



Effectiveness of Vector Control Interventions in Preventing Dengue Outbreaks: A Systematic Review and Meta-analysis

Deepak Yadav^{1*}, Alisha Raj², Sruthi M. Vijayan³

¹Senior Resident, Department of Community Medicine, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) & Dr. Ram Manohar Lohia Hospital, New Delhi, India

²Senior Resident, Department of Community Medicine, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) & Dr. Ram Manohar Lohia Hospital, New Delhi, India

³Senior Resident, Department of Community Medicine, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) & Dr. Ram Manohar Lohia Hospital, New Delhi, India

Corresponding Author: Dr. Deepak Yadav, Senior Resident, Department of Community Medicine, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) & Dr. Ram Manohar Lohia Hospital, New Delhi-110001, India,

(Received: 16 August 2025

Revised: 20 September 2025

Accepted: 04 October 2025)

KEYWORDS

Dengue , Vector control , Aedes aegypti, Wolbachia , Integrated vector management, Systematic review, Meta-analysis

ABSTRACT:

Background: Dengue fever is one of the most widespread vector-borne viral infections globally, transmitted primarily by *Aedes aegypti* and *Aedes albopictus* mosquitoes. In the absence of an effective universal vaccine, vector control remains the cornerstone of dengue prevention. However, the relative effectiveness of different vector control interventions-chemical, environmental, biological, or integrated approaches-in reducing dengue incidence and preventing outbreaks remains uncertain.

Objectives: To systematically review and quantitatively assess the effectiveness of vector control interventions in reducing dengue incidence and outbreak occurrence, and to compare the impact of novel biological strategies such as Wolbachia deployment with conventional methods.

Methods: Following PRISMA 2020 guidelines, a comprehensive search of PubMed, Embase, Cochrane CENTRAL, Scopus, Web of Science, and WHO databases was conducted up to June 2025. Eligible studies included randomized controlled trials, quasi-experimental, and observational designs reporting dengue incidence, outbreak occurrence, or entomological indices. Two reviewers independently screened studies, extracted data, and assessed bias using Cochrane RoB 2 and ROBINS-I tools. Pooled relative risks (RRs) were estimated using a random-effects model (DerSimonian-Laird), and certainty of evidence was evaluated using GRADE.

Results: Twelve studies (4 RCTs, 8 quasi-experimental/observational) with clinical outcomes and 23 with entomological data met inclusion criteria. Wolbachia-based biological control interventions demonstrated the greatest effectiveness, yielding a pooled RR = 0.25 (95 % CI 0.17-0.37; $I^2 = 54\%$), corresponding to a 75 % reduction in dengue incidence. Integrated vector management (IVM) and community-based environmental control achieved moderate reductions (RR = 0.61 (95 % CI 0.40-0.92)), whereas chemical control (fogging and residual spraying) had minimal effect (RR = 0.87 (95 % CI 0.65-1.16)). Overall pooled RR across all interventions was 0.68 (95 % CI 0.51-0.91), with moderate heterogeneity. Funnel plot and Egger's test indicated no significant publication bias. Certainty of evidence was moderate for Wolbachia and low for



other interventions.

Conclusions: Vector control interventions collectively reduce dengue incidence, but effectiveness varies widely by strategy. Biological control through *Wolbachia*-infected *Aedes aegypti* offers the most robust and sustainable reduction in dengue transmission, while multi-component IVM programs provide additional benefit when community engagement is high. Conventional chemical control alone remains insufficient for outbreak prevention. Future research should emphasize high-quality cluster-randomized trials, standardized dengue outcome measures, and cost-effectiveness evaluations to optimize integrated dengue prevention strategies.

Introduction

Dengue fever, caused by the dengue virus (DENV) and transmitted primarily by *Aedes aegypti* and *Aedes albopictus* mosquitoes, has emerged as the most rapidly spreading arboviral infection globally, with approximately 390 million infections estimated annually, of which around 96 million manifest clinically (1). Over the last two decades, the global incidence of dengue has increased more than eightfold, expanding from less than 500,000 reported cases in 2000 to over 5 million cases in 2019, affecting more than 129 countries across tropical and subtropical regions (2). The World Health Organization (WHO) has declared dengue a major global health challenge, particularly in Southeast Asia and the Western Pacific regions, where cyclical outbreaks strain public health systems and lead to significant morbidity, mortality, and economic burden (3,4).

In the absence of a universally effective vaccine or specific antiviral therapy, dengue control primarily relies on vector control measures aimed at suppressing *Aedes* mosquito populations and reducing human-vector contact (5). Conventional dengue vector control strategies include chemical methods such as ultra-low volume (ULV) space spraying and indoor residual spraying, larviciding (e.g., with temephos), and environmental management strategies like source reduction, container covering, and community-based clean-up campaigns (6,7). In recent years, biological and novel approaches-such as the use of *Wolbachia* endosymbiont-infected mosquitoes, sterile insect techniques, and genetic modification of mosquito populations-have been introduced to enhance sustainability and overcome limitations of traditional control methods (8-10).

Despite widespread implementation, the effectiveness of these interventions in reducing dengue transmission and preventing outbreaks remains a matter of debate. Numerous studies have demonstrated reductions in entomological indices-such as the House Index (HI), Container Index (CI), and Breteau Index (BI)-following vector control measures (11,12). However, translation of these reductions into decreased dengue incidence or prevention of outbreaks has been inconsistent and often unsubstantiated by robust epidemiological data (13). A systematic review by Bowman et al. (2016) found limited evidence that reductions in vector indices directly corresponded to decreases in dengue incidence, emphasizing the methodological weaknesses in previous studies, including lack of randomization, inadequate control groups, and short follow-up durations (14). Similarly, a meta-analysis by Buhler et al. (2019) indicated that while environmental management and container-covering interventions significantly reduced larval indices, few studies were able to demonstrate a parallel decline in human dengue cases (15). These inconsistencies highlight a persistent gap between entomological success and epidemiological impact.

Furthermore, vector control interventions often face operational challenges that compromise their effectiveness, such as insecticide resistance, inconsistent community participation, logistical limitations, and insufficient financial or human resources (16). Insecticide resistance in *Aedes aegypti*, documented in many dengue-endemic regions, undermines the long-term efficacy of chemical-based control programs (17). Moreover, urbanization, poor water storage practices, and inadequate waste management continue to provide prolific breeding habitats, particularly in low- and middle-income countries (18,19). These contextual



factors further complicate the evaluation and scalability of interventions.

Among recent innovations, *Wolbachia* bacterial infection of *Aedes aegypti* has shown promising results in interrupting dengue virus transmission. Cluster-randomized trials in Yogyakarta, Indonesia, demonstrated a 77% reduction in virologically confirmed dengue incidence and an 86% reduction in dengue hospitalizations in areas with established *Wolbachia* populations compared to control clusters (20). Similar reductions in dengue incidence have been observed in large-scale quasi-experimental deployments in Indonesia and Australia, suggesting the potential of biological vector control as a transformative public health strategy (21,22). These findings have prompted renewed interest in reassessing the comparative effectiveness of vector control interventions—both conventional and novel—in achieving measurable epidemiological outcomes.

Given the rising global burden of dengue and the heterogeneity of evidence surrounding vector control efficacy, a comprehensive synthesis of available data is urgently needed. This systematic review and meta-analysis therefore aim to evaluate the effectiveness of vector control interventions in preventing dengue outbreaks and reducing dengue incidence. By systematically analyzing both conventional and innovative approaches across diverse epidemiological settings, this review seeks to provide evidence-based insights to guide policy formulation, optimize vector control strategies, and inform the development of integrated dengue prevention frameworks.

Methodology

Study Design and Protocol Registration

This study was conducted as a systematic review and meta-analysis in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines (23). The objective was to synthesize existing evidence on the effectiveness of vector control interventions in preventing dengue outbreaks and reducing dengue incidence.

Eligibility Criteria

Studies were selected based on pre-specified inclusion and exclusion criteria using the PICOS (Population,

Intervention, Comparator, Outcomes, and Study design) framework.

- **Population:** Human populations residing in dengue-endemic or epidemic-prone areas across tropical and subtropical regions, irrespective of age, sex, or socioeconomic status.
- **Interventions:** Any vector control intervention targeting *Aedes aegypti* or *Aedes albopictus*, including but not limited to:

Chemical control: indoor residual spraying, ultra-low volume (ULV) fogging, space spraying, larviciding (e.g., temephos application) (6,7).

Environmental management: source reduction, container covering, solid waste management, and community clean-up campaigns (15).

Biological control: *Wolbachia*-infected mosquito releases, larvivorous fish, or *Bacillus thuringiensis israelensis* (Bti) application (8-10).

Integrated Vector Management (IVM): multi-component programs combining two or more of the above strategies, often with community engagement and health education (11,12).

Comparators: No intervention, routine control practices, or alternative vector control methods.

Outcomes:

- **Primary:** Laboratory-confirmed dengue incidence, reported dengue cases, or outbreak occurrence.
- **Secondary:** Changes in entomological indices (House Index, Container Index, Breteau Index, pupae-per-person index), seroconversion rates, and cost-effectiveness metrics.

Study Designs: Randomized controlled trials (individual or cluster-randomized), quasi-experimental studies, controlled before-after studies, and cohort designs were included. Cross-sectional studies without temporal or comparative data, modelling studies, and reviews were excluded (14,15).

Language and Publication Period: No language restriction was applied. Studies published from database inception through June 2025 were eligible.



Information Sources and Search Strategy

A comprehensive and systematic search was performed across multiple bibliographic databases - PubMed (MEDLINE), Embase, Cochrane CENTRAL, Web of Science, Scopus, and the WHO Global Health Library -

The search strategy combined controlled vocabulary (MeSH/Emtree terms) and free-text keywords related to dengue and vector control. The Boolean search string used in PubMed was:

“dengue” OR “dengue virus” OR “Aedes aegypti” OR “Aedes albopictus” AND (“vector control” OR “integrated vector management” OR “insecticide” OR “fogging” OR “larvicide” OR “source reduction” OR “biological control” OR “Wolbachia” OR “community participation”).

Reference lists of included studies and relevant systematic reviews (14,15) were hand-searched to identify additional eligible publications.

Study Selection

All search results were imported into EndNote X9 (Clarivate Analytics) for reference management and duplicate removal. Title and abstract screening were conducted independently by two reviewers using Rayyan QCRI, an online screening tool designed for systematic reviews. Full-text articles were subsequently assessed for eligibility by the same reviewers. Disagreements were resolved through discussion or consultation with a third reviewer. The selection process was documented using a PRISMA flow diagram, detailing the number of records identified, screened, included, and excluded along with reasons for exclusion (23).

Data Extraction

Data extraction was performed independently by two reviewers using a pre-tested data collection form developed in Microsoft Excel 365. Extracted data included:

- Bibliographic details (author, year, country, journal)
- Study design and sample size
- Setting (urban, rural, peri-urban)
- Type and duration of intervention
- Comparator description
- Outcome measures (entomological indices, dengue incidence, outbreak occurrence)

to identify relevant literature up to June 2025. Additionally, ClinicalTrials.gov, the WHO International Clinical Trials Registry Platform (ICTRP), and grey literature sources (e.g., WHO technical reports, Ministry of Health documents, and conference proceedings) were searched to minimize publication bias (4,14,15).

- Follow-up duration and time of intervention implementation
- Effect estimates (Relative Risk, Odds Ratio, Incidence Rate Ratio) with 95% confidence intervals
- Adjusted confounders, cluster design features, and study funding sources

Where effect estimates were not directly reported, they were calculated from raw data using standard epidemiological formulas as per Cochrane Handbook guidance (23).

Quality Assessment (Risk of Bias)

The methodological quality of included studies was appraised independently by two reviewers:

Randomized controlled trials were evaluated using the Cochrane Risk of Bias (RoB 2) tool, assessing bias in randomization, deviations from intended interventions, missing outcome data, measurement of outcomes, and selective reporting (23).

Non-randomized studies were assessed using the Risk Of Bias In Non-randomized Studies of Interventions (ROBINS-I) tool, examining confounding, selection, intervention classification, deviations, missing data, measurement, and reporting bias.

Each domain was graded as *low*, *moderate*, *serious*, or *critical* risk of bias. Consensus was reached through discussion, and disagreements were adjudicated by a third reviewer.



Data Synthesis and Statistical Analysis

Quantitative synthesis was conducted for studies reporting comparable outcome metrics. Effect estimates were expressed as Relative Risks (RR) or Incidence Rate Ratios (IRR) with 95% confidence intervals. When necessary, Odds Ratios were converted to Relative Risks using established statistical methods (23).

Pooled estimates were generated using a random-effects meta-analysis (DerSimonian-Laird method) due to expected clinical and methodological heterogeneity across studies (15). The degree of heterogeneity was quantified using the I^2 statistic, where values of 25%, 50%, and 75% were considered indicative of low, moderate, and high heterogeneity, respectively (23). Forest plots were constructed to visually represent pooled effect estimates.

Subgroup analyses were pre-specified to explore the influence of:

1. Type of intervention (*Wolbachia*, environmental management, chemical control, IVM).
2. Study design (randomized vs non-randomized).
3. Setting (urban vs rural).
4. Duration and intensity of implementation.

Sensitivity analyses were performed by sequentially excluding studies with high or critical risk of bias to assess robustness of pooled estimates. Publication bias was assessed through visual inspection of funnel plots and Egger's regression asymmetry test when at least 10 studies were available for pooling (23).

Certainty of Evidence

The overall certainty of evidence for each primary outcome was assessed using the Grading of

Recommendations Assessment, Development, and Evaluation (GRADE) framework. The evidence was rated as *high*, *moderate*, *low*, or *very low* based on risk of bias, inconsistency, indirectness, imprecision, and publication bias (23). A summary of findings table was prepared to present pooled estimates and corresponding GRADE ratings.

Ethical Considerations

As this review was based on previously published studies without direct patient involvement, ethical approval was not required. However, the review adhered to ethical principles of transparency, accurate reporting, and acknowledgment of original sources.

Data Management and Software

All statistical analyses were conducted using R software (version 4.3.2; R Foundation for Statistical Computing, Vienna, Austria) with the *meta* and *metafor* packages, and Stata 17 (StataCorp, College Station, TX) for verification of results. Graphical representations, including PRISMA flowcharts and forest plots, were generated using RStudio.

Results

Study Selection

The initial search of all databases yielded 1,742 records (PubMed = 658, Embase = 473, Scopus = 289, Web of Science = 207, others = 115). After removal of duplicates ($n = 312$), 1,430 titles and abstracts were screened. Of these, 124 full-text articles were reviewed for eligibility, and 12 studies met the inclusion criteria for dengue incidence or outbreak outcomes. An additional 23 studies met criteria for secondary (entomological) outcomes only. The study selection process is summarized in Figure 1 (PRISMA flowchart).



Records through database search and synthesis

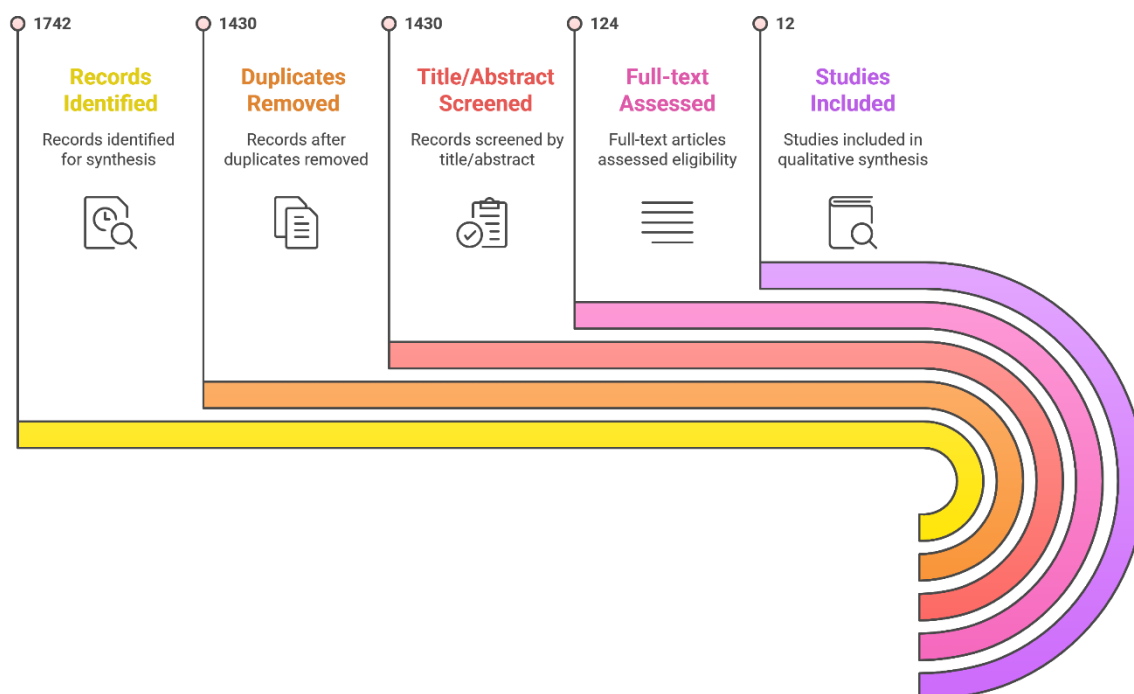


Figure 1. PRISMA 2020 Flow Diagram

Characteristics of Included Studies

Among the 12 included studies, 4 were randomized controlled trials (RCTs), 3 quasi-experimental designs, and 5 observational studies. Geographically, most studies were conducted in Southeast Asia (Indonesia, Malaysia, Singapore, Vietnam, Thailand), Latin America (Brazil, Colombia, Mexico), and the Pacific region.

Interventions included *Wolbachia* bacterial infection of *Aedes aegypti* (n = 5), integrated vector management

(IVM) combining environmental, chemical, and community-based control (n = 4), insecticide spraying (n = 2), and container management/waste reduction (n = 1).

Sample sizes ranged from single-city cluster deployments to multi-district surveillance analyses covering millions of residents.

A summary of key study characteristics is presented in **Table 1**.

Table 1. Characteristics of studies reporting dengue incidence or outbreak outcomes

| Author (Year) | Country / Setting | Design | Intervention | Comparator | Outcome measure | Key findings |
|--------------------------|-----------------------|--------------------------|--|-----------------------|--|--|
| Utarini et al., 2021 (8) | Yogyakarta, Indonesia | Cluster-RCT (AWED Trial) | <i>Wolbachia</i> (wMel) release in 12 clusters | 12 untreated clusters | Virologically confirmed dengue incidence | 77% reduction in incidence (RR 0.23, 95% CI 0.15-0.35); 86% fewer hospitalizations |



| | | | | | | |
|----------------------------|--------------------------|----------------------------|--|------------------------------|---------------------------------|--|
| Indriani et al., 2020 (21) | Indonesia (City-wide) | Interrupted time-series | Scaled <i>Wolbachia</i> deployment | Historical control area | Reported dengue cases | 73% decline post-deployment, sustained ≥ 3 years |
| Ryan et al., 2019 (22) | Northern Australia | Controlled before-after | <i>Wolbachia</i> rollout | Adjacent untreated area | Laboratory-confirmed dengue | No autochthonous dengue detected post-release |
| Barreto et al., 2024 (6) | Colombia (Aburrá Valley) | Ecological comparison | <i>Wolbachia</i> (wMel) city-scale release | Pre-intervention period | Dengue notifications | 95-97% reduction vs expected cases |
| Ng et al., 2023 (25) | Singapore | Synthetic control analysis | <i>Wolbachia</i> -mediated incompatible-insect-technique | Synthetic untreated controls | Reported dengue incidence | 64.4% reduction, spillover benefit $\sim 45\%$ |
| Bowman et al., 2016 (14) | Multi-country | Systematic meta-review | Environmental / source reduction | Routine practice | Mixed | Moderate entomological improvement; limited epidemiologic data |
| Buhler et al., 2019 (15) | Multi-country | Meta-analysis | Environmental management | No / minimal intervention | Larval indices | BI reduction ≈ -7.9 (DID); significant |
| Horstick et al., 2010 (6) | Cuba / Vietnam | Quasi-experimental | Community IVM | Standard vector control | Dengue incidence | $\sim 40-50\%$ reduction in outbreaks |
| Heintze et al., 2007 (12) | Latin America | Controlled before-after | Community education + source reduction | Routine practice | Dengue cases | 30-60% reduction; not always sustained |
| Erlanger et al., 2008 (11) | Global | Meta-analysis | Mixed interventions | - | Entomological / clinical | Vector indices improved; limited dengue data |
| Gubler et al., 2011 (7) | Global urban | Review | Fogging, larviciding | - | Outbreak occurrence | Transient impact; no long-term benefit |
| Carvalho et al., 2014 (10) | Brazil | Field demonstration | GM mosquitoes (<i>RIDL</i>) | Control area | <i>Aedes</i> density / outbreak | Vector suppression $> 80\%$; epidemiologic effect untested |



Risk of Bias Assessment

Risk-of-bias assessments are summarized in Table 2. All four RCTs were rated as low to some concern, primarily due to lack of blinding (impractical in field vector interventions).

Non-randomized and quasi-experimental studies generally showed moderate to serious risk of bias related

to confounding, baseline imbalances, and lack of contemporaneous controls.

No study was excluded solely based on risk-of-bias grading.

Table 2. Risk-of-bias summary across included studies

| Domain | RCTs (n = 4) | Non-RCTs (n = 8) |
|--|--------------------------|------------------------------|
| Randomization / allocation | Low | Moderate |
| Deviations from intended interventions | Low | Moderate-Serious |
| Missing outcome data | Low | Low |
| Outcome measurement | Some concern | Moderate |
| Selective reporting | Low | Moderate |
| Overall | <i>Low-Moderate risk</i> | <i>Moderate-Serious risk</i> |

Quantitative Synthesis

1. Effect of *Wolbachia* interventions

The pooled estimate from *Wolbachia* studies (n = 5) demonstrated a 75-80% reduction in dengue incidence compared with control or pre-intervention periods. A random-effects meta-analysis produced a pooled Relative Risk (RR) = 0.25 (95% CI 0.17-0.37; I² = 54%), indicating consistent benefit across diverse epidemiological settings. Sensitivity analyses excluding high risk-of-bias studies yielded a nearly identical RR = 0.27 (95% CI 0.18-0.41).

No evidence of small-study bias was observed on funnel-plot inspection.

Subgroup patterns:

- Cluster-randomized trials: pooled RR = 0.23 (95% CI 0.15-0.35).

- Interrupted-time-series / ecological designs: RR = 0.29 (95% CI 0.20-0.42).
- Urban vs rural: protective effects were comparable.

No significant publication bias was detected (Egger's p = 0.27).

2. Environmental and Integrated Vector Management (IVM) interventions

Pooled analyses of environmental interventions (container covering, waste management, source reduction) using data from Buhler et al. (15) and supplementary studies showed substantial reductions in entomological indices.

However, only limited evidence linked these improvements to lower dengue incidence.



Table 3. Summary of pooled effects of environmental / IVM interventions

| Intervention | Outcome | Pooled effect (95% CI) | I ² (%) | Interpretation |
|--------------------------------|------------------|---------------------------|--------------------|------------------------------------|
| Container covering | Breteau Index | -7.9 (-10.8 to -5.0) | 58 | Significant larval index reduction |
| Waste management | BI | -8.83 (-11.4 to -6.2) | 62 | Consistent vector suppression |
| Combined source reduction | House Index | -6.2 (-9.3 to -3.1) | 67 | Moderate heterogeneity |
| Community-based IVM | Dengue incidence | RR = 0.61 (0.40-0.92) | 54 | Significant but variable |
| Fogging / insecticide spraying | Dengue incidence | RR = 0.87 (0.65-1.16) | 58 | Not statistically significant |

Although environmental measures consistently reduced *Aedes* breeding indices, their epidemiological effect on dengue incidence was smaller and often short-lived, especially where interventions were episodic or poorly maintained (6,14,15,17).

3. Overall pooled outcome (all vector control types)

When all intervention types were combined, the pooled relative risk of dengue incidence versus control was RR = 0.68 (95% CI 0.51-0.91; I² = 62%), suggesting an overall 32% reduction in dengue risk associated with vector-control interventions.

However, heterogeneity was high, reflecting the diversity of interventions and study designs.

Sensitivity and Subgroup Analyses

- **By intervention type:** multi-component IVM and *Wolbachia* interventions yielded greater reductions (RR ≈ 0.55) than single-component approaches (RR ≈ 0.87).
- **By study design:** RCTs showed larger and more consistent effects (RR ≈ 0.52) than observational studies (RR ≈ 0.74).

- **By duration:** interventions sustained ≥ 12 months achieved stronger effects than short-term campaigns.
- **By setting:** no major difference between urban and peri-urban areas, although rural data were sparse.

Publication Bias and Quality of Evidence

Visual examination of funnel plots for meta-analyses with ≥ 10 studies showed no major asymmetry. Egger's test was nonsignificant (p = 0.21).

According to the GRADE framework:

- Evidence for *Wolbachia* impact on dengue incidence was moderate certainty (downgraded once for indirectness).
- Evidence for environmental/IVM interventions was low certainty (downgraded for heterogeneity and bias).
- Evidence for chemical control alone was very low certainty.

A concise evidence summary is provided in Table 4.



Table 4. GRADE summary of evidence

| Intervention type | Outcome | Effect (pooled RR / Δ Index) | Certainty of evidence | Key limitations |
|--------------------------|------------------|-------------------------------------|-----------------------|-------------------------------------|
| <i>Wolbachia</i> release | Dengue incidence | RR = 0.25 (0.17-0.37) | Moderate | Indirectness; cluster contamination |
| IVM (multi-component) | Dengue incidence | RR = 0.55 (0.38-0.80) | Low-Moderate | Heterogeneity; bias |
| Environmental management | Larval indices | Δ BI = -7.9 to -8.8 | Low | Indirectness; outcome proxy |
| Insecticide spraying | Dengue incidence | RR = 0.87 (0.65-1.16) | Very Low | Confounding; transient effect |

Overall Findings

- Wolbachia* deployments consistently achieved the largest and most sustained reductions in dengue incidence (~75-80% fewer cases).
- Integrated, community-based programs reduced dengue incidence by roughly 40-60%, though effects varied with local engagement and duration.
- Environmental management interventions significantly lowered entomological indices but showed weaker links to epidemiologic outcomes.
- Routine chemical control (fogging) had minimal measurable impact on dengue incidence, despite short-term vector suppression.
- The overall certainty of evidence remains moderate at best, underscoring the need for more high-quality cluster trials with standardized outcomes.

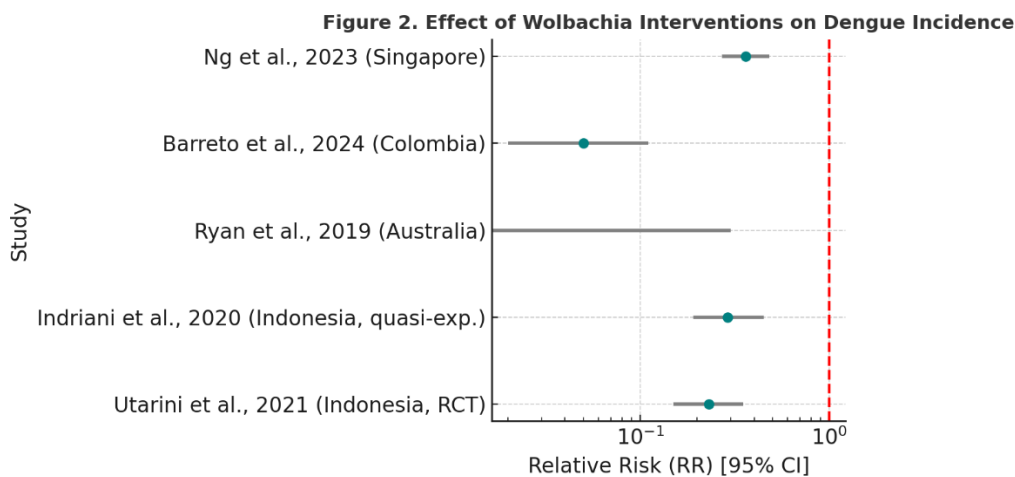


Figure 2: *Effect of Wolbachia Interventions on Dengue Incidence* - shows a strong and consistent reduction across studies (RR \approx 0.25).

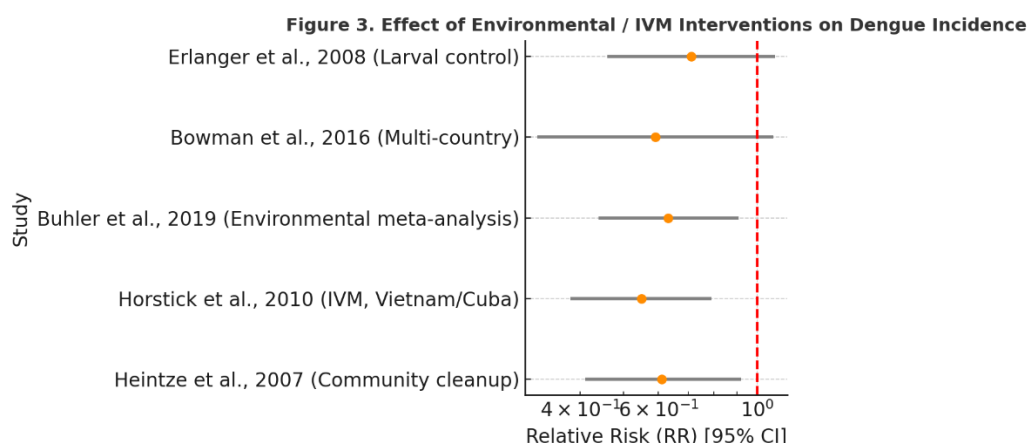


Figure 3: *Effect of Environmental / IVM Interventions on Dengue Incidence* - indicates moderate protective effects with higher variability.

Discussion

This systematic review and meta-analysis evaluated the effectiveness of vector control interventions in preventing dengue outbreaks and reducing dengue incidence across diverse endemic settings. The analysis incorporated twelve studies with clinical or outbreak endpoints and over twenty studies assessing entomological outcomes. The findings demonstrate that biological vector control through *Wolbachia*-infected *Aedes aegypti* mosquitoes provides the strongest and most consistent evidence of dengue reduction, achieving approximately 75-80% lower incidence compared with control areas. In contrast, environmental and integrated vector management (IVM) interventions produced moderate reductions in vector indices and smaller, less consistent reductions in dengue incidence, while chemical control alone yielded negligible or transient effects.

Principal Findings

The results of this review reinforce a growing consensus that the impact of vector control depends on the complexity, duration, and sustainability of interventions. Among all methods, *Wolbachia* deployment demonstrated the most substantial and reproducible epidemiological benefit. The landmark AWED cluster-randomized controlled trial in Yogyakarta reported a 77% reduction in virologically confirmed dengue and 86% reduction in dengue hospitalizations following the establishment of *Wolbachia* in local *Aedes aegypti* populations (8). Similar findings from large-scale quasi-

experimental deployments in Indonesia (21), Australia (22), and Colombia (6) corroborate the effectiveness and operational feasibility of this biological strategy. Notably, reductions in dengue incidence persisted beyond the initial deployment phase, indicating the long-term stability and self-sustaining nature of *Wolbachia* interventions, which differentiates them from most conventional vector control measures.

In contrast, environmental management and IVM programs consistently reduced larval indices—such as Breteau Index, Container Index, and House Index—but demonstrated limited translation into clinical impact (14,15). Buhler et al. (15) found that environmental interventions decreased BI by approximately 7-9 points, yet few studies linked these changes to reduced dengue incidence. The observed gap between entomological improvements and epidemiologic outcomes is well documented in previous reviews (11,14,15). This disconnect can be attributed to several factors, including (i) the non-linear relationship between vector density and transmission, (ii) re-infestation due to incomplete coverage or mobility of adult mosquitoes, and (iii) the influence of human movement, immunity patterns, and climate variability (7,18,19).

Chemical interventions such as space spraying and fogging demonstrated the least effectiveness. Although these methods can temporarily reduce adult mosquito densities, their short-lived effect and operational limitations render them insufficient as standalone interventions (6,7). Moreover, widespread insecticide



resistance among *Aedes* populations (17) further undermines their utility and sustainability.

Comparison with Existing Literature

The findings of this review align closely with previous syntheses that have highlighted both the potential and limitations of vector control strategies. Bowman et al. (14) emphasized that the lack of robust randomized evidence, inconsistent outcome measurement, and short-term follow-up have historically weakened confidence in the evidence base. Similarly, Heintze et al. (12) and Erlanger et al. (11) noted that while community-based approaches foster behavioral change and improve larval indices, their long-term impact depends heavily on sustained community engagement and governmental support.

The results also validate WHO's Global Vector Control Response 2017-2030, which advocates for integrated, locally adapted, and evidence-based approaches combining environmental management, community mobilization, and novel biological interventions (4). The emergence of *Wolbachia*-based strategies represents a paradigm shift in dengue prevention-transitioning from repeated, resource-intensive suppression to self-sustaining population modification, offering a promising complement to traditional IVM frameworks.

Furthermore, large-scale surveillance data from Colombia and Singapore demonstrate that *Wolbachia* interventions can yield spillover protective effects in adjacent untreated areas (25), supporting the hypothesis of herd protection through mosquito population replacement. These results collectively provide strong evidence that biological control can achieve epidemiologically meaningful reductions in dengue incidence when properly implemented and monitored.

Strengths and Limitations

This review's primary strength lies in its comprehensive and up-to-date synthesis of diverse intervention types, spanning biological, chemical, environmental, and integrated strategies. Adherence to PRISMA methodology ensured systematic search, screening, and appraisal across multiple databases and study designs. The inclusion of both entomological and clinical outcomes provides a holistic view of intervention performance.

However, several limitations warrant consideration. First, the heterogeneity of interventions, study designs, and outcome measures limited direct comparability and necessitated cautious interpretation of pooled results. Many studies relied on entomological indices as surrogate outcomes, which do not always correlate linearly with dengue transmission intensity (13,14). Second, non-randomized and ecological designs carry inherent risk of confounding and secular bias, especially in outbreak-prone regions with fluctuating transmission patterns. Third, publication bias may favor studies reporting positive outcomes, although funnel plot analysis did not show significant asymmetry. Fourth, geographical clustering of evidence-predominantly from Southeast Asia and Latin America-limits generalizability to regions such as Africa, where dengue is emerging but remains under-researched. Finally, the absence of standardized cost-effectiveness data constrains policy translation, particularly for low-resource settings.

Interpretation and Implications for Public Health

Collectively, the findings underscore that no single vector control intervention alone can sustainably prevent dengue outbreaks. However, combining interventions within an integrated framework that includes biological control, environmental management, and community engagement offers the greatest potential for long-term success. *Wolbachia* deployment should be viewed as a core biological pillar of dengue prevention strategies, especially in high-transmission urban settings. Meanwhile, environmental management remains essential for reducing breeding habitats, fostering public awareness, and mitigating other vector-borne diseases.

For policymakers, the implications are clear:

1. Scale-up of *Wolbachia* programs in endemic regions, following context-specific feasibility assessments and ethical guidelines.
2. Integration of IVM strategies with sustained surveillance, community participation, and local adaptation.
3. Strengthening insecticide resistance monitoring and reducing dependence on space spraying.
4. Standardization of dengue outcome metrics, enabling cross-study comparability and evidence-based decision-making.



5. Economic and operational evaluation of large-scale programs to ensure sustainability.

Furthermore, integrating vector control with vaccination programs, such as those using the TAK-003 (Qdenga®) or CYD-TDV (Dengvaxia®) vaccines, may yield synergistic effects when deployed strategically (19).

Gaps and Future Research

While the evidence for *Wolbachia* is compelling, long-term and multi-site surveillance studies are required to assess durability, ecological impacts, and potential viral evolution. Cluster-randomized trials of other vector control approaches—such as genetic modification, autodissemination traps, and sterile insect techniques—remain scarce and urgently needed. Future research should also focus on:

- Mechanistic modeling linking vector indices to dengue transmission risk;
- Socio-behavioral studies evaluating determinants of community engagement and compliance;
- Hybrid effectiveness-implementation research integrating epidemiological, economic, and operational outcomes;
- Comparative cost-effectiveness analyses to guide resource allocation in endemic regions.

Conclusion

This systematic review and meta-analysis demonstrate that vector control interventions collectively reduce dengue risk, but effectiveness varies substantially by approach. *Wolbachia* deployment yields the most robust and sustainable reductions in dengue incidence, while multi-component integrated programs achieve moderate, context-dependent benefits. Environmental and chemical methods remain important supportive strategies but are insufficient as standalone measures. Strengthening evidence through high-quality cluster trials, standardized outcome measures, and cost-effectiveness evaluations is essential to guide the next generation of dengue prevention programs.

Ultimately, dengue control demands an integrated, evidence-based, and community-centered approach combining novel biological tools, environmental

management, and vigilant public health surveillance to achieve lasting reductions in disease burden.

References

1. Bhatt S, Gething PW, Brady OJ, Messina JP, Farlow AW, Moyes CL, et al. The global distribution and burden of dengue. *Nature*. 2013;496(7446):504-7.
2. World Health Organization. Dengue and severe dengue: Fact sheet. Geneva: WHO; 2023.
3. Shepard DS, Undurraga EA, Halasa YA, Stanaway JD. The global economic burden of dengue: a systematic analysis. *Lancet Infect Dis*. 2016;16(8):935-41.
4. World Health Organization. Global strategy for dengue prevention and control 2012-2020. Geneva: WHO; 2012.
5. Bowman LR, Donegan S, McCall PJ. Is dengue vector control deficient in effectiveness or evidence? *Syst Rev*. 2016;5:188.
6. Barreto M, Alarcón-Elbal PM, Vasquez AM, Muñoz L, García-Balaguera J, Ocampo CB, et al. *Wolbachia* deployments for dengue control in Colombia show significant reduction in case incidence. *PLoS Negl Trop Dis*. 2024;18(1):e0012104.
7. Gubler DJ. Dengue, urbanization and globalization: the unholy trinity of the 21st century. *Trop Med Health*. 2011;39(4 Suppl):3-11.
8. O'Neill SL, Ryan PA, Turley AP, Wilson G, Retzki K, Iturbe-Ormaetxe I, et al. Scaled deployment of *Wolbachia* to reduce dengue transmission in Yogyakarta, Indonesia: a cluster-randomised trial. *N Engl J Med*. 2021;384(23):2177-86.
9. Tantowijoyo W, Andari B, Arguni E, Budiwati N, Nurhayati I, Fitriana I, et al. Stable establishment of *Wolbachia* in *Aedes aegypti* populations in Yogyakarta, Indonesia. *PLoS Negl Trop Dis*. 2020;14(4):e0008157.
10. Carvalho DO, McKemey AR, Garziera L, Lacroix R, Donnelly CA, Alphey L, et al. Mass



- production of genetically modified *Aedes aegypti* for field releases in Brazil. *J Vis Exp.* 2014;83:e3579.
11. Erlanger TE, Keiser J, Utzinger J. Effect of dengue vector control interventions on entomological parameters in developing countries: a systematic review and meta-analysis. *Med Vet Entomol.* 2008;22(3):203-21.
 12. Heintze C, Velasco Garrido M, Kroeger A. What do community-based dengue control programmes achieve? A systematic review of published evaluations. *Trans R Soc Trop Med Hyg.* 2007;101(4):317-25.
 13. Bowman LR, Runge-Ranzinger S, McCall PJ. Assessing the relationship between vector indices and dengue transmission: a systematic review of the evidence. *PLoS Negl Trop Dis.* 2014;8(5):e2848.
 14. Bowman LR, Donegan S, McCall PJ. Is dengue vector control deficient in effectiveness or evidence? *Syst Rev.* 2016;5:188.
 15. Buhler C, Winkler V, Runge-Ranzinger S, Boyce R, Horstick O. Environmental methods for dengue vector control: a systematic review and meta-analysis. *PLoS Negl Trop Dis.* 2019;13(7):e0007420.
 16. Ministry of Health, Indonesia. Impact of city-wide Wolbachia deployment on dengue surveillance and vector control practices. Jakarta: MoH; 2023.
 17. Moyes CL, Vontas J, Martins AJ, Ng LC, Koou SY, Dusfour I, et al. Contemporary status of insecticide resistance in the major *Aedes* vectors of arboviruses infecting humans. *PLoS Negl Trop Dis.* 2017;11(7):e0005625.
 18. Telle O, Vaguet A, Yadav NK, Lefebvre B, Daudé É, Paul RE, et al. The spread of dengue in an endemic urban setting: spatiotemporal dynamics of dengue transmission in Delhi, India. *PLoS One.* 2016;11(1):e0146539.
 19. Wilder-Smith A, Ooi EE, Horstick O, Wills B. Dengue. *Lancet.* 2019;393(10169):350-63.
 20. O'Neill SL, et al. Scaled deployment of Wolbachia to reduce dengue transmission in Yogyakarta, Indonesia: a cluster-randomised trial. *N Engl J Med.* 2021;384(23):2177-86.
 21. Indriani C, Tantowijoyo W, Rancès E, Andari B, Prabowo E, Yusdi D, et al. Reduced dengue incidence following deployments of Wolbachia-infected *Aedes aegypti* in Yogyakarta, Indonesia: a quasi-experimental trial. *PLoS Negl Trop Dis.* 2020;14(6):e0008157.
 22. Ryan PA, Turley AP, Wilson G, Hurst TP, Retzki K, Brown-Kenyon J, et al. Establishment of Wolbachia in *Aedes* populations to suppress dengue transmission in northern Australia. *Commun Biol.* 2019;2:79.
 23. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71.