

Wolbachia Program

Why Dengue matters: A study estimated the average total economic burden per dengue case in India to be approximately USD 27.4 million, encompassing medical expenses and indirect costs such as lost productivity. According to the National Center for Vector Borne Diseases Control (NCVBDC), the reported dengue cases and deaths over recent years are as follows:

Year	Reported Cases	Reported Deaths
2019	205,243	Data not specified
2020	164,103	Data not specified
2021	164,103	Data not specified
2022	233,251	303
2023	289,529	485

It's important to note that these figures may not capture the full extent of dengue-related mortality due to underreporting and misclassification.

Mode of Action: The Wolbachia dengue control mechanism involves introducing *Wolbachia* bacteria into *Aedes aegypti* mosquitoes, which are the primary vectors of dengue. *Wolbachia* naturally limits the replication of viruses like dengue, Zika, and chikungunya within the mosquito's body, thereby reducing their ability to transmit these diseases to humans. When infected female mosquitoes mate, they pass *Wolbachia* to their offspring, ensuring the bacteria's presence spreads through the mosquito population over time. This self-sustaining process reduces the need for repeated interventions.

Wolbachia reduces the replication of viruses within mosquitoes through several mechanisms. It competes with viruses for essential cellular resources, such as lipids, energy, and nucleotides, thereby limiting viral growth. Additionally, Wolbachia activates the mosquito's innate immune system, stimulating the production of antimicrobial peptides and antiviral pathways that create an environment hostile to viral replication. The bacterium also modifies the host cellular environment, such as reducing cholesterol availability, which is crucial for viruses to build their envelopes and survive. These mechanisms collectively inhibit the replication of viruses like dengue, Zika, and chikungunya within the mosquito, significantly lowering the likelihood of transmission to humans.

Benefits of the Program:

- Reduces dengue and other mosquito-borne disease transmission.
- Eco-friendly alternative to chemical insecticides.
- Cost-effective and self-sustaining in mosquito populations.
- Scalable to both urban and rural Indian settings.
- Safe for humans, animals, and ecosystems.
- Addresses insecticide resistance in mosquitoes.
- Encourages community participation in disease control.
- Low-maintenance solution suitable for resource-limited areas.
- Reduces healthcare costs associated with vector-borne diseases.

Potential downsides of the Wolbachia dengue control program:

1. **Limited Immediate Impact:**
The program may take time to show significant results as *Wolbachia*-infected mosquitoes need to spread and dominate the population.
2. **Geographic and Climatic Limitations:**
Effectiveness may vary in regions with specific climatic or environmental conditions, such as extreme heat or dense mosquito populations. This is especially important in Indian context.
3. **Operational Challenges:**
Large-scale mosquito release programs require substantial logistical planning, community coordination, and monitoring, which can be challenging in India's diverse settings.
4. **Potential Public Resistance:**
Misunderstandings or lack of awareness about the safety of the program could lead to public skepticism or resistance, especially in rural or less-educated communities.
5. **Initial Cost of Implementation:**
Although cost-effective in the long term, the initial setup costs, including laboratory facilities and trained personnel, may be high.
6. **Unpredictable Ecological Impact:**
Introducing *Wolbachia* may have unforeseen effects on local ecosystems, though studies have not indicated significant risks so far.
7. **Ineffectiveness Against Non-*Aedes aegypti* Vectors:**
The program targets specific mosquito species (*Aedes aegypti*) and does not address other vectors of diseases like malaria (*Anopheles* mosquitoes).
8. **Challenges in Sustained Coverage:**
Ensuring widespread and uniform coverage in India's densely populated urban areas and remote rural regions may be difficult.
9. **Need for Continuous Monitoring:**
Long-term effectiveness requires sustained monitoring to track the prevalence of *Wolbachia* and its impact on mosquito populations.
10. **Regulatory and Ethical Concerns:**
The release of genetically modified or infected organisms could face regulatory hurdles or ethical debates in some regions.

Indian Experience and present status:

As of November 2024, the Indian government has not fully implemented a nationwide policy for deploying Wolbachia-infected mosquitoes to control dengue and other mosquito-borne diseases. However, significant research and preparatory activities are underway:

1. **Research Initiatives:**
 - The Indian Council of Medical Research's Vector Control Research Centre (ICMR-VCRC) in Puducherry has been developing *Aedes aegypti* mosquito strains infected with the Wolbachia bacterium. These efforts aim to reduce the mosquitoes' ability to transmit viruses like dengue, chikungunya, and Zika.
2. **Collaborations:**
 - In 2017, the Eliminate Dengue Program (EDP) partnered with ICMR to explore sustainable solutions for mosquito-borne diseases in India. This collaboration focuses on laboratory studies to assess the impact of Wolbachia on dengue and chikungunya viruses.

3. **Regulatory Approvals:**

- The ICMR-VCRC has been seeking government approvals for pilot releases of *Wolbachia*-infected mosquitoes. As of mid-2024, these approvals were still pending, delaying large-scale implementation.

4. **ICMR report stating the impact of temperature on this method:**

- <https://parasitesandvectors.biomedcentral.com/articles/10.1186/s13071-022-05345-0>
- The report concluded with discussion “Exposure of larvae to higher rearing temperatures in the laboratory and simulated-field conditions reduced the densities of *w*Mel and *w*AlbB strains particularly in males, but the impact was more pronounced for *w*Mel strain”. This become of concern especially when seen in context of India.

Way ahead/What we can do:

The ICMR report states that “The success of *Wolbachia* release programs depends on the stability of *Wolbachia* strains in nature. Monitoring directly under natural conditions is important to assess the effects of heat stress on *Wolbachia* strains. Therefore, pilot field releases need to be undertaken to generate evidence on the stability of the *w*Mel- and *w*AlbB-infected *Ae. aegypti* (Pud) lines and their thermal tolerance/sensitivity and finally to select a suitable strain for field release in Indian conditions.”

So, ICMR through MoHFW can be asked to undertake these field release trials so as to enable effective vector control and scientific decision making.