi.org/10.4269/ajtmh.16-0963 PMID: 28719283

72. O’Donnell KL, Bixby MA, Morin KJ, Bradley DS, Vaughan JA. Potential of a Northern Population of Aedes vexans (Diptera: Culicidae) to Transmit Zika Virus. J Med Entomol. 2017; https://doi.org/10.1093/jme/tjx087 PMID: 28499036

73. Amraoui F, Atyame-Ntenc C, Vega-Ruán A, Lourenc¸ o-de-Oliveira R, Vazeille M, Failloux AB. Culex mosquitoes are experimentally unable to transmit Zika virus. Vector Borne Zoonotic Dis Larchmt N. 2016; 16: 673–676. https://doi.org/10.1089/vbz.2016.2058 PMID: 27556838

74. Guo X-X, Li C-X, Deng Y-Q, Xing D, Liu Q-M, Wu Q, et al. Culex pipiens quinquefasciatus: a potential vector to transmit Zika virus. Emerg Microbes Infect. 2016; 5: e102. https://doi.org/10.1038/emi.2016.102 PMID: 27599470

75. Simpson DI. ZIKA VIRUS INFECTION IN MAN. Trans R Soc Trop Med Hyg. 1964; 58: 335–338. PMID: 14175744

76. Fagbami AH. Zika virus infections in Nigeria: virological and seroepidemiological investigations in Oyo State. J Hyg (Lond). 1979; 83: 213–219.

77. Franz AWE, Kantor AM, Passarelli AL, Clem RJ. Tissue Barriers to Arbovirus Infection in Mosquitoes. Viruses. 2015; 7: 3741–3767. https://doi.org/10.3390/v7072795 PMID: 26184281

78. Haddow AD, Schuh AJ, Yasuda CY, Kasper MR, Heang V, Huy R, et al. Genetic Characterization of Zika Virus Strains: Geographic Expansion of the Asian Lineage. PLoS Negl Trop Dis. 2012; 6: e1477. https://doi.org/10.1371/journal.pntd.0001477 PMID: 22389730
80. Olson JG, Ksiazek TG, Suhandiman null, Triwibowo null. Zika virus, a cause of fever in Central Java, Indonesia. Trans R Soc Trop Med Hyg. 1981; 75: 389–393. PMID: 6275577
81. Ioos S, Mallet H-P, Lepart Goffart I, Gauthier V, Cardoso T, Herida M. Current Zika virus epidemiology and recent epidemics. Med Mal Infect. 2014; 44: 302–307. https://doi.org/10.1016/j.medmal.2014.04.008 PMID: 25001879
82. Toghareli J, Ulooa S, Villagra E, Lagos J, Aguayo C, Fonse R, et al. A report on the outbreak of Zika virus on Easter Island, South Pacific, 2014. Arch Virol. 2016; 161: 665–668. https://doi.org/10.1007/s00705-015-2695-5 PMID: 26611910
83. Molaei G, Andreidis TG, Armstrong PM, Bueno R, Dennett JA, Real SV, et al. Host feeding pattern of Culex quinquefasciatus (Diptera: Culicidae) and its role in transmission of West Nile virus in Harris County, Texas. Am J Trop Med Hyg. 2007; 77: 73–81. PMID: 17620633
84. Baer A, Kehn-Hall K. Viral Concentration Determination Through Plaque Assays: Using Traditional and Novel Overlay Systems. J Vis Exp JoVE. 2014; https://doi.org/10.3791/52065 PMID: 25407402
85. Huang Y-JS, Lyons AC, Hsu W-W, Park SL, Higgs S, Vanlantingham DL. Differential outcomes of Zika virus infection in Aedes aegypti orally challenged with infectious blood meals and infectious protein meals. PloS One. 2017; 12: e0182386. https://doi.org/10.1371/journal.pone.0182386 PMID: 28796799
86. Gonçalves CM, Melo FF, Bezerra JMT, Chaves BA, Silva BM, Silva LD, et al. Distinct variation in vector competence among nine field populations of Aedes aegypti from a Brazilian dengue-endemic risk city. Parasit Vectors. 2014; 7: 320. https://doi.org/10.1186/1756-3305-7-320 PMID: 25015526
87. Kraemer MUG, Sinka ME, Duda KA, Mylne AQN, Shearer FM, Barker CM, et al. The global distribution of the arbovirus vectors Aedes aegypti and Ae. albopictus. eLife. 2015; 4: e08347. https://doi.org/10.7554/eLife.08347 PMID: 26126267
88. Medlock JM, Hansford KM, Schaffner F, Versteirt V, Hendrickx G, Zeller H, et al. A Review of the Invasive Mosquitoes in Europe: Ecology, Public Health Risks, and Control Options. Vector Borne Zoonotic Dis. 2012; 12: 435–447. https://doi.org/10.1089/vbz.2011.0814 PMID: 22448724
89. Reiter P, Fontenille D, Paupy C. Aedes albopictus as an epidemic vector of chikungunya virus: another emerging problem? Lancet Infect Dis. 2006; 6: 463–464. https://doi.org/10.1016/S1473-3099(06)70531-X PMID: 16870524
90. Mousson L, Dauga C, Garrigues T, Schaffner F, Vazeille M, Failloux A-B. Phylogeography of Aedes (Stegomyia) aegypti (L.) and Aedes (Stegomyia) albopictus (Skuse) (Diptera: Culicidae) based on mitochondrial DNA variations. Genet Res. 2005; 86: 1–11. https://doi.org/10.1017/S0016672305007627 PMID: 16181519
91. Gratz NG. Critical review of the vector status of Aedes albopictus. Med Vet Entomol. 2004; 18: 215–227. https://doi.org/10.1111/j.0269-283X.2004.00513.x PMID: 15347388
92. Vega-Rúa A, Zouache K, Girod R, Failloux A-B, Lourenço-de-Oliveira R. High level of vector competence of Aedes aegypti and Aedes albopictus from ten American countries as a crucial factor in the spread of chikungunya virus. J Virol. 2014; 88: 6294–6306. https://doi.org/10.1128/JVI.00370-14 PMID: 24672026
93. Kraemer MUG, Sinka ME, Duda KA, Mylne AQN, Shearer FM, Barker CM, et al. The global distribution of the arbovirus vectors Aedes aegypti and Ae. albopictus. eLife. 2015; 4: e08347. https://doi.org/10.7554/eLife.08347 PMID: 26126267
94. Medlock JM, Hansford KM, Schaffner F, Versteirt V, Hendrickx G, Zeller H, et al. A Review of the Invasive Mosquitoes in Europe: Ecology, Public Health Risks, and Control Options. Vector Borne Zoonotic Dis. 2012; 12: 435–447. https://doi.org/10.1089/vbz.2011.0814 PMID: 22448724
95. Reiter P, Fontenille D, Paupy C. Aedes albopictus as an epidemic vector of chikungunya virus: another emerging problem? Lancet Infect Dis. 2006; 6: 463–464. https://doi.org/10.1016/S1473-3099(06)70531-X PMID: 16870524
96. Mousson L, Dauga C, Garrigues T, Schaffner F, Vazeille M, Failloux A-B. Phylogeography of Aedes (Stegomyia) aegypti (L.) and Aedes (Stegomyia) albopictus (Skuse) (Diptera: Culicidae) based on mitochondrial DNA variations. Genet Res. 2005; 86: 1–11. https://doi.org/10.1017/S0016672305007627 PMID: 16181519
97. Gratz NG. Critical review of the vector status of Aedes albopictus. Med Vet Entomol. 2004; 18: 215–227. https://doi.org/10.1111/j.0269-283X.2004.00513.x PMID: 15347388
98. Vega-Rúa A, Zouache K, Caro V, Diancourt L, Delaunay P, Grandadam M, et al. High efficiency of temperate Aedes albopictus to transmit chikungunya and dengue viruses in the Southeast of France. PloS One. 2013; 8: e59716. https://doi.org/10.1371/journal.pone.0059716 PMID: 23527259
99. Gardner LM, Chen N, Sarkar S. Global risk of Zika virus depends critically on vector status of Aedes albopictus. Lancet Infect Dis. 2016; 16: 522–523. https://doi.org/10.1016/S1473-3099(16)00176-6 PMID: 26997578
100. Greenberg JA, Lujan DA, DiMenna MA, Wearing HJ, Hofkin BV. Identification of Blood Meal Sources in Aedes vexans and Culex quinquefasciatus in Bernalillo County, New Mexico. J Insect Sci. 2013; 13. https://doi.org/10.1673/031.013.7501 PMID: 24224615
101. Gubler DJ. Transmission of Ross River virus by Aedes polynesiensis and Aedes aegypti. Am J Trop Med Hyg. 1981; 30: 1303–1306. PMID: 7325287
102. Gilotra SK, Shah KV. Laboratory studies on transmission of Chikungunya virus by mosquitoes. Am J Epidemiol. 1986; 86: 379–385. PMID: 34833438
103. Rosen L, Rozeboom LE, Sweet BH, Sabin AB. The transmission of dengue by Aedes polynesiensis Marks. Am J Trop Med Hyg. 1954; 3: 878–882. PMID: 13197723
104. Braught AC, Foy BD, Myles KM, Kelly CLH, Higgs S, Weaver SC, et al. Infection patterns of o’nyong nyong virus in the malaria-transmitting mosquito, Anopheles gambiae. Insect Mol Biol. 2004; 13: 625–635. https://doi.org/10.1111/j.0962-1075.2004.00521.x PMID: 15608811
105. Beemtsen BT, James AA, Christensen BM. Genetics of Mosquito Vector Competence. Microbiol Mol Biol Rev. 2000; 64: 115–137. PMID: 10704476

PLOS Neglected Tropical Diseases | https://doi.org/10.1371/journal.pntd.0005933 November 16, 2017 20 / 22
Vorou R. Zika virus, vectors, reservoirs, amplifying hosts, and their potential to spread worldwide: 114.

Dusfour I, Thalmensy V, Gaborit P, Issaly J, Carinci R, Girod R. Multiple insecticide resistance in

Bueno MG, Martinez N, Abdalla L, Duarte Dos Santos CN, Chame M. Animals in the Zika Virus Life

Cycle: What to Expect from Megadiverse Latin American Countries. PLoS Negl Trop Dis. 2016; 10: e0004681. https://doi.org/10.1371/journal.pntd.0004681 PMID: 27128312

Strode C, Wondji CS, David J-P, Hawkes NJ, Lumjuan N, Nelson DR, et al. Genomic analysis of detoxification genes in the mosquito Aedes aegypti. Insect Mol Biol. 2007; 16: 785–798. https://doi.org/10.1111/j.1365-2583.2007.00774.x PMID: 18093007

Li, et al. A mutation in the voltage-gated sodium channel gene associated with pyrethroid resistance in Aedes aegypti (Diptera: Culicidae) populations compromises the effectiveness of dengue vector control in French Guiana. Mem Inst Oswaldo Cruz. 2011; 106: 346–352. PMID: 21655824

McMeniman CJ, Lane RV, Cass BN, Fong AWC, Sidhu M, Wang Y-F, et al. Stable introduction of a transgenic Aedes aegypti in Brazil: risk perception and assessment. Bull World Health Organ. 2016; 94: 766–771. https://doi.org/10.1016/S0140-6736(16)00014-9

Enfissi A, Codrington J, Roosblad J, Kazanjii M, Rosset D. Zika virus genome from the Americas. Lancet Lond Engl. 2016; 387: 227–228. https://doi.org/10.1016/S0140-6736(16)00003-9

Rosen L, Shroyer DA, Tesh RB, Freier JE, Lien JC. Transovarial Transmission of Dengue Viruses by Mosquitoes: Aedes albopictus and Aedes aegypti. Am J Trop Med Hyg. 1983; 32: 1108–1119. https://doi.org/10.4269/ajtmh.1983.32.1108 PMID: 6625066

Diallo M, Thonnon J, Fontenille D. Vertical transmission of the yellow fever virus by Aedes aegypti (Diptera, Culicidae): dynamics of infection in F1 adult progeny of infected females. Am J Trop Med Hyg. 2000; 62: 151–156. PMID: 10761742

Thangamani S, Huang J, Hart CE, Guzman H, Tesh RB. Vertical Transmission of Zika Virus in Aedes aegypti Mosquitoes. Am J Trop Med Hyg. 2016; 95: 1169–1173. https://doi.org/10.4269/ajtmh.16-0448 PMID: 27573623

Ciota AT, Bialosuknia SM, Ehrbar DJ, Kramer LD. Vertical Transmission of Zika Virus by Aedes aegypti and Aedes albopictus Mosquitoes. Emerg Infect Dis. 2017; 23: 880–882. https://doi.org/10.3201/eid2305.1602041 PMID: 28277199

Carlson CJ, Dougherty ER, Getz W. An Ecological Assessment of the Pandemic Threat of Zika Virus. PLoS Negl Trop Dis. 2016; 10: e0004968. https://doi.org/10.1371/journal.pntd.0004968 PMID: 27564232

Paz S, Semenza JC. El Niño and climate change—contributing factors in the dispersal of Zika virus in the Americas? Lancet Lond Engl. 2016; 387: 745. https://doi.org/10.1016/S0140-6736(16)00256-7

Caminade C, Turner J, Metelmann S, Hesson JC, Blagrove MSC, Solomon T, et al. Global risk model for vector-borne transmission of Zika Virus reveals the role of El Niño 2015. Proc Natl Acad Sci U S A. 2017; 114: 119–124. https://doi.org/10.1073/pnas.1614303114 PMID: 27994145

Adde A, Roucou P, Mangeas M, Ardillon V, Desenclos J-C, Rousset D, et al. Predicting Dengue Fever Outbreaks in French Guiana Using Climate Indicators. PLoS Negl Trop Dis. 2016; 10: e0004681. https://doi.org/10.1371/journal.pntd.0004681 PMID: 27128312

Scott TW, Clark GG, Lorenz LH, Amerasinghe PH, Reiter P, Edman JD. Detection of multiple blood feeding in Aedes aegypti (Diptera: Culicidae) during a single gonotrophic cycle using a histologic technique. J Med Entomol. 1993; 30: 94–99. PMID: 8433550

Soper FL. The Elimination of Urban Yellow Fever in the Americas Through the Eradication of Aedes aegypti. Am J Public Health Nations Health. 1963; 53: 7–16.

McMeniman CJ, Lane RV, Cass BN, Fong AWC, Sidhu M, Wang Y-F, et al. Stable introduction of a life-shortening Wolbachia infection into the mosquito Aedes aegypti. Science. 2009; 323: 141–144. https://doi.org/10.1126/science.1165326 PMID: 19119237

Paes de Andrade P, Araújo FJL, Colli W, Dellagostin OA, Finardi-Filho F, Hirata MH, et al. Use of transgenic Aedes aegypti in Brazil: risk perception and assessment. Bull World Health Organ. 2016; 94: 766–771. https://doi.org/10.2471/BLT.16.173377 PMID: 27843167

Vorou R. Zika virus, vectors, reservoirs, amplifying hosts, and their potential to spread worldwide: what we know and what we should investigate urgently. Int J Infect Dis IJID Off Publ Int Soc Infect Dis. 2016; 48: 85–90. https://doi.org/10.1016/j.ijid.2016.05.014 PMID: 27208633

Bueno MG, Martínez N, Abdalla L, Duarte Dos Santos CN, Chame M. Animals in the Zika Virus Life Cycle: What to Expect from Megadiverse Latin American Countries. PLoS Negl Trop Dis. 2016; 10: e0005073. https://doi.org/10.1371/journal.pntd.0005073 PMID: 28005902

Saavedra-Rodriguez K, Urdaneta-Marquez L, Rajatileka S, Mouton M, Flores AE, Fernandez-Salas I, et al. A mutation in the voltage-gated sodium channel gene associated with pyrethroid resistance in Latin American Aedes aegypti. Insect Mol Biol. 2007; 16: 785–798. https://doi.org/10.1111/j.1365-2583.2007.00774.x PMID: 18093007

Dusfour I, Thalmensy V, Gaborit P, Issaly J, Carinci R, Girod R. Multiple insecticide resistance in Aedes aegypti (Diptera: Culicidae) populations compromises the effectiveness of dengue vector control in French Guiana. Mem Inst Oswaldo Cruz. 2011; 106: 346–352. PMID: 21655824

Dusfour I, Zorrilla P, Guizè A, Issaly J, Girod R, Guillaumot L, et al. Deltamethrin Resistance Mechanisms in Aedes aegypti Populations from Three French Overseas Territories Worldwide. PLoS Negl Trop Dis. 2015; 9: e0004226. https://doi.org/10.1371/journal.pntd.0004226 PMID: 26588076

Strode C, Wondji CS, David J-P, Hawkes NJ, Lumjuan N, Nelson DR, et al. Genomic analysis of detoxification genes in the mosquito Aedes aegypti. Insect Biochem Mol Biol. 2008; 38: 113–123. https://doi.org/10.1016/j.ibmb.2007.09.007 PMID: 18070670

Marcombe S, Poupardin R, Darriet F, Reynaud S, Bonnet J, Strode C, et al. Exploring the molecular basis of insecticide resistance in the dengue vector Aedes aegypti: a case study in Martinique Island (French West Indies). BMC Genomics. 2009; 10: 494. https://doi.org/10.1186/1471-2164-10-494 PMID: 19857255
121. Marcombe S, Mathieu RB, Pocquet N, Riaz M-A, Poupardin R, Sélior S, et al. Insecticide resistance in the dengue vector Aedes aegypti from Martinique: distribution, mechanisms and relations with environmental factors. PloS One. 2012; 7: e30989. https://doi.org/10.1371/journal.pone.0030989 PMID: 22363529

122. Maciel-de-Freitas R, Avendano FC, Santos R, Sylvestre G, Araujo SC, Lima JBP, et al. Undesirable Consequences of Insecticide Resistance following Aedes aegypti Control Activities Due to a Dengue Outbreak. PLOS ONE. 2014; 9: e92424. https://doi.org/10.1371/journal.pone.0092424 PMID: 24676277

123. Alout H, Djègbè I, Chandre F, Djogbènou LS, Dabiré RK, Corbel V, et al. Insecticide exposure impacts vector-parasite interactions in insecticide-resistant malaria vectors. Proc Biol Sci. 2014; 281. https://doi.org/10.1098/rspb.2014.0389 PMID: 24850924

124. Alout H, Yameogo B, Djogbènou LS, Chandre F, Dabiré RK, Corbel V, et al. Interplay between Plasmodium infection and resistance to insecticides in vector mosquitoes. J Infect Dis. 2014; 210: 1464–1470. https://doi.org/10.1093/infdis/jiu276 PMID: 24829465

125. Alout H, Ndam NT, Sandeu MM, Djègbè I, Chandre F, Dabiré RK, et al. Insecticide resistance alleles affect vector competence of Anopheles gambiae s.s. for Plasmodium falciparum field isolates. PloS One. 2013; 8: e63849. https://doi.org/10.1371/journal.pone.0063849 PMID: 23704944

126. McCarroll L, Paton MG, Karunaratne SH, Jayasuriya HT, Kalpage KS, Hemingway J. Insecticides and mosquito-borne disease. Nature. 2000; 407: 961–962. https://doi.org/10.1038/35039671 PMID: 11069167

127. McCarroll L, Hemingway J. Can insecticide resistance status affect parasite transmission in mosquitoes? Insect Biochem Mol Biol. 2002; 32: 1345–1351. PMID: 12225925