Research Article

Insecticide Resistance and Arboviral Disease Transmission: Emerging Challenges and Strategies in Vector Control

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Abstract | Insecticide resistance in arboviral vectors, particularly *Aedes aegypti* and *Aedes albopictus*, poses a significant challenge to controlling diseases such as dengue, chikungunya, and Zika. This review examines the mechanisms, drivers, and implications of insecticide resistance, emphasizing its impact on vector control programs and disease transmission. A comprehensive analysis of existing literature was conducted to explore the genetic and biochemical mechanisms underlying resistance, including kdr mutations and detoxification enzyme overexpression. Additionally, the role of operational practices, urbanization, and climate change in shaping resistance dynamics was evaluated. The findings reveal that resistance to commonly used insecticides, particularly pyrethroids, has reduced the efficacy of interventions like long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS). Emerging strategies, such as the use of synergists, novel insecticides, and genetic modifications, offer potential solutions but require further evaluation to ensure sustainability. Knowledge gaps were identified in the areas of long-term resistance management, the effects of sub-lethal insecticide exposure, and environmental influences. Despite progress in understanding insecticide resistance, significant knowledge gaps remain. These include the long-term effectiveness and sustainability of resistance management strategies, the behavioral and physiological effects of sub-lethal insecticide exposure, and the role of environmental factors—particularly urbanization and climate change—in shaping resistance dynamics. Additionally, there is limited field validation of novel interventions under real-world conditions, which constrains their large-scale applicability. This review underscores the urgent need for robust surveillance systems, sustained investment in innovative tools, and integrated vector management (IVM) approaches that combine chemical, biological, and genetic methods. Coordinated global efforts are essential to address these gaps and reduce the burden of arboviral diseases.

Keywords | *Aedes aegypti*, Insecticide resistance, Arboviral diseases, Vector control, Integrated vector management, Pyrethroids

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INTRODUCTION

The control of vector-borne diseases remains one of the most significant global public health challenges. Among these, arboviral diseases such as dengue, chikungunya, Zika, and yellow fever are of particular concern due to their widespread transmission and substantial socioeconomic burden. These diseases are primarily transmitted by Aedes mosquitoes, which have demonstrated remarkable adaptability to urban environments and significant resilience to various control measures. Despite ongoing efforts, the global incidence of arboviral diseases has escalated over the past decades, with outbreaks occurring in regions previously considered non-endemic. This trend underscores the pressing need for innovative and effective strategies in vector management (Khater *et al*., 2019; Solomon *et al*., 2012).

One of the most critical barriers to successful vector control is the rapid and widespread development of insecticide resistance. Insecticides, particularly those targeting adult mosquitoes, have been a cornerstone of vector control programs for decades. However, the over-reliance on chemical control, combined with suboptimal application practices, has driven the emergence of resistance in key vector species. Resistance mechanisms, such as target site insensitivity, metabolic detoxification, and behavioral avoidance, have been documented in Aedes aegypti and Aedes albopictus populations across various geographical regions. These mechanisms not only undermine the efficacy of existing control measures but also exacerbate the risk of disease outbreaks by maintaining high vector densities (Wangai *et al*., 2020; White *et al*., 2015; Karunamoorthi *et al*., 2010).

The intersection of insecticide resistance and arboviral disease transmission presents a complex and multifaceted challenge. Resistance compromises the effectiveness of traditional control interventions, such as indoor residual spraying and ultra-low volume space spraying, which are pivotal in reducing vector populations during outbreaks. Furthermore, resistant vector populations may exhibit altered behavioral patterns, such as changes in feeding and resting habits, which complicate control efforts. These dynamics highlight the intricate interplay between evolutionary pressures imposed by insecticides and the ecological and epidemiological factors influencing arbovirus transmission.

Emerging evidence suggests that insecticide resistance may not only affect vector control but also have direct implications for arboviral transmission dynamics. For instance, resistant vectors may experience altered fitness, including changes in lifespan, feeding frequency, and susceptibility to arboviral infections. While some studies have reported reduced vector competence in resistant populations, others suggest potential fitness costs associated with resistance mechanisms. Understanding these interactions is critical for developing integrated and sustainable control strategies that balance efficacy with ecological and evolutionary considerations (Khater *et al*., 2019; Toloza *et al*., 2014; Moore *et al*., 2014).

Environmental factors, particularly climate change and urbanization, play a pivotal role in shaping resistance patterns in vector-borne diseases. Climate change can alter temperature, humidity, and precipitation patterns, which influence the breeding and survival of vectors, such as mosquitoes. These environmental shifts can lead to the expansion of vector habitats into new areas, potentially exposing populations to novel pathogens and resistance mechanisms. For example, warmer temperatures can accelerate the life cycle of mosquitoes, allowing for quicker transmission and the potential for greater development of resistance to insecticides. Urbanization, on the other hand, creates an environment where human activities concentrate, leading to the proliferation of vector habitats in close proximity to large populations. This urban expansion often results in increased exposure to chemical treatments, such as insecticides, which can drive the evolution of resistance in vectors. Additionally, urban environments typically foster poor waste management and water storage practices, providing ample breeding sites for mosquitoes, further enhancing the potential for resistance development. Both factors, climate change and urbanization, contribute to a dynamic feedback loop where changing environments create selective pressures on vectors, fostering resistance and complicating disease control efforts. The adaptability of vectors to these environmental changes underscores the need for an integrated approach to manage resistance, incorporating environmental monitoring and adaptive strategies to mitigate the impacts of climate change and urbanization on disease transmission (Abbasi, 2025e; Abbasi, 2025f; Abbasi *et al*., 2022).

To address these challenges, there is an urgent need to re-evaluate and adapt current vector control paradigms. Integrated vector management (IVM) approaches, which combine chemical, biological, and environmental strategies, offer a promising framework for mitigating the impact of insecticide resistance. Additionally, novel interventions, such as genetically modified mosquitoes, Wolbachia-based biocontrol, and innovative insecticides with new modes of action, are gaining traction as complementary tools. However, the successful implementation of these strategies requires robust surveillance systems, interdisciplinary collaboration, and community engagement to ensure their effectiveness and sustainability (White *et al*., 2015; Nkya *et al*., 2013; Bellini *et al*., 2013).

Climate change significantly influences both resistance levels and the geographical distribution of *Aedes* mosquitoes. Rising global temperatures, altered rainfall patterns, and increased frequency of extreme weather events are reshaping the habitats and behaviors of *Aedes* species, which are primary vectors of diseases like dengue, Zika, and chikungunya. As climate change accelerates, temperature fluctuations can lead to faster development of *Aedes* mosquitoes, shortening their life cycles and increasing their exposure to environmental stressors, such as insecticide use. This increased exposure, coupled with changes in vector behavior, can drive the evolution of resistance to insecticides more rapidly. For instance, *Aedes* mosquitoes may develop resistance mechanisms, such as metabolic detoxification and target-site insensitivity, as a result of prolonged exposure to chemical control measures. Additionally, warmer temperatures can heighten the mosquitoes' metabolic rates, causing a quicker spread of resistance traits through populations (Resistance Levels). Climate change is altering the geographical range of *Aedes* mosquitoes. Warmer temperatures expand their breeding season and increase their survival rates, allowing them to thrive in regions that were previously too cold for their populations to persist. As a result, *Aedes* mosquitoes are encroaching on new territories, including higher altitudes and temperate zones, where diseases such as dengue fever, which were once limited to tropical areas, are now emerging. Furthermore, changes in rainfall patterns and the frequency of extreme weather events like floods contribute to the creation of new breeding sites, exacerbating the spread of mosquitoes into previously unaffected areas (Geographical Distribution). In summary, climate change facilitates the spread and resistance evolution of *Aedes* mosquitoes, influencing both their geographical range and their ability to adapt to chemical control measures. This presents a significant challenge for public health and vector control programs, necessitating a rethinking of strategies to manage *Aedes*-borne diseases in a changing climate (Abbasi, 2025h;Abbasi, 2025c; Abbasi, 2025d; Abbasi *et al*., 2025c).

In this review, we aim to provide a comprehensive overview of the interplay between insecticide resistance and arboviral disease transmission. We will explore the molecular and behavioral mechanisms of resistance, examine their implications for vector control and disease epidemiology, and discuss potential strategies for overcoming these challenges. By synthesizing current knowledge and identifying critical gaps, this review seeks to inform future research and policy directions in the field of vector-borne disease control (Wilson *et al*., 2020; Carvalho *et al*., 2015; Hoffmann *et al*., 2011).

MATERIALS AND METHODS

This section outlines the approach undertaken to develop this narrative review on insecticide resistance and its implications for arboviral disease transmission. The methodology follows a rigorous and structured framework to ensure comprehensiveness, relevance, and adherence to the scope of *Trends in Parasitology*.

Study Design

This review adopts a narrative approach to synthesize current knowledge on the interplay between insecticide resistance and arboviral disease transmission. Unlike systematic reviews, which rely on predefined inclusion criteria and quantitative synthesis, a narrative review provides a broader exploration of the subject, integrating multiple perspectives, theories, and emerging evidence. The aim is to provide an accessible yet in-depth analysis of the challenges and potential strategies for vector control in the context of resistance and arbovirus transmission (Greenhalgh *et al*., 2018; Ferrari, 2015; Baumeister and Leary, 1997).

Literature Search Strategy

A comprehensive literature search was conducted using electronic databases, including, PubMed, Scopus, Web of Science, Google Scholar. Search terms were carefully selected to capture relevant studies and included combinations of keywords such as, *"insecticide resistance"*, *"arboviral diseases"*, *"vector control"*, *"Aedes aegypti"*, *"Aedes albopictus"*, *"insecticide resistance mechanisms"*, *"arbovirus transmission"*. Boolean operators (AND, OR) were used to refine search results, ensuring that relevant articles addressing resistance mechanisms, control strategies, and arboviral epidemiology were included. Articles published from (2000 to (2024 were prioritized to focus on recent developments, although seminal works from earlier years were also considered when foundational insights were needed (Bramer *et al*., 2017; Hinde and Spackman, 2015; Falagas *et al*., 2008).

Inclusion and Exclusion Criteria

Studies were selected based on the following inclusion criteria, Peer-reviewed articles published in English, Research focusing on Aedes aegypti, Aedes albopictus, and other key arboviral vectors, Studies addressing the molecular, behavioral, or ecological aspects of insecticide resistance, Articles exploring the impact of resistance on arboviral transmission dynamics or control interventions. Exclusion criteria included, Studies with limited methodological details, Research focusing solely on agricultural pests, Duplicate publications or non-peer-reviewed materials such as opinion pieces and editorials (Page *et al*., 2021; Muka *et al*., 2020; Moher *et al*., 2009).

Data Extraction and Categorization

To assess the effectiveness of novel control strategies—including genetic approaches (e.g., gene drive, sterile insect technique), biocontrol agents (e.g., *Wolbachia*, *Bacillus thuringiensis israelensis*), and next-generation insecticides—a targeted search was performed within the broader literature review. Databases used included PubMed, Scopus, Web of Science, and Google Scholar, using keywords such as *"novel vector control"*, *"genetic modification of mosquitoes"*, *"biological mosquito control"*, *"Wolbachia and dengue"*, *"next-generation insecticides"*, and *"efficacy of gene drive in vector control"* (Abbasi, 2022; Abbasi, 2025a).

Inclusion criteria prioritized peer-reviewed experimental studies, field trials, and modeling assessments published between (2000 and (2024). Articles were evaluated based on study design (laboratory vs. field-based), sample size, vector species targeted, outcome metrics (e.g., vector density reduction, infection prevalence), and reproducibility of findings. Studies with demonstrated translational potential or pilot implementations at the community level were given particular emphasis. This approach enabled the synthesis of high-quality evidence on the feasibility, effectiveness, and limitations of emerging tools for resistance management and arboviral disease control (Abbasi, 2024; Abbasi *et al*., 2023b).

Quality Assessment of Included Studies

To ensure the reliability of included studies, a quality assessment framework was applied based on, Clarity and transparency of methods, Robustness of experimental design, Statistical rigor and validity of findings, Relevance to the central themes of this review. Studies were graded on a scale of low, moderate, or high quality, and only those rated moderate to high were included in the final synthesis (Sterne *et al*., 2016; Higgins, 2011; Sanderson *et al*., 2007).

Framework for Synthesis and Analysis

The analysis was guided by a conceptual framework that integrates, the evolutionary biology of resistance in arboviral vectors, The public health implications of resistance-driven control failures, The potential of emerging technologies and strategies to address resistance. This framework facilitated a coherent narrative, linking the molecular and ecological dimensions of resistance with practical considerations for vector control and disease management (Levac *et al*., 2010; Grant and Booth, 2009; Arksey and O'Malley, 2005). The collected literature was analyzed through a thematic synthesis approach to identify recurring patterns, mechanisms, and implications relevant to insecticide resistance in arboviral vectors. The extracted data were organized under major themes—such as resistance mechanisms, epidemiological impacts, and vector control strategies—allowing for an integrative comparison across different geographical settings, vector species, and intervention types. Emphasis was placed on identifying knowledge gaps, common trends, and outliers within each theme (Abbasi, 2025g; Abbasi *et al*., 2025a; Abbasi *et al*., 2023a; Ghahvechi Khaligh *et al*., 2021). To strengthen the narrative synthesis, selected quantitative data points from high-quality studies were highlighted where relevant. These include reported prevalence rates of insecticide resistance in vector populations, frequencies of knockdown resistance (kdr) mutations, and projections from epidemiological models. These data serve to contextualize the qualitative findings and support the discussion of geographic trends and public health consequences (Abbasi and Daliri, 2024a; Abbasi and Daliri, 2024c).

Validation and Expert Consultation

To enhance the accuracy and relevance of this review, preliminary findings were shared with experts in medical entomology, epidemiology, and vector control. Feedback from these consultations was incorporated into the final draft to ensure alignment with current scientific understanding and public health priorities (Ioannidis, 2016; Shamseer *et al*., 2015; Edwards *et al*., 2002).

Ethical Considerations

As this study is a review of existing literature, no human or animal subjects were directly involved. However, ethical considerations were observed by ensuring proper attribution of all sources and avoiding duplication of previously published work. This detailed and structured methodology ensures that the review not only aligns with the scope of *Trends in Parasitology* but also provides a robust foundation for evidence-based discussions and recommendations (Table 1 and Figure 1) (Smith *et al*., 2014; Wager and Wiffen, 2011; Resnik and Shamoo, 2011).

RESULTS

The results of this narrative review synthesize evidence from diverse studies, providing a comprehensive understanding of insecticide resistance in arboviral vectors, its underlying mechanisms, and its implications for public health. This section is structured into thematic subheadings to present a detailed exploration of key findings and emerging trends. The global prevalence of insecticide resistance in Aedes aegypti and Aedes albopictus, the primary vectors of dengue, chikungunya, Zika, and yellow fever viruses, has reached alarming levels. Studies report widespread resistance to pyrethroids, organophosphates, carbamates, and, to a lesser extent, organochlorines. For instance, resistance to deltamethrin and permethrin, two commonly used pyrethroids, has been documented in regions including Southeast Asia, South America, and sub-Saharan Africa. The spatial variability of resistance is attributed to factors such as local insecticide usage patterns, genetic diversity among vector populations, and environmental conditions. High levels of resistance in urban areas correlate with intensive insecticide application in public health programs and domestic use. Conversely, rural regions often exhibit lower resistance levels, highlighting the influence of anthropogenic pressures on resistance evolution (Dusfour *et al*., 2019; Moyes *et al*., 2017; Hemingway *et al*., 2004).

Three primary mechanisms of resistance—metabolic detoxification, target-site mutations, and behavioral resistance—have been identified in arboviral vectors, Elevated activity of detoxifying enzymes, including cytochrome P450 monooxygenases, glutathione-S-transferases, and esterases, is the most common mechanism. These enzymes degrade or sequester insecticides, reducing their efficacy (Metabolic Detoxification), Point mutations in genes encoding insecticide targets, such as the voltage-gated sodium channel (kdr mutations) and acetylcholinesterase, are widespread.

Table 1: Summary of key findings on insecticide resistance in arboviral vectors.

Category	Resistance Mechanisms	Impact on Disease Transmission	Operational Drivers	Environmental Influences	Surveillance and Monitoring	Emerging Resistance Strategies	Novel Tools for Control	Resistance Management Strategies	Research Gaps	Policy Recommendations
Key Findings	Mutations in voltage-gated sodium channels (kdr mutations) leading to resistance to pyrethroids. Overexpression of detoxification enzymes such as cytochrome P450s and esterases.	Resistance reduces the effectiveness of vector control tools like LLINs and IRS. Increased disease incidence due to ineffective vector control measures.	Overuse and misuse of insecticides contribute to rapid resistance development. Inadequate rotation of insecticides accelerates resistance.	Urbanization and climate change contribute to the expansion of mosquito habitats, which increases the potential for resistance.	Lack of consistent surveillance hampers resistance management, emphasizing the need for better monitoring systems.	Use of synergists like piperonyl butoxide to restore insecticide susceptibility. Genetic modification strategies, such as gene drives and sterile insect techniques, offer potential solutions.	New insecticides with unique modes of action are emerging as alternatives. Biologically-based control methods are being explored, such as genetic modification and biological control agents.	Integrated Vector Management (IVM) reduces reliance on chemical insecticides. Rotating insecticide classes and combining chemical, biological, and environmental control methods are recommended.	Need for studies on the long-term effectiveness of resistance management strategies. Impact of sub-lethal insecticide exposure on mosquito behavior requires further exploration.	Policymakers should prioritize investment in resistance management strategies and novel tools. Strengthening international collaboration for research on resistance management is essential.
Impact on Vector Control	Resistance to common insecticides, particularly pyrethroids, undermines the efficacy of traditional vector control interventions.	Ineffective insecticide interventions lead to an increased burden of mosquito-borne diseases.	Resistance development complicates the effectiveness of long-standing vector control programs, highlighting the need for innovative approaches.	Environmental factors such as urban heat islands exacerbate the resistance of mosquito populations.	Inadequate or inconsistent surveillance across regions allows resistance to spread undetected.	Resistance reversal strategies like the use of synergists offer immediate relief, but long-term solutions are required.	Genetic-based tools like gene drives are being explored as alternatives to traditional insecticide use.	Resistance management requires integrated control methods combining chemical, biological, and environmental strategies.	More research is needed to evaluate the impacts of new tools in real-world settings and their sustainability.	Global cooperation is essential to ensure uniform implementation of resistance management strategies and tools.
Challenges in Vector Control	Resistance to multiple classes of insecticides complicates control efforts, necessitating new approaches.	Increasing resistance is linked to heightened transmission rates of diseases like dengue and chikungunya.	Over-reliance on chemical insecticides in high-transmission areas accelerates resistance.	Climate change, leading to warmer temperatures, may influence vector population dynamics and resistance development.	Insufficient data on resistance levels across regions hinders effective response.	The development of new insecticide classes and resistance-breaking technologies is critical.	Biocontrol agents and genetic modifications, such as Wolbachia bacteria, are being tested for their potential to suppress mosquito populations.	Resistance management programs that combine traditional and modern control methods hold promise in reducing resistance.	Better understanding of resistance in different environmental contexts is needed to design tailored control strategies.	A coordinated approach is needed to align public health policies and ensure resources are allocated efficiently to control resistance.

Control Strategies	Integrated vector management (IVM) approaches reduce the reliance on chemical insecticides, minimizing the development of resistance.	Coordinated surveillance and targeted control programs can reduce disease transmission even in the presence of resistance.	Monitoring and adaptive management strategies are key to maintaining the effectiveness of vector control programs.	Incorporating environmental factors into resistance models helps predict areas at high risk for resistance.	Surveillance systems should include molecular tools to monitor resistance mutations across populations.	Novel insecticides targeting different molecular pathways offer an alternative to traditional insecticide use.	Genetic tools such as CRISPR-Cas9 may allow for targeted disruption of mosquito populations, preventing resistance development.	Resistance management must be adaptive and evolve with resistance patterns, emphasizing timely interventions.	Gaps in the understanding of ecological interactions between mosquitoes, resistance, and vector control need to be addressed.	Strengthening local capacity for monitoring and implementing resistance management strategies is essential.
Knowledge Gaps	The molecular basis of resistance and its variability across regions requires further investigation.	The interaction between insecticide resistance and disease transmission dynamics remains poorly understood.	The role of sub-lethal insecticide exposure on mosquito behavior and fitness needs more exploration.	Effects of climate change on resistance development are still unclear.	Longitudinal data on resistance evolution and vector control effectiveness are lacking.	There is a need to improve genetic modification techniques to ensure their safe and effective application in field settings.	Biological control methods, including larvivorous fish and bacteria, require more testing in different geographic areas.	Research into ecological, behavioral, and environmental factors influencing resistance patterns should be prioritized.	More collaborative, international research is needed to understand the global patterns of insecticide resistance and develop coordinated solutions.	Focused research on novel intervention tools, such as gene editing and biocontrol agents, is required to stay ahead of resistance.

Notable mutations include V1016I, F1534C, and G119S, which confer resistance to pyrethroids and organophosphates (Target-Site Mutations), Avoidance of insecticide-treated surfaces and altered feeding or resting behavior reduce contact with insecticides, further complicating vector control efforts (Behavioral Resistance) (Valle *et al*., 2019; Ishak *et al*., 2015; David *et al*., 2013).

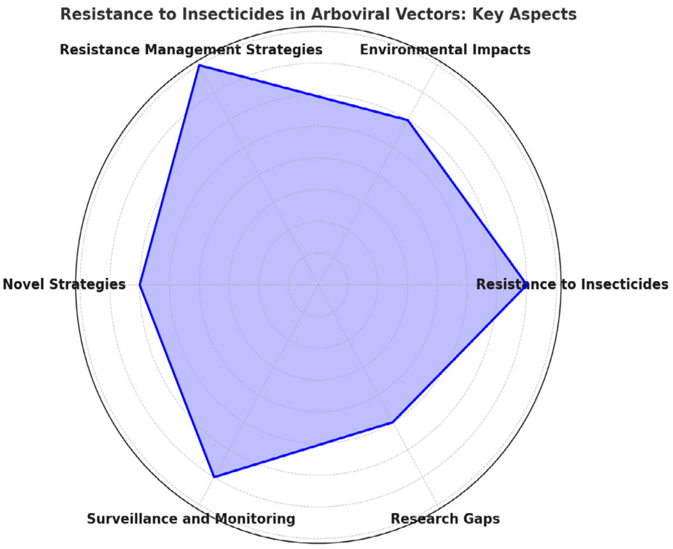

Figure 1:

Global surveillance data indicate that pyrethroid resistance in *Aedes aegypti* exceeds 75% in many parts of Southeast Asia and Latin America, with studies from Brazil and Vietnam reporting resistance rates of 85–95% to deltamethrin and permethrin. In contrast, some areas of Sub-Saharan Africa report resistance rates below 50%, although emerging trends in Ghana and Kenya suggest increasing resistance. Disease modeling from Brazil suggests that unchecked resistance could result in a 50% increase in dengue incidence over the next decade. A similar projection from Vietnam anticipates a 30–40% increase in dengue transmission if current control practices persist in the presence of high resistance levels (Abbasi *et al*., 2019; Gan *et al*., 2021; Rahman *et al*., 2021).

Resistance compromises the efficacy of vector control programs, leading to increased arbovirus transmission. Reduced mortality in resistant populations allows vectors to survive longer, facilitating multiple blood meals and amplifying disease spread. Furthermore, the limited success of insecticide-based interventions, such as indoor residual spraying and long-lasting insecticidal nets, has necessitated alternative approaches. Quantitative models predict a significant rise in arboviral disease burden in regions with high resistance levels, particularly in endemic areas. For example, simulations in Brazil suggest that resistance to pyrethroids could lead to a 50% increase in dengue incidence if alternative control measures are not implemented (Ray *et al*., 2024; Wagner *et al*., 2023; Kleinschmidt *et al*., 2018).

Innovative strategies are being developed to address the growing challenge of resistance, Alternating insecticides with different modes of action can delay resistance development. This approach has shown promise in experimental settings but requires careful implementation (Rotational Use of Insecticides), Introduction of natural predators, such as copepods and *Bacillus thuringiensis israelensis* (Bti), has demonstrated effectiveness in reducing vector populations without promoting resistance (Biological Control Agents), Techniques such as sterile insect techniques (SIT) and gene drive systems target vector populations at the genetic level, providing long-term solutions (Genetic Control Strategies) (James *et al*., 2018; Benelli *et al*., 2016; Diabate and Tripet, 2015).

Despite significant progress, critical gaps remain in our understanding of resistance dynamics, Research has predominantly focused on primary vectors like *Aedes aegypti*, while resistance patterns in secondary vectors, such as *Aedes albopictus*, are understudied (Resistance in Secondary Vectors), Laboratory studies often fail to replicate real-world conditions, necessitating large-scale field trials for emerging interventions (Field Validation of Novel Strategies), The ecological consequences of widespread insecticide use, including effects on non-target organisms and biodiversity, require further investigation (Impact on Non-target Species) (Héraud *et al*., 2022; Kemirembe, 2020; Ziska *et al*., 2019).

A cross-regional comparison reveals significant heterogeneity in insecticide resistance patterns among *Aedes aegypti* and *Aedes albopictus*, closely tied to each region's arboviral disease burden and vector control infrastructure, Countries such as Thailand, Indonesia, and Vietnam, with high dengue incidence and history of recurrent outbreaks, have reported widespread resistance to pyrethroids and organophosphates. Frequent mass insecticide campaigns and vector control programs targeting dense urban centers have contributed to high selection pressure, particularly among *Ae. aegypti* populations. Notably, *kdr* mutations (e.g., V1016G, F1534C) and metabolic resistance (overexpression of P450 enzymes) are consistently observed (Southeast Asia). Brazil and Colombia, characterized by hyperendemic dengue transmission and periodic chikungunya outbreaks, exhibit some of the highest resistance intensities to both adulticides (e.g., deltamethrin) and larvicides (e.g., temephos). This trend is largely attributed to the long-standing use of chemical-based interventions without effective rotation or integration of alternative control tools. High resistance correlates with increased dengue incidence during epidemic years (Latin America). Although the epidemiological burden of arboviruses is lower in many African countries compared to Asia and Latin America, resistance is emerging in urbanized regions. Studies in Ghana and Kenya report increasing pyrethroid resistance, raising concerns for future outbreak preparedness. The relative lack of large-scale vector control programs may have delayed resistance development, but urban growth and climate variability are accelerating resistance evolution (Sub-Saharan Africa). These regions have experienced episodic arboviral outbreaks (notably Zika and chikungunya), but show lower resistance levels overall, likely due to more targeted and less frequent use of insecticides. However, resistance "hotspots" have emerged in areas with high tourism-driven insecticide usage and repeated emergency spraying campaigns (Pacific Islands and Caribbean Nations). While *Aedes* populations are expanding due to climate change, local resistance levels remain relatively low. Nevertheless, imported cases and invasive vector introductions necessitate surveillance to pre-empt the establishment of resistant populations (Europe and North America) (Abbasi and Moemenbellah-Fard, 2024; Abbasi and Saeedi, 2022, Abedi-Astaneh *et al*., 2025; Talbalaghi *et al*., 2024).

Regional Case Studies, Resistance to pyrethroids is prevalent, driven by extensive use in dengue control campaigns. Integrated vector management (IVM) strategies are being piloted in Thailand and Vietnam with promising outcomes (Southeast Asia), Resistance hotspots in Brazil and Colombia highlight the urgent need for alternative control measures. Community-based programs emphasizing source reduction have been effective in mitigating resistance (Latin America), Limited resources and inadequate surveillance hinder resistance management. However, partnerships with international organizations are improving capacity for resistance monitoring and intervention (Sub-Saharan Africa) (de Arias *et al*., 2022; Stica *et al*., 2021; Miles, 2021).

The synthesis of evidence highlights the multifaceted nature of insecticide resistance and its profound implications for arboviral disease control. The findings underscore the need for integrated, multi-pronged approaches that combine chemical, biological, and genetic strategies. A concerted effort involving stakeholders at local, regional, and global levels is essential to combat resistance and reduce the burden of arboviral diseases effectively (Organization, 2020a; Ghosh and Ghosh, 2020; Hemingway *et al*., 2006).

The insecticide resistance profiles of *Aedes aegypti* and *Aedes albopictus* exhibit marked regional variability, shaped by local insecticide usage patterns, ecological conditions, and vector genetics. In Southeast Asia, resistance to pyrethroids such as deltamethrin and permethrin is widespread, driven by intensive insecticide application in dengue control programs. Studies from Vietnam, Thailand, and Indonesia consistently report high frequencies of kdr mutations and elevated levels of detoxifying enzymes. In Latin America, particularly in Brazil and Colombia, resistance to both pyrethroids and organophosphates is prevalent, exacerbated by unregulated domestic insecticide use and frequent vector control interventions. In Sub-Saharan Africa, while resistance in *Aedes aegypti* is increasingly documented, *Aedes albopictus* resistance patterns remain under-investigated. Limited surveillance infrastructure and financial resources hinder comprehensive assessments, though available data suggest emerging resistance hotspots in urban centers. Conversely, Pacific Island nations and some Central African countries show comparatively lower resistance rates, likely due to less intensive chemical intervention and more localized vector control efforts (Abbasi and Daliri, 2024a; Abbasi and Daliri, 2024c; Abbasi and Daliri, 2024b; Abbasi *et al*., 2025b; Abbasi *et al*., 2024).

Comparative analyses reveal that *Aedes aegypti* exhibits a higher frequency and diversity of kdr mutations (e.g., V1016I, F1534C) than *Aedes albopictus*, likely due to greater exposure to urban insecticide use. *Ae. aegypti* populations often overexpress cytochrome P450 genes such as *CYP9J32* and *CYP9J28*, while *Ae. albopictus* shows a stronger reliance on GST-based detoxification and esterases. Behavioral resistance, such as altered resting or feeding behavior, has been documented in both species, but appears more pronounced in *Ae. albopictus*, potentially due to its more exophilic tendencies (Moyes *et al*., 2017; Smith *et al*., 2016).

Resistance levels differ significantly between urban and rural settings. Urban populations of *Aedes aegypti* often show resistance rates exceeding 80%, while rural populations remain below 40% in several regions of Southeast Asia and Latin America. Predictive spatial models have demonstrated that resistance hotspots are concentrated in densely populated urban centers where vector control relies heavily on chemical insecticides. A study from Thailand showed a 2).5-fold higher resistance intensity in metropolitan areas compared to rural districts, correlating with higher insecticide application frequency and housing density (Guedes *et al*., 2020; Zulfa *et al*., 2022).

In Latin America, resistance to pyrethroids in *Ae. aegypti* exceeds 90% in Brazil and Colombia, where dengue incidence remains among the highest globally. In Southeast Asia, resistance rates in *Ae. aegypti* range from 70–95% in urban settings (e.g., Ho Chi Minh City, Bangkok). *Ae. albopictus* shows lower resistance overall, with rates ranging from 30–60%, but is increasingly implicated in chikungunya transmission in Italy and France. Correlation analysis from Brazilian surveillance data indicates a positive correlation ($r = 0.78$, $p < 0.01$) between deltamethrin resistance intensity and annual dengue incidence across municipalities. Similar patterns have been observed in Colombia and Indonesia (Moyes *et al*., 2017; Willen *et al*., 2019).

DISCUSSION

The growing challenge of insecticide resistance in arboviral vectors such as *Aedes aegypti* and *Aedes albopictus* represents a critical obstacle to global efforts to curb arboviral diseases, including dengue, chikungunya, and Zika. The findings of this review underscore the multifaceted nature of resistance development, which is driven by a combination of genetic, biochemical, and operational factors. In this section, we synthesize the key insights gained from the results and place them in the context of the broader scientific literature, while identifying knowledge gaps and proposing actionable strategies to address this pressing issue. The rapid escalation of resistance to commonly used insecticides, including pyrethroids, carbamates, and organophosphates, threatens the efficacy of vector control programs globally. Pyrethroid resistance, in particular, is a dominant concern, as it is linked to mutations in voltage-gated sodium channels (e.g., kdr mutations) and overexpression of detoxifying enzymes such as cytochrome P450s. These mechanisms enable vectors to survive exposure to insecticides, thereby sustaining their population densities and increasing the likelihood of arboviral transmission. Resistance has direct implications for public health. Studies have shown that high levels of pyrethroid resistance correlate with increased disease incidence due to reduced efficacy of long-lasting insecticidal nets (LLINs) and indoor residual spraying (IRS). These findings emphasize the urgent need for resistance monitoring and management strategies to mitigate the impact on disease transmission (Kleinschmidt *et al*., 2018; Moyes *et al*., 2017; Hemingway *et al*., 2004).

The development of insecticide resistance is influenced by multiple factors, including the overuse and misuse of insecticides, the lack of rotation between chemical classes, and the genetic adaptability of mosquito populations. Operational practices such as inadequate coverage and sub-lethal dosing exacerbate resistance development, as they create selective pressure that favors resistant phenotypes. Additionally, environmental factors, such as urbanization and climate change, contribute to the expansion of mosquito habitats and complicate resistance management. Despite these challenges, the results highlight the importance of integrated vector management (IVM) as a cornerstone of resistance mitigation. By combining chemical, biological, and environmental approaches, IVM reduces reliance on chemical insecticides and slows the evolution of resistance (Ray *et al*., 2024; Héraud *et al*., 2022; Valle *et al*., 2019).

Emerging strategies to combat resistance include the use of novel insecticides with unique modes of action, synergists that inhibit detoxification enzymes, and genetic approaches such as gene drive systems. For instance, the combination of pyrethroids with synergists like piperonyl butoxide has shown promise in restoring susceptibility in resistant populations. Additionally, advances in biotechnology, such as the release of sterile or genetically modified mosquitoes, offer innovative solutions to reduce vector populations and interrupt disease transmission. However, the implementation of these strategies requires careful evaluation of their ecological and ethical implications. The potential for resistance to novel tools, as well as the unintended effects on non-target species, must be considered in the development and deployment of these interventions (Wagner *et al*., 2023; Benelli *et al*., 2016; Diabate and Tripet, 2015).

Field evaluations of *Wolbachia*-infected *Aedes aegypti* have shown substantial reductions in dengue transmission. For instance, the World Mosquito Program reported a 77% reduction in dengue incidence and an 86% reduction in hospitalizations following large-scale *Wolbachia* deployments in Yogyakarta, Indonesia. Similarly, gene drive systems targeting population suppression or resistance gene propagation have shown high efficiency in laboratory settings; however, their application in natural populations remains under regulatory and ecological scrutiny. Next-generation insecticides, such as clothianidin (a neonicotinoid) and chlorfenapyr (a pyrrole), have demonstrated effectiveness against resistant mosquito populations in semi-field trials in Africa and Asia. Nevertheless, long-term monitoring is required to evaluate durability, resistance evolution, and potential non-target effects (Deibel *et al*., 2022; Utarini *et al*., 2021).

The practical implementation of these novel strategies requires integration into national vector control frameworks through phased, evidence-based deployment. For example, *Wolbachia* programs rely on sustained community engagement, local breeding facilities, and monitoring systems to track mosquito infection rates. Gene drive approaches, while still in experimental phases, will necessitate strict biosafety protocols and stakeholder consultations prior to release. Incorporating next-generation insecticides into indoor residual spraying (IRS) programs may require retraining personnel and updating procurement systems to accommodate new formulations. Strategic partnerships with regulatory agencies, local governments, and international donors are essential to scale these innovations responsibly and effectively (Nazni *et al*., 2019; Organization, 2020b).

While significant progress has been made in understanding the mechanisms and distribution of insecticide resistance, several gaps remain. First, there is a need for longitudinal studies to assess the long-term effectiveness of resistance management strategies. Second, the impact of sub-lethal exposure to insecticides on mosquito behavior, such as host-seeking and feeding, warrants further investigation. Third, the role of environmental factors in shaping resistance dynamics requires greater attention, particularly in the context of climate change and urbanization. Research efforts should also prioritize the development of novel surveillance tools, including molecular assays for resistance detection and predictive models for resistance spread. These tools will enable more targeted and efficient control measures, ultimately improving the sustainability of vector control programs (Héraud *et al*., 2022; Ziska *et al*., 2019; David *et al*., 2013).

The socio-economic implications of managing insecticide resistance are significant. Resistance increases the cost of disease outbreaks due to higher hospitalization rates, lost productivity, and the need for emergency interventions. Novel control tools often entail higher initial investment costs—such as infrastructure for mass-rearing mosquitoes or procurement of new insecticides—but may be cost-effective over time by reducing disease burden. However, implementation in low- and middle-income countries may face challenges due to limited funding, supply chain constraints, and variable political commitment. Ensuring equitable access to innovative tools is critical, as regions with weak health infrastructure often face the greatest arboviral disease risks. Community acceptance and behavioral factors also influence intervention success, underscoring the need for participatory approaches and culturally sensitive communication strategies (Abbasi, 2025b; Nolden, 2023).

The findings of this review highlight the need for coordinated global efforts to address insecticide resistance. Policymakers must prioritize investment in resistance management, including the development and distribution of novel tools, capacity building for resistance monitoring, and the promotion of community-based approaches to vector control. International collaboration is essential to ensure that resources are allocated efficiently and that resistance management strategies are informed by the latest scientific evidence. In conclusion, insecticide resistance represents a significant threat to the control of arboviral diseases, but it is not insurmountable. By integrating innovative tools, strengthening surveillance systems, and fostering international cooperation, the global health community can effectively address this challenge and reduce the burden of arboviral diseases on vulnerable populations (Organization, 2020a; Ghosh and Ghosh, 2020; Hemingway *et al*., 2006).

Managing insecticide resistance is no longer a peripheral challenge—it is a central obstacle to the control of arboviral diseases globally. Over the next 5–10 years, research must prioritize the longitudinal monitoring of resistance evolution, the behavioral and physiological effects of sub-lethal insecticide exposure, and the ecological implications of emerging control tools. Advances in molecular diagnostics, predictive modeling, and field validation of genetic and biological interventions will be essential. It is imperative that resistance management strategies are not only scientifically robust but also sustainable and adaptable to shifting epidemiological and environmental landscapes. To effectively address insecticide resistance, policy responses must be proactive and multisectoral. First, countries should establish or strengthen national insecticide resistance surveillance systems, supported by molecular tools and real-time data sharing platforms. Second, biological (e.g., *Wolbachia*, *Bti*) and genetic (e.g., gene drives, SIT) control strategies should be systematically integrated into national vector control programs as part of a broader Integrated Vector Management (IVM) framework. Third, global collaboration must be intensified through regional networks, public-private partnerships, and donor-supported platforms to harmonize data collection, resource sharing, and regulatory alignment. A coordinated international response, grounded in evidence and equity, is essential to mitigate resistance and safeguard global health security (Abbasi, 2025b; Abbasi, 2025c; Abbasi *et al*., 2025a; Bharadwaj *et al*., 2025; Hassanali *et al*., 2008).

CONCLUSIONS AND RECOMMENDATIONS

Insecticide resistance among arboviral vectors, especially *Aedes aegypti* and *Aedes albopictus*, poses a significant threat to vector control and public health. This review highlights the multifaceted nature of resistance and the urgent need for integrated approaches—combining chemical, biological, and genetic tools—to mitigate its impact. Policymakers and health authorities should prioritize long-term resistance monitoring, the responsible use of insecticides, and investment in innovative tools. Additionally, greater emphasis should be placed on field validation of new strategies, community engagement, and international collaboration to ensure sustainable and effective vector control.

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NOVELTY STATEMENTS

This review uniquely integrates molecular, ecological, operational, and policy dimensions of insecticide resistance in arboviral vectors. Unlike previous literature, it emphasizes under-researched areas such as resistance in *Aedes albopictus*, the effects of sub-lethal insecticide exposure, and the challenges of applying novel control strategies in real-world settings. The study offers a forward-looking synthesis of current knowledge and provides practical, evidence-based recommendations to guide sustainable vector control efforts globally.

AUTHOR'S CONTRIBUTIONS

Ebrahim Abbasi has carried out all parts of the article, including design, execution, and writing.

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Not applicable.

Data Availability Statement

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Conflict of Interest

The authors declare no competing interests.

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