

Applying *Wolbachia* to Eliminate Dengue - A randomised controlled trial

Yogyakarta, Indonesia

June 2021



Trial results show a

77% 

reduction* in dengue incidence and

86% 

reduction** in dengue hospitalizations in *Wolbachia*-treated communities.

 population of study site
312,000

size of study site 
26 km²

Between **9** and **14** biweekly releases

 **93.0%**
Wolbachia prevalence in treated clusters

Protective efficacy was similar across all **4** dengue virus serotypes

* (95% confidence interval: 65.3%, 84.9%)
** (95% confidence interval: 66.2%, 94.3%)

Dengue and other diseases transmitted by *Aedes aegypti* mosquitoes present an increasing public health challenge in tropical regions. The World Mosquito Program's self-sustaining intervention uses natural bacteria called *Wolbachia* to reduce the ability of mosquitoes to transmit viruses between people.

The approach works by releasing *Wolbachia*-carrying mosquitoes into target wild mosquito populations. Over the subsequent months, the prevalence of *Wolbachia* in the local mosquito population increases, until virtually all mosquitoes in the area carry the bacteria.

Methodology

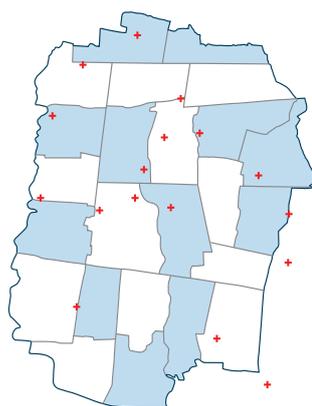
In order to measure the efficacy of the *Wolbachia* method in preventing dengue, WMP conducted a cluster randomised controlled trial (RCT) within a 26km² area of Yogyakarta City, Indonesia. RCTs are considered the gold standard trial design for demonstrating the efficacy of a public health intervention.

In collaboration with the community, the study site was subdivided into 24 clusters, each with an area of approximately 1km². Among the 24 clusters, 12 were randomly selected to receive *Wolbachia* deployments. The other 12 remained untreated.

The aim of the study was to determine whether deployment of *Wolbachia*-carrying *Aedes aegypti* mosquitoes leads to a reduced incidence of dengue in treated areas, compared with untreated areas.

Following the successful establishment of *Wolbachia* in the intervention clusters, patients presenting to health clinics across Yogyakarta City with fever were invited to enrol in the study. Consenting participants' residential location and recent travel history were recorded, and a blood sample collected and tested for dengue.

The efficacy of *Wolbachia* was calculated by comparing the distribution of 5921 test-negative patients between treated and untreated study arms, with the distribution of 385 confirmed dengue cases. Test-negative patients were located throughout the study area, whereas the dengue cases occurred predominantly in the areas not treated with *Wolbachia*.



Yogyakarta City

24 clusters
12 receive *Wolbachia*
12 untreated

-  Primary care clinics
-  RCT intervention clusters
-  RCT untreated clusters

COMMUNITY ACCEPTANCE

Extensive effort was invested in local community engagement leading up to the trial, from collaboration with community leaders and key stakeholders to engaging with local media and the general public. Community engagement activities aim to inform the community about the planned *Wolbachia* releases and to address any questions or concerns.

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We are happiest when everyone in the community is healthy. We will be happy when the World Mosquito Program's *Wolbachia* mosquitoes are spread evenly, worldwide. I am proud to be involved directly in supporting the program. It's a personal feeling of honour.

- Erlin Tri Rahayu

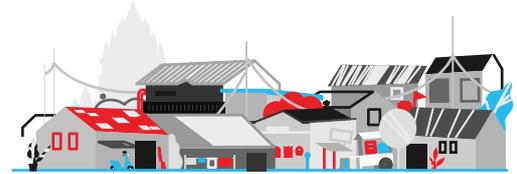


What is a cluster randomised controlled trial?

A cluster randomised controlled trial is considered a gold-standard method for evaluating the efficacy of health interventions delivered at the community level. It involves the comparison of disease outcomes amongst individuals living in areas with versus without an intervention. The result represents an unbiased estimate of the effect of the intervention on the disease of interest.

Why Yogyakarta?

Yogyakarta has regularly ranked among the top ten provinces in Indonesia for annual dengue incidence, over the past three decades. Previous pilot studies have demonstrated successful and durable *Wolbachia* establishment, as well as strong community support. These factors made it well-suited as the site for the first efficacy trial of WMP's *Wolbachia* method.



Where do the *Wolbachia*-carrying mosquitoes come from?

The *Wolbachia*-infected mosquitoes are from a mosquito colony that has been maintained in Yogyakarta since 2013. Frequent outcrossing of the colony since 2013 with local wild-type mosquitoes ensures the genetic background of the mosquitoes is always well-matched to the mosquitoes flying around in Yogyakarta.

Did you have consent from all residents of the treated areas to release *Wolbachia*-carrying mosquitoes in their community?

Approval for releases was given by community leaders after extensive community consultation, with individual residents' consent obtained for hosting a mosquito release container at their property.

Will the intervention eventually eliminate dengue from Yogyakarta?

Wolbachia remains at a high level in the trial area more than 3 years after completion of releases, and in January 2021 *Wolbachia* releases were completed throughout all remaining areas of Yogyakarta city. We expect this will lead to an even greater reduction in dengue incidence - and potentially even local elimination of dengue - in years to come, although enhanced case finding and diagnosis will be needed to track progress towards and achievement of any elimination goal.

What do these results mean for other dengue endemic settings?

In general, we expect that in other locations where *Wolbachia* is established at a high level, we will see similarly significant reductions in local arboviral disease incidence. The main caveat in replicating these results elsewhere is that differences in ecology, climate, altitude and the complexity of the urban environment are likely to affect the trajectory of *Wolbachia* establishment, and consequently the timing of the impact on disease.

RCT partners and supporters:



About us

The World Mosquito Program is an international, not-for-profit initiative that works to protect the global community from mosquito-borne diseases including dengue, Zika, chikungunya and yellow fever.

Our approach has widespread support from communities, governments, research institutes and philanthropic partners around the world. Through collaboration and innovation, we can make a difference to millions of lives.

Currently the World Mosquito Program works in 11 countries in Asia, the Pacific and the Americas. Our ambition is to protect 75 million people over the next five years.

In addition to the Oceania Office in Melbourne, Australia, the World Mosquito Program has a regional Asian Hub in Ho Chi Minh City, Vietnam. These hubs support projects in their respective regions and contribute to core global operations.

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