# Zika virus outbreak in the Americas: the need for novel mosquito control methods

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Local transmission of Zika virus (ZIKV) in the Americas was first confirmed in February, 2014, on Easter Island. In May, 2015, 16 patients from the Brazilian states of Bahia and Rio Grande do Norte were found to be ZIKV-positive. 22 countries and territories have subsequently identified autochthonous transmission within the region (figure). Until recently, ZIKV infection was only associated with mild symptoms (headache, rash, joint pain, conjunctivitis) but a possible link between ZIKV infection during pregnancy and subsequent birth defects (most notably microcephaly) was identified in November, 2015.[1] Approaching 4000 cases of suspected ZIKV-related microcephaly have arisen in Brazil alone where initial figures suggest between 440 000 and 1·3 million people have been infected so far.[2] Concern in the region is escalating, with public health authorities in Colombia, Ecuador, El Salvador, and Jamaica all issuing an unprecedented health notice warning their residents to avoid pregnancy until 2018.

ZIKV is a flavivirus related to dengue virus (DENV) and historically has been transmitted by the same mosquito species, *Aedes aegypti* (figure). There is no available treatment or vaccine so disease control is limited to the management of mosquitoes which currently relies on either insecticides or the destruction of larval breeding sites. In Brazil, ultra-low-volume space spraying is recommended only during dengue outbreaks. However, widespread insecticide resistance (including high pyrethroid resistance rates)[3] and the impracticality of identifying and eliminating standing pools of water on a city-wide scale provide little hope for the containment of this disease. Vaccine development is anticipated to take several years; in the more immediate term, what options are left for the control of ZIKV?

Two novel approaches that have shown considerable promise in recent years are the genetic control of *A aegypti* mosquitoes and the development of mosquitoes that are resistant to arbovirus infection. The first field-trialled genetic control strategy is known as RIDL (the Release of Insects carrying Dominant Lethal genes) and involves the mass rearing of *A aegypti* that have been genetically modified to express a repressible lethal gene.[4] During their rearing in insectaries, the mosquitoes are provided with a dietary supplement not present in nature (eg, tetracycline), and this supplement represses the lethal gene activation. Only male mosquitoes are released and these compete with wild males to mate with wild females. Offspring do not survive to the adult stage because they do not receive the dietary additive in the wild. Lines of RIDL males have been shown to have minimal fitness costs (ie, they are competitive with wild males) and the recent field release in Bahia, Brazil, reportedly achieved a 95% reduction in local mosquito populations.[5]

An alternative approach is the use of endosymbiotic bacteria to prevent arboviruses replicating within the mosquito. The Eliminate Dengue project has been able to demonstrate that *Wolbachia* bacteria from *Drosophila* fruit flies can prevent DENV transmission in *A aegypti* mosquitoes without significant fitness costs.[6]

For the **Eliminate Dengue project** see http://www.eliminatedengue.com/

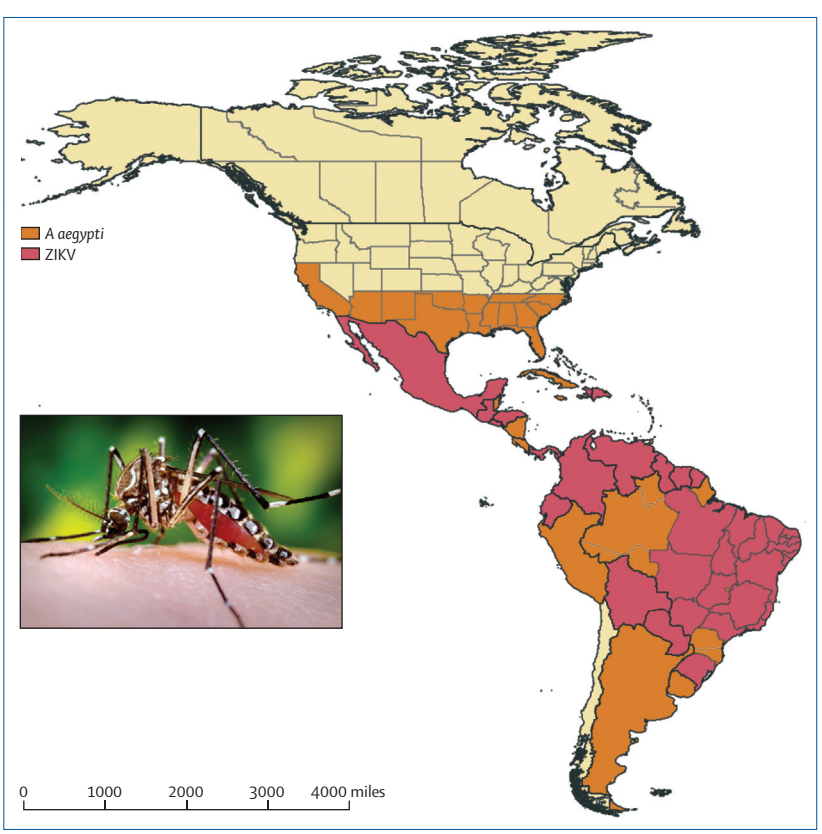


***Figure:*** **Current distribution of *Aedes aegypti* and suspected distribution of ZIKV in the Americas (Brazil and USA are shown at state level)**
Inset: *Aedes aegypti* mosquito shown blood-feeding.

*Wolbachia* has also been shown to inhibit the replication of additional arboviruses such as chikungunya virus and yellow fever virus, strongly suggesting potential inhibitory effects against ZIKV.

Whereas RIDL is a self-limiting approach (the genetic modification is not perpetuated in wild populations), *Wolbachia*-based control strategies rely on this endosymbiont successfully invading wild mosquito populations through a reproductive phenotype known as cytoplasmic incompatibility. This phenotype results in the generation of inviable offspring when an uninfected female mates with a *Wolbachia*-infected male. By contrast, *Wolbachia*-infected females can produce viable progeny when they mate with both infected and uninfected males, resulting in a reproductive advantage over uninfected females. *Wolbachia*-infected *A aegypti* mosquitoes were released and successfully invaded wild populations in Australia[7] and releases are ongoing in DENV-endemic countries such as Indonesia, Vietnam, and Brazil.

What effect either RIDL or *Wolbachia* will have on arboviral transmission and epidemiology in the field remains uncertain. Mathematical models of DENV transmission incorporating the dynamics of viral infection in humans and mosquitoes predict that one strain of *Wolbachia* (*w*Mel) would reduce the basic reproduction number, R0, of DENV transmission by 70%.[8] Models of DENV transmission control with RIDL also project high efficacy in reducing disease burden.[9] These projections suggest that such strategies could have a direct impact on transmission of arboviruses such as ZIKV in countries such as Brazil where *A aegypti* is the principle vector.

An important benefit of these environmentally friendly, species-specific approaches is the reduced dependence they pose for insecticides—an increasingly important feature of future disease vector control. Moreover, suppressing the mosquito population, or rendering it arbovirus-resistant, holds great potential in the simultaneous control of ZIKV, DENV, chikungunya, and yellow fever viruses. 150 countries presently have *A aegypti* and are vulnerable to future outbreaks with all of these viruses. The costs of implementing these novel technologies in Brazil and across the tropics must be considered in the context of the multifaceted benefits they pose in controlling several emerging infectious diseases.

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We declare no competing interests.



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