

HIGHLIGHT

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WOLBACHIA

making dengue mosquitoes harmless

The objective of our project is to replace wild dengue-transmitting mosquito populations with populations that are unable to transmit dengue, Zika or chikungunya viruses to people. This will be done using bacteria called *Wolbachia*, which are naturally found inside many insects including mosquitoes and are passed from female insects to their offsprings. However, *Wolbachia* is not naturally found in *Aedes aegypti*. *Wolbachia* are already safely being used in several countries around the world to reduce disease transmission. The replacement strategy we are using involves the release of male and female *Aedes* mosquitoes carrying *Wolbachia*, usually for a period of around 8-12 weeks (depending on the characteristics of the release area) which will then mate with wild mosquitoes. This process enables *Wolbachia* to spread by itself to high levels in the mosquito population of that area.

KEY MESSAGES

- Once *Wolbachia* has spread through a mosquito population it remains at a very high level for a long term, re-application is not required.
- It is natural, safe and a form of biocontrol that does **NOT involve genetic modification.**
- A sustainable strategy and cost effective way to reduce dengue, zika and chikungunya.

Wolbachia in nature

60-70%

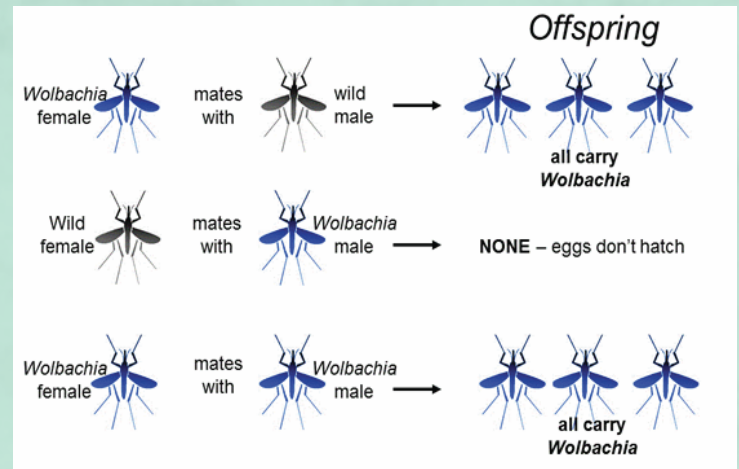
- insects are naturally infected with *Wolbachia* including flies, butterflies, grasshoppers, spiders etc.
- However, *Aedes aegypti* is not naturally infected with *Wolbachia*.

It can **ONLY** live inside host cells, not in the environment.

It cannot be transmitted between insects naturally.

Since it cannot survive outside cells, *Wolbachia* infections in a new host species are created by injecting *Wolbachia* into the eggs using a technique called microinjection.

How the microinjected *Wolbachia* affects *Aedes* mosquito?



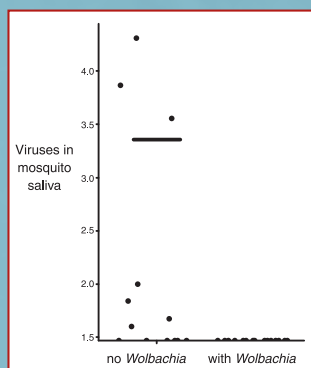
- Wolbachia* has become a master of manipulation in the reproduction of its hosts. Males with *Wolbachia* are a 'dead end' host because their sperm are unable to successfully fertilize eggs. This is known as cytoplasmic incompatibility.
- Female insects that carry *Wolbachia* have a major advantage – they can mate and produce offsprings successfully with any male in the population.
- If both males and females carry *Wolbachia* they can mate and produce offspring successfully.

Creating mosquitoes that block virus transmission

Since *Wolbachia* cannot survive outside cells, *Wolbachia* infections in a new host species are created by injecting the eggs using a technique called **microinjection**. The eggs are hatched and lines with a high density of *Wolbachia* are selected and colonised.

In our partner lab led by Professor Steven Sinkins at Glasgow University, Scotland, a number of lines of *Ae. aegypti* and *Aedes albopictus* have now been created that carry various different *Wolbachia* strains.

Compatible lines are chosen to take forward into field trials have the most favourable combination of *Wolbachia* inheritance and virus transmission-blocking capacity, at minimal cost to the fitness of the mosquito (and thus easier to spread).



Microinjection Technique

microneedle

mosquito eggs

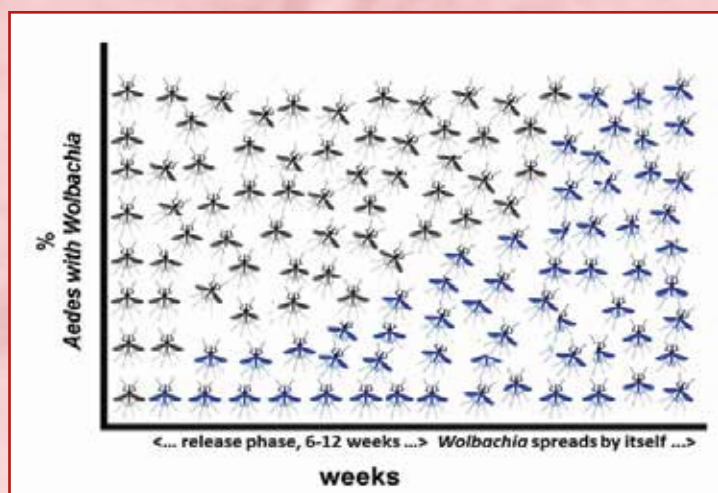


The microinjection technique involves the transfer of *Wolbachia* into individual freshly laid mosquito eggs.

Wolbachia-based population replacement strategy

The goal of population replacement is to replace the wild mosquito populations with *Wolbachia*-infected mosquitoes. The replacement strategy involves the release of **MALES AND FEMALES** infected with *Wolbachia* over a number of weeks and these *Wolbachia* infected mosquitoes then mate with the wild mosquito population.

Wolbachia is maternally transmitted and passed on from generation to generation. Over time, the percentage of mosquitoes carrying *Wolbachia* grows until it remains high without any further release.



Wolbachia-infected mosquitoes are unable to transmit viruses to people and therefore, reducing the risk of outbreaks in the released areas. Studies have shown that *Wolbachia* can sustain itself in mosquito populations without continual re-application, which makes this method sustainable and cost effective in the long term.

To date, a number of countries have conducted field releases of *Wolbachia*-carrying mosquitoes, including Australia, Brazil, China, Colombia, Indonesia, Singapore, Tahiti, Thailand and Vietnam. Our partner Professor Ary Hoffmann, University of Melbourne, is a leader in the field implementation of this approach.



The Institute for Medical Research (IMR) has been given mandate to conduct *Wolbachia* -based control strategy utilizing the **population replacement** approach to stop the escalating number of dengue cases every year. This study is a collaboration with University of Glasgow, Scotland, University of Melbourne, Australia and Institute for Health Behavioural Research (IHBR). The 5-year duration project is fully funded by the Wellcome Trust, UK.

Public Engagements & Stakeholders Meeting

"The pre-requisite of a successful implementation of *Wolbachia* Technology relies on effective public engagement."



FAQ

Q *Is Wolbachia a GMO?*

A No, *Wolbachia* has not been genetically modified, and is classed as a biological control agent. It already exists in the environment naturally (within invertebrate hosts). It is also not being used as a biopesticide because we are not using it to suppress populations.

Q *Are the Wolbachia strains that will be released occur naturally in Malaysia?*

A Yes, in the common *Drosophila* fruit flies and in other mosquito species.

Q *If Wolbachia occurs naturally in Aedes albopictus, why don't they block dengue transmission?*

A Natural *Wolbachia* strains occur at lower density and don't have a big impact on virus transmission, while the introduced *Wolbachia* will be at much higher density within the mosquito cells and will block dengue.

Q *Can Wolbachia be transmitted to humans?*

A No, *Wolbachia* or *Wolbachia* proteins are not transmitted in mosquito saliva. These *Wolbachia* can only grow in insect cells; no *Wolbachia* can survive / grow in vertebrate cells. Humans have been exposed to *Wolbachia* in countless ways for millions of years and there is no evidence that there has ever been transmission to humans.

Q *Can Wolbachia cause ecological damage in the environment?*

A No, *Wolbachia* can only survive and replicate inside host invertebrate cells, they do not escape and cause damage.

Q *Why do female mosquitoes have to be released?*

A *Wolbachia* population spread is dependent on female release due to its mode of maternal transmission, it is not transmitted by males. So only by releasing females will the *Wolbachia* be introduced into a population.

Q *Why not just release males to suppress the mosquito population?*

A This is a much less efficient strategy that requires ongoing intervention—a much larger scale of release would be needed and it would have to be conducted continuously to have any effect on dengue transmission, so would be prohibitively expensive. As soon as male releases are stopped, the mosquito population bounces back. In contrast, the replacement strategy requires just a short period of release, then *Wolbachia* spreads by itself and maintains itself stably at a high frequency from then on, blocking virus transmission.

Q *Will people notice an increase in mosquito biting?*

A This is extremely unlikely - releases are conducted during drier times of lower mosquito population density, for a short period only, and the released males would be 'sterilizing' wild females – so any increase (if detected at all) would only be minor. Wild mosquito populations can also be suppressed with insecticides prior to starting releases. *Aedes* (the mosquito being released) are not the main mosquito biting nuisance in cities, *Culex* are much more common.

Q *How long will the Wolbachia effects last?*

A Their effects are permanent. Mosquitoes will stay infected with *Wolbachia*, it is a self-maintaining control method.

Q *Can we still undertake our usual mosquito suppression measures while releases are occurring?*

A Yes completely. All normal methods of mosquito control like suppressing breeding sites continue while releases are undertaken.

Q *What happens when there is a dengue outbreak in the area where releases are being undertaken?*

A The release can be continued in conjunction with dengue control activities.

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In Collaboration with :



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