

STRATEGIES FOR VECTOR CONTROL – THE WOLBACHIA STORY

SEPTEMBER 15, 2021

INTRODUCTION

Due to the ongoing COVID-19 pandemic, 5th Asia Dengue Summit has been postponed to January 2022. In the meantime, the Asia Dengue Voice and Action (ADVA) Group, in collaboration with the Global Dengue and Aedes transmitted Diseases Consortium (GDAC), Fondation Merieux (FMx), International Society for Neglected Tropical Diseases (ISNTD) and Southeast Asian Ministers of Education Tropical Medicine and Public Health Network (SEAMEO) bring a series of online meetings titled “Decimate Dengue: The Pre-Summit Webinars.” **The fourth webinar in the series titled “Strategies for vector control – The Wolbachia story”** was held on September 15, 2021. **Prof. Zulkifli Ismail**, Consultant Pediatrician and Pediatric Cardiologist at KPJ Selangor Specialist Hospital, Malaysia, and **Prof. Sri Rezeki Hadinegoro** from the University of Indonesia, chaired the webinar. The webinar featured talks by **Dr. Sakunthala Janaki**, Entomologist at National Dengue Control Unit, Ministry of Health, Sri Lanka, **Dr. Norhayati Mokhtar**, Public Health Physician at Ministry of Health Malaysia and **Dr. Claudia Surjadja**, Regional Director Asia, World Mosquito Program (WMP).

PILOT IMPLEMENTATION OF WOLBACHIA PROJECT IN COLOMBO, SRI LANKA



Dr. Sakunthala Janaki

Entomologist, National Dengue Control Unit
Ministry of Health, Sri Lanka

1. National Action Plan for Prevention and Control of Dengue in Sri Lanka¹

- Developed by the National Dengue Control Unit for the duration of 2019-2023
- Project objectives include achieving dengue incidence below 100/100,000 population and reducing and maintaining case fatality rate below 0.1% by the year 2023
- Major strategies for dengue control include monitoring disease surveillance, vector surveillance, integrated vector management (IVM), evidence-based clinical care, inter-sectoral coordination and social mobilization, risk communication, outbreak preparedness and response, and research

- IVM includes environmental management, chemical methods, biological and bio-chemical methods, intersectoral collaboration, health education and law enforcement

2. Wolbachia project in Sri Lanka was first established in 2017

- Research collaboration partners include Government of Australia, Monash University, WMP, Government of Sri Lanka, Ministry of health and National Dengue Control Unit (NDCU)
- Local collaborating agencies include Colombo Municipal council and Kotte Municipal council (under the Ministry of Local Government)
- Necessary approvals and permits were obtained, most important being approval for release of eggs from the Department of Animal production and Health in 2018
- Other permits for Aedes eggs export approval and Larval foods import approval were obtained from relevant authorities
- An independent observing committee assesses the environment risk assessment of the Wolbachia project

Wolbachia project implementation

Set up of operation

Set up the project team

- ~48 staff of the fulltime and part time
- ~24 Field staff (only for BG trap collection & Aedes eggs release)




Setup facilities

- Diagnostic lab established
- To perceive the establishment of the Wolbachia inf. Aedes
- Project field office (on a rental basis)
- meeting facility/egg capsule preparation/BG traps identification
- Upgraded the Entomology laboratory capacity at the NDCU



Egg capsules release- field activities

Release areas



Population: 129,795* 89,071
Area: 7.3 km² 12.1 km²



Release quality assurance monitoring

- ➔ Visually -at the field
- ➔ Mosquito emerging - at the laboratory

Release box availability

- ➔ Cephalothorax counting for selected release boxes

Deployment repeated every weeks, until Wolbachia levels are self-sustaining



3. Capacity building activities for Wolbachia included:
- Workshop on "Introduction of Wolbachia Infected Aedes aegypti to Control Dengue Transmission "in June 2017
 - Study tour for Ministry of Health technical officials at Queensland Health (Townsville, Cairns, Brisbane) in November 2017
 - Local training programs by WMP

4. Stages in Wolbachia project implementation
- Study area selection is based on dengue incidence and vector distribution
 - First Wolbachia mosquito releases took place in Colombo area in the year 2020
 - Set up of project team included 48 fulltime and part time staff and 24 field staff (only for BG trap collection and Aedes eggs release)
 - Setup facilities established included diagnostic lab to perceive the establishment of the Wolbachia infected Aedes mosquitos, project field office for meeting facility, egg capsule preparation, and BG traps identification and upgraded entomology laboratory capacity at the NDCU.

5. Field and laboratory-based entomology activities include:

Field activities		
Ovitrap collections <ul style="list-style-type: none"> ✓ Sensitive, economical, and operationally viable surveillance method ✓ Eggs collected to <ul style="list-style-type: none"> • Rear adult mosquitos and test for insecticide resistance • For backcrossing Wolbachia mosquito lines • For out crossing to maintain Sri Lankan Wolbachia mosquito colony 	BG trap collections <ul style="list-style-type: none"> ✓ Superior trap for mosquito surveillance and monitoring ✓ To determine mosquito density pre-Wolbachia implementation ✓ To monitor Wolbachia infected population replacement during and post release 	Mosquito release <ul style="list-style-type: none"> ✓ Wolbachia infected mosquito release, to establish a self-sustaining population replacement

Laboratory activities		
Insecticide resistance test <ul style="list-style-type: none"> ✓ To determine insecticide resistance profile of Aedes aegypti populations in release area before backcrossing to create a local Wolbachia line ✓ Conducted in Sri Lanka, Australia 	Back crossing <ul style="list-style-type: none"> ✓ Mating wild-type male mosquitoes with Wolbachia-carrying females to produce Wolbachia-carrying mosquitos with the same genetic background as the local wild mosquitoes ✓ Conducted in Australia 	Mass egg production <ul style="list-style-type: none"> ✓ Conducted in Australia

6. Stages of egg capsule preparation, release, and monitoring
- Egg capsule preparation needs less space and is an economical method for Wolbachia mosquito release compared to adult mosquito release
 - Mass rearing of Sri Lankan Wolbachia Ae.aegypti line for mass eggs production is conducted in Australia
 - Wolbachia infected eggs batches are exported to the Sri Lanka for release
 - Egg capsules are prepared in project laboratory with approximately 300 Wolbachia infected Ae.aegypti eggs per capsule with necessary larval food.
 - Mosquito release containers (MRCs) are placed in selected households, and public areas
 - Field staff is trained for field release, MRCs setup, quality assurance monitoring, and data management
 - MRC deployment is repeated every week until Wolbachia levels are self-sustaining
 - Wolbachia establishment needs to be monitored during release and post-release. Repeat monitoring will be conducted every 6 months from December 2021-2026 by placing BG traps and Ovitrap.

Wolbachia operationalization in Malaysia



Dr. Norhayati Mokhtar
Public Health Physician
Ministry of Health, Malaysia

1. Reduced dengue incidence in urban Malaysia has been demonstrated after establishment of Wolbachia Strain wAlbB²
 - Aedes aegypti mosquitoes carrying wAlbB were released at 6 diverse sites in greater Kuala Lumpur, Malaysia
 - wAlbB was established and maintained at high population frequency.
 - Dengue case reduction of 40.3% was reported at intervention sites compared to control sites
2. Phases of Wolbachia mosquito operationalization for dengue control in Malaysia

PHASE 1	PHASE 2	PHASE 3
7 July 2019	November 2019	2021 – 2022
11 localities ✓ Selangor: 8 localities ✓ WPKL & Putrajaya: 3 localities	8 localities ✓ WPKL & Putrajaya: 3 localities ✓ Pulau Pinang: 3 localities ✓ Selangor: 2 localities	11 localities ✓ WPKL & Putrajaya: 1 locality ✓ Kelantan: 2 Localities ✓ Pulau Pinang: 2 localities ✓ Selangor: 2 localities ✓ Johor: 1 locality ✓ Melaka: 1 locality ✓ N. Sembilan: 1 locality ✓ Pahang: 1 locality

3. Operationalization of Wolbachia started in Malaysia
 - Wolbachia strain used is wAlbB
 - Wolbachia mosquito colony is produced at Institute for Medical Research (IMR)
 - Operating budget (staff, equipment, Wolbachia insectariums) is under Ministry of Health Malaysia (District Health Offices & State Health Offices)
 - Multidisciplinary team comprises of Epidemiologists, Entomologists, Health Inspectors, Health Education Officers, community leaders, residential building management body, local municipal.
 - Prevention and control activities at Wolbachia mosquito release sites do not allow fogging. Dengue enforcement is maintained as usual
4. Preliminary findings of epidemiological and entomological endpoints include
 - Epidemiological endpoint (Weekly confirmed dengue cases reported in the area) – reported a 93.6% reduction
 - Entomological endpoints - Wolbachia frequency (%) in the environment

- Median number of batches needed for Wolbachia mosquito releases to achieve 80% (of Wolbachia frequency) for 2 consecutive month \approx 14 batches
- Median number of weeks needed for Wolbachia mosquito to sustain at frequency of 80% \approx 34 weeks (8 months)
- Median number of booster releases needed to achieve back 80% (of Wolbachia frequency) for 2 consecutive month \approx 8 batches
- These results imply after 14 batches of release, Wolbachia frequency will be stable in the environment for 8 months, however after 8 months, 8 batches of booster release are required to maintain Wolbachia in the environment

5. Initial result of Wolbachia mosquito operationalization appears to be promising
 - 15 out of 17 localities, (89.5%) have shown dengue cases reduction by 67% - 100% after 1 year of implementation. Remaining 2 localities did not show significant increase
 - 7 out of 17 localities (41.1%) did not report any case after 1 year of Wolbachia mosquito release.
 - 16 out of 17 localities (94.1%) manage to reach Wolbachia frequency of >80% for 2 consecutive months and release has been stopped. However, Wolbachia frequency in 5 localities dropped till < 60%, hence booster release initiated.
6. Operational challenges in Wolbachia implementation in Malaysia
 - Not all hotspots are suitable for Wolbachia mosquito release. Site selection depends on
 - type of dwelling (terrace, low level flats, clustered high rise)
 - natural boundaries (highways, river, vegetation, open space, industrial sites)
 - Wolbachia strain has no efficacy against Aedes albopictus
 - Dengue outbreak could still occur
 - Search and destroy activities must be sustained, however, fogging should be avoided
 - Invasion of wild Aedes aegypti and Aedes albopictus can occur
 - Environmental cleanliness must be maintained
 - Buffer zone area receive similar intervention for sustainability
 - COVID-19 pandemic slowed down project operationalization
 - Due to competing priorities for financial support and synergistic collaboration from stakeholders
 - Sub-optimal coverage at Wolbachia mosquito release site where full lock down was implemented

Community Engagement Before Release of Wolbachia Mosquito in Petaling



Preparation Before Release of Adult Wolbachia Mosquito



Mosquito Story: From Indonesia to the World



Dr Claudia Surjadjaja
Regional Director Asia
World Mosquito Foundation

1. The World Mosquito Program (WMP) is a not-for-profit initiative that is protecting communities around the world from mosquito-borne diseases.³
 - WMP Wolbachia Innovation is safe, sustainable, and cost-effective.
 - To date WMP has released Wolbachia-carrying mosquitos in 11 countries reaching 7.7 million people.
 - In areas where Wolbachia is self-sustaining at high level, notified dengue and Chikungunya incidence has been significantly reduced.



2. Establishment of wMel strain Wolbachia in *Aedes aegypti* mosquitoes in Cairns and northern Queensland, Australia has decreased dengue incidence⁴
 - Wolbachia was established in local mosquito populations over mean release period of 11 weeks
 - Wolbachia frequency remained stable in mosquito populations for up to 8 years
 - 96% reduction in dengue incidence was reported in Wolbachia treated population
3. Reduced incidence of dengue and chikungunya reported in Wolbachia-treated areas in Niterói, Brazil⁵
 - Adult wMel-infected *Aedes aegypti* mosquitoes were deployed in Niterói, Brazil during 2017–2019
 - Total area covered was 83 km² with a population of 373,000
 - Resulted in 69% reduction in dengue incidence, 56% reduction in chikungunya incidence and 37% reduction in Zika incidence

4. WMP Indonesia is the only randomized controlled trial that demonstrated a reduction against virologically confirmed dengue case incidence⁶
 - Cluster randomized trial conducted in Yogyakarta, Indonesia.
 - 3721 participants lived in wMel intervention clusters, and 4423 participants lived in control clusters
 - 77.1% reduction in dengue case incidence was reported in intervention clusters
 - 86.2% efficacy against hospitalized dengue was demonstrated in wMel intervention clusters
5. Thirteenth meeting of the WHO Vector Control Advisory Group 2021 concluded that⁷
 - The data on wMel introgression into populations of *Aedes aegypti* reveals public health value against dengue
 - There is sufficient data for WHO to initiate the guidelines development process to recommend use of this wMel intervention for dengue control
6. Wolbachia intervention in high density urban areas in Indonesia is expected to be highly cost-effective⁸
 - Averted dengue cases would translate into annual cost savings from \$980,000 in Yogyakarta to \$27.1 million in Jakarta
 - Expected to be cost-saving over a 10-years through savings in healthcare costs, and societal costs (E.g., lost wages)
 - Protect against other diseases like chikungunya, Zika and yellow fever
7. WMP National deployment plan in Indonesia
 - WMP intends to target major population centers across Java, Bali, and Sulawesi.
 - WMP will deploy Wolbachia mosquitoes in four stages over 5 years across major population centers in Indonesia
 - The national rollout will protect a population of greater than 17 million Indonesians and is expected to avert more than 7 million dengue cases
 - The first stage of deployment will be in Bali starting from 2022
 - Mosquito mass production facility will be built to produce mosquitoes for release in Indonesia
8. Upcoming WMP plan in Asia
 - Sri Lanka - Wider Colombo release in 2022
 - Southern Vietnam - Two sites outside Ho Chi Minh City (My Tho City in Tien Giang Province and Thu Dau Mot City in Binh Duong Province) release in February 2022
 - Lao PDR: baseline entomological study conducted in 2020, partnering with Ministry of Health first releases in Vientiane in 2022



Q AND A SESSION

1. How does WMP select countries for Wolbachia project?

Dr Claudia Surjadaja

- WMP selects the country for Wolbachia based on dengue incidence, climate suitability and funding.
- WMP collaborates with Ministry of health, University, or research institute in the country

2. What has the program cost and what is the source of funding? And what is the number of populations protected?

Dr Norhayati Mokhtar

- For Malaysia the cost for Wolbachia operationalization is covered by the Ministry of Health. Capital cost for initiation (~40,000 USD excluding cost of the mosquitoes) and maintenance cost is ~23,850 USD).
- For Malaysia the time from training to full implementation is about 6 months.
- Currently there are 22 localities with an aim to have 30 localities by next year. Population coverage is ~250,000.

Dr Sakunthala Janaki

- 220,000 population covered in Sri Lanka to date.

3. Are there any challenges from community for this program?

Dr Sakunthala Janaki

- Community engagement is a major part of the Wolbachia project. Sri Lanka has a dedicated helpline number for community members to ask questions and seek information.

Dr Norhayati Mokhtar

- Success of this project greatly depends on community acceptance and participation. Community engagement is necessary throughout the project. Special hotline number for public is available to answer questions.

4. What is role of Wolbachia implementation in bigger picture of dengue control?

Dr Norhayati Mokhtar

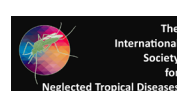
- Wolbachia method should be implemented as a preventive measure in dengue control.

Dr Claudia Surjadaja

- Wolbachia can be implemented in combination with other vector control measures and can be used as a complementary strategy in dengue control.
- Wolbachia strategy is a long-term, self-sustaining solution to reducing mosquito-borne diseases. It is compatible with other methods such as insecticides and vaccines.

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