

Advances in Vector-Borne Protozoan Diseases and Control: Challenges, Innovations, and Future Directions – A Review

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ARTICLE INFO

Received: February 20, 2025

Accepted: March 17, 2025

Volume: 5

Issue: 1

KEYWORDS

Vector-pathogen, Interactions, Transmission, Protozoan-diseases, Insecticide resistance, One Health approach, Wolbachia-based biocontrol, Zoonotic spillover.

ABSTRACT

Vector-borne protozoan diseases, including malaria, Chagas disease, leishmaniasis, and African trypanosomiasis, remain significant global health challenges. These diseases, transmitted by arthropod vectors such as mosquitoes, triatomine bugs, sandflies, and tsetse flies, disproportionately affect tropical and subtropical regions, causing substantial morbidity, mortality, and socio-economic burdens. This review synthesizes recent advances in understanding vector-pathogen interactions, highlights innovative control strategies, and addresses emerging challenges such as insecticide resistance, zoonotic spillover, and climate change. The paper emphasizes the importance of integrated, multi-disciplinary approaches, including genetic, ecological, and one health frameworks, to achieve sustainable disease control. By integrating findings from studies published between 2020–2024, this paper provides a comprehensive overview of the current state of knowledge and outlines critical directions for future research and policy.

1. Introduction

Vector-borne protozoan diseases remain a formidable challenge to global health, disproportionately affecting resource-limited regions in tropical and subtropical areas (WHO, 2023). These diseases, transmitted by arthropod vectors such as mosquitoes, sandflies, and triatomine bugs, are caused by protozoan parasites including *Plasmodium*, *Trypanosoma*, and *Leishmania* species. Collectively, they account for over 1 million deaths annually and impose significant socio-economic burdens, particularly in low- and middle-income countries (Burza *et al.*, 2023; PAHO, 2023; WHO, 2023). Despite decades of control efforts, the persistence and resurgence of these diseases highlight the complex interplay of biological, environmental, and socio-economic factors (Hotez *et al.*, 2020; Rocklöv and Dubrow, 2024).

The global burden of vector-borne protozoan diseases has been exacerbated by emerging threats such as insecticide resistance, climate change, and urbanization. For instance, the invasion of *Anopheles stephensi*, an urban-adapted malaria vector, into Africa has raised concerns about malaria resurgence in regions previously on the brink of elimination (Ahmed *et al.*, 2023). Similarly, climate-driven shifts in vector distribution are expanding the geographic range of diseases like leishmaniasis into non-endemic areas, including southern Europe (Ready, 2023). These trends underscore the urgent need for innovative and integrated approaches to disease control.

The World Health Organization (WHO) has identified vector-borne diseases as a priority for the 2030 Global Health Agenda, with specific targets for malaria elimination and control of Neglected Tropical Diseases (NTDs) such as leishmaniasis and Chagas disease (WHO, 2021). However, achieving these targets is increasingly challenging due to the rapid evolution of pathogens and vectors, as well as the socio-economic disparities that hinder effective intervention in endemic regions. This review is timely because it synthesizes the latest research on vector-pathogen interactions and control strategies, providing a roadmap for addressing these challenges in the context of global health priorities.

Recent advances in molecular biology and genomics have deepened our understanding of vector-pathogen interactions, revealing intricate mechanisms of immune evasion, genetic adaptation, and co-evolution. For example, studies have identified *Plasmodium falciparum* proteins like PfGEST that manipulate mosquito midgut microbiota to enhance parasite survival (Wang *et al.*, 2024). Similarly, *Leishmania exosomes* have been shown to modulate sandfly immune responses, facilitating parasite transmission. These discoveries are paving the way for novel interventions, including gene drives, Wolbachia-based biocontrol, and next-generation vaccines (Atayde *et al.*, 2023).

However, the translation of these innovations into field applications faces significant hurdles. Insecticide resistance, for instance, has been reported in over 80% of malaria-endemic countries, undermining the efficacy of long-standing control tools like insecticide-treated bed nets (ITNs) and indoor residual spraying (IRS) (Hemingway *et al.*, 2023). Moreover, socio-economic disparities and inadequate healthcare infrastructure in endemic regions exacerbate the burden of these diseases, particularly among vulnerable populations such as children, pregnant women, and immunocompromised individuals (Alvar *et al.*, 2022; Desai *et al.*, 2022; Lee *et al.*, 2022).

While significant progress has been made in understanding vector-borne protozoan diseases, several critical gaps remain. First, there is a lack of integrated approaches that combine genetic, ecological, and socio-economic strategies to achieve sustainable disease control. Most studies focus on isolated aspects of disease transmission, such as vector biology or drug development, without considering the broader ecological and socio-economic context. Second, the impact of emerging threats like climate change and zoonotic spillover on disease dynamics is not fully understood. Finally, there is limited research on the scalability and cost-effectiveness of innovative control tools, such as gene drives and Wolbachia-based biocontrol, in resource-limited settings.

This review aims to address these gaps by providing a comprehensive synthesis of recent advances in vector-pathogen interactions, innovative control strategies, and the socio-economic factors that influence disease transmission. By integrating findings from studies published between 2020–2024, we highlight the importance of multi-disciplinary approaches and identify critical directions for future research and policy.

This review is divided into five (5) main sections to provide a structured and comprehensive overview of the current state of knowledge:

Epidemiology and Vectors: We examine the global burden of major protozoan diseases, including malaria, Chagas disease, leishmaniasis, and African trypanosomiasis, and discuss the role of their respective vectors in disease transmission.

Molecular and Ecological Insights: We explore recent advances in understanding vector-pathogen interactions, including genetic adaptations, immune evasion mechanisms, and the impact of climate change on transmission dynamics.

Disparities and Socio-Economic Costs: We assess how vector-borne protozoan diseases cause not only substantial morbidity and mortality but also exacerbate socio-economic inequalities, perpetuating cycles of poverty and hindering development.

Control Strategies: We review innovative approaches to disease control, such as gene drives, Wolbachia-based biocontrol, and next-generation vaccines, and discuss the challenges of translating these innovations into field applications.

Emerging Challenges and Future Directions: We highlight key challenges, including insecticide resistance, zoonotic spillover, and the impacts of climate change, and outline critical areas for future research and policy.

2. LITERATURE REVIEW

2.1 Major Protozoan Diseases: Epidemiology and Vectors

2.1.1 Malaria

Vector: *Anopheles* spp., particularly *An. gambiae* and *An. stephensi*, are the primary vectors. *An. gambiae* is highly efficient in transmitting *Plasmodium falciparum*, the deadliest malaria parasite, while *An. stephensi* is an emerging threat due to its adaptability to urban environments (Sinka *et al.*, 2021; Tadesse *et al.*, 2022; Ahmed *et al.*, 2023).

Burden: In 2022, malaria caused 249 million cases and 608,000 deaths globally, with sub-Saharan Africa accounting for 95% of cases and 96% of deaths. Children under 5 years old are the most vulnerable, representing 80% of malaria-related deaths (WHO, 2023).

Recent Findings: The invasion of *An. stephensi* into Africa, particularly in Ethiopia, Sudan, and Djibouti, poses a significant threat to malaria control. Unlike other *Anopheles* species, *An. stephensi* thrives in urban settings, breeding in artificial water

containers such as water storage tanks and discarded tires (Sinka *et al.*, 2021; Carter *et al.*, 2023). This adaptability increases the risk of malaria resurgence in urban areas, where populations are often immunologically naive and healthcare systems are overburdened (Ahmed *et al.*, 2023).

Key Stat: Insecticide resistance has been reported in over 80% of malaria-endemic countries, complicating vector control efforts (Hemingway *et al.*, 2023).

Critical Analysis: While the spread of *An. stephensi* is well-documented, there is limited understanding of its long-term ecological impact and interactions with other vector species. For example, studies have shown conflicting results on whether *An. stephensi* competes with or displaces native *Anopheles* species, which could have implications for malaria transmission dynamics (Tadesse *et al.*, 2022; Carter *et al.*, 2023). Additionally, the role of urbanization in driving *An. stephensi* adaptation remains understudied, particularly in peri-urban areas where human-vector contact is highest (Ahmed *et al.*, 2023).

2.1.2 Chagas Disease

Vector: Triatomine bugs, including *Triatoma infestans* and *Rhodnius prolixus*, are the primary vectors. These nocturnal insects transmit *Trypanosoma cruzi* through their faeces, which contaminate bite wounds or mucous membranes (López *et al.*, 2021; Nóbrega *et al.*, 2022; Garcia *et al.*, 2023).

Burden: Chagas disease affects 6–7 million people globally, with 12,000 deaths annually. The disease is endemic in 21 Latin American countries, but globalization and migration have spread cases to non-endemic regions such as the United States and Europe (PAHO, 2023).

Emerging Trends: Oral transmission, particularly in the Amazon Basin, has become a significant route of infection. Outbreaks are linked to the consumption of contaminated food or beverages, such as açai juice, which can harbor *T. cruzi* from crushed triatomine bugs. This mode of transmission is associated with higher parasite loads and more severe acute symptoms (Nóbrega *et al.*, 2022).

Key Stat: Chronic Chagas cardiomyopathy develops in 30% of infected individuals, leading to heart failure and sudden death (Lee *et al.*, 2022).

Critical Analysis: Despite advances in understanding oral transmission, there are significant gaps in knowledge about the ecological and behavioral factors driving this route of infection. For example, the role of deforestation and land-use changes in increasing human contact with triatomine bugs is not fully understood (Chaves *et al.*, 2023). Additionally, the impact of urbanization on triatomine bug populations and disease transmission in non-endemic regions remains understudied (Garcia *et al.*, 2023).

2.1.3 Leishmaniasis

Vectors: *Phlebotomus* sandflies in the Old World (e.g., Europe, Asia, Africa) and *Lutzomyia* sandflies in the New World (e.g., Americas) transmit *Leishmania* parasites (Ready, 2023; Valero *et al.*, 2023).

Burden: Leishmaniasis causes approximately 1 million new cases annually. *Visceral leishmaniasis* (VL), the most severe form, has a fatality rate of 95% if untreated. *Cutaneous leishmaniasis* (CL), while less fatal, causes disfiguring skin lesions that lead to social stigma and economic hardship (Burza *et al.*, 2023).

Climate Impact: Rising global temperatures are expanding the geographic range of sandflies into southern Europe, including countries like Italy and Spain. This shift increases the risk of leishmaniasis in regions previously considered non-endemic (Ready, 2023).

Key Stat: Over 90% of VL cases occur in just 10 countries, including India, Brazil, and Sudan, highlighting the concentrated burden in specific regions (WHO, 2023).

Critical Analysis: While the impact of climate change on sandfly distribution is well-documented, there is limited research on the ecological interactions between sandflies and their vertebrate hosts in newly endemic areas. For example, the role of

domestic animals as reservoirs for *Leishmania* parasites in southern Europe is not fully understood (Valero *et al.*, 2023). Additionally, the socio-economic factors driving the spread of leishmaniasis, such as poverty and inadequate housing, require further investigation (Burza *et al.*, 2023).

2.1.4 African Trypanosomiasis (Sleeping Sickness)

Vector: Tsetse flies (*Glossina* spp.) transmit *Trypanosoma brucei gambiense* (West African form) and *T. b. rhodesiense* (East African form) (Auty *et al.*, 2022; Franco *et al.*, 2023; Rock *et al.*, 2022).

Burden: In 2022, fewer than 1,000 cases were reported, reflecting the success of sustained control efforts, including vector control, screening, and treatment programs. The disease is now concentrated in remote areas of the Democratic Republic of Congo and Central African Republic (WHO, 2023).

Challenges: Animal reservoirs, particularly cattle, sustain zoonotic transmission of *T. b. rhodesiense*. This complicates elimination efforts, as tsetse flies can transmit the parasite between animals and humans (Auty *et al.*, 2022).

Key Stat: The WHO aims to eliminate *gambiense* sleeping sickness as a public health problem by 2030, but achieving this goal requires addressing zoonotic transmission and improving surveillance in conflict-affected regions (WHO, 2023).

Critical Analysis: While significant progress has been made in reducing human cases, the role of animal reservoirs in sustaining transmission remains a major challenge. For example, studies have shown conflicting results on the effectiveness of targeting cattle reservoirs in reducing human cases (Auty *et al.*, 2022; Franco *et al.*, 2023). Additionally, the impact of climate change on tsetse fly distribution and disease transmission is not fully understood (Rock *et al.*, 2022).

Table 1: Global Distribution of Major Protozoan Diseases and Their Vectors

Disease	Primary Vectors	Geographic Distribution	Key Statistics
Malaria	<i>Anopheles gambiae</i> , <i>An. Stephensi</i>	Sub-Saharan Africa (95% of cases), Asia, Latin America	249 million cases, 608,000 deaths annually (WHO, 2023). Children under 5 account for 80% of deaths.
Chagas Disease	<i>Triatoma infestans</i> , <i>Rhodnius prolixus</i>	Endemic in 21 Latin American countries; spreading to the US and Europe due to migration	6–7 million cases, 12,000 deaths annually. Chronic cardiomyopathy develops in 30% of cases (PAHO, 2023).
Leishmaniasis	<i>Phlebotomus</i> spp. (Old World), <i>Lutzomyia</i> spp. (New World)	South Asia, East Africa, Latin America; expanding to southern Europe due to climate change	1 million new cases annually. Visceral leishmaniasis has a 95% fatality rate if untreated (Burza <i>et al.</i> , 2023).
African Trypanosomiasis	<i>Glossina</i> spp. (tsetse flies)	Democratic Republic of Congo, Central African Republic	Fewer than 1,000 cases reported in 2022. Zoonotic transmission from cattle complicates control (WHO, 2023).

Comparative Analysis

A comparative analysis of the epidemiology and control challenges of malaria, Chagas disease, leishmaniasis, and African trypanosomiasis reveals both unique and shared features:

Malaria: High burden in sub-Saharan Africa, driven by *Anopheles* vectors and exacerbated by urbanization and insecticide resistance.

Chagas Disease: Concentrated in Latin America, with emerging threats from oral transmission and urbanization.

Leishmaniasis: Expanding geographic range due to climate change, with a high burden in South Asia, East Africa, and Latin America.

African Trypanosomiasis: Low case numbers but persistent challenges from zoonotic transmission and animal reservoirs.

These comparisons highlight the need for tailored control strategies that address the unique ecological and socio-economic contexts of each disease.

2.2 Vector-Pathogen Interactions: Molecular and Ecological Insights

The transmission of protozoan diseases by arthropod vectors involves complex interactions at the molecular and ecological levels. These interactions determine the efficiency of pathogen transmission, the survival of vectors, and the overall disease burden. Recent advances in genomics, molecular biology, and climate modelling have provided unprecedented insights into these processes, revealing new targets for intervention and highlighting the impact of environmental changes on disease dynamics (Cirimotich *et al.*, 2021; Molina-Cruz *et al.*, 2023; Wang *et al.*, 2024).

2.2.1 Genetic Adaptations

Malaria:

Plasmodium falciparum, the deadliest malaria parasite, has evolved sophisticated mechanisms to manipulate its mosquito vector, *Anopheles gambiae*. Recent research has identified a secreted protein, PfGEST, which alters the composition of the mosquito midgut microbiota, creating a favorable environment for parasite development. By suppressing commensal bacteria that compete for resources, PfGEST enhances the survival of *Plasmodium* sporozoites, increasing the likelihood of transmission to humans (Smith *et al.*, 2022; Gómez-Díaz *et al.*, 2023; Wang *et al.*, 2024).

Another critical adaptation is the expression of *Pfs47*, a surface protein that enables *Plasmodium* to evade the mosquito's immune system. *Pfs47* inhibits the activation of the mosquito's complement-like system, particularly the thioester-containing protein 1 (TEP1), which would otherwise target and destroy the parasite (Molina-Cruz *et al.*, 2023).

Mechanistic Depth: PfGEST achieves this by modulating the expression of key microbial genes involved in nutrient acquisition and immune regulation. For example, PfGEST downregulates the expression of *Acinetobacter* spp. genes that produce antimicrobial peptides, thereby reducing competition for resources in the mosquito midgut (Wang *et al.*, 2024). A proposed pathway for PfGEST-mediated microbiota manipulation is illustrated in Table 2.

Table 2: Pathway for PfGEST-Mediated Manipulation of Mosquito Microbiota

Step	Mechanism	Outcome
PfGEST Secretion	<i>Plasmodium falciparum</i> secretes PfGEST into the mosquito midgut.	PfGEST interacts with midgut microbiota.
Microbiota Modulation	PfGEST suppresses commensal bacteria (e.g., <i>Acinetobacter</i> spp.) by downregulating antimicrobial peptide production.	Reduced competition for resources in the midgut.
Nutrient Availability	Suppression of competing bacteria increases nutrient availability for <i>Plasmodium</i> .	Enhanced survival and development of <i>Plasmodium</i> sporozoites.
Immune Evasion	PfGEST indirectly modulates mosquito immune responses by altering microbiota.	Reduced immune activation against <i>Plasmodium</i> .

Key Insight: PfGEST enhances *Plasmodium* survival by manipulating the mosquito midgut microbiota, creating a favorable environment for parasite development (Wang *et al.*, 2024; Smith *et al.*, 2022; Gómez-Díaz *et al.*, 2023).

Emerging Research: Recent studies have highlighted the role of vector microbiota in shaping pathogen transmission. For instance, the gut microbiota of *Anopheles* mosquitoes has been shown to influence the susceptibility to *Plasmodium* infection,

with certain bacterial species enhancing or inhibiting parasite development (Gómez-Díaz et al., 2023). However, there is ongoing debate about the relative importance of specific microbial taxa and their interactions with the mosquito immune system (Cirimotich et al., 2021).

Leishmaniasis:

Leishmania parasites secrete exosomes—small vesicles containing proteins, lipids, and RNA—that modulate the immune response of their sandfly vectors. For example, *Leishmania exosomes* have been shown to downregulate the expression of immune-related genes such as *SPRNK1* in *Phlebotomus papatasi* sandflies. This suppression of the vector’s immune system allows the parasite to establish and persist in the midgut, facilitating transmission to humans (Atayde et al., 2023).

Additionally, *Leishmania* manipulates the sandfly’s feeding behaviour by altering the production of salivary proteins, increasing the frequency of bites and enhancing the chances of transmission (Rogers et al., 2022).

Mechanistic Depth: *Leishmania* exosomes achieve immune modulation by delivering microRNAs that target key immune signaling pathways in the sandfly. For instance, miR-71 has been shown to inhibit the expression of *SPRNK1*, a gene involved in the sandfly’s immune response to *Leishmania* infection (Atayde et al., 2023). A proposed pathway for exosome-mediated immune evasion is illustrated in Table 3.

Table 3: Pathway for Leishmania Exosome-Mediated Immune Evasion in Sandflies

Step	Mechanism	Outcome
Exosome Secretion	<i>Leishmania</i> parasites secrete exosomes containing microRNAs (e.g., miR-71).	Exosomes are taken up by sandfly midgut cells.
Immune Gene Suppression	Exosomal miR-71 targets and downregulates immune-related genes (e.g., <i>SPRNK1</i>).	Suppression of sandfly immune responses.
Parasite Survival	Reduced immune activation allows <i>Leishmania</i> to establish and persist in the midgut.	Enhanced transmission to humans.

Key Insight: *Leishmania* exosomes modulate sandfly immune responses, facilitating parasite survival and transmission (Atayde et al., 2023; Rogers et al., 2022).

Emerging Research: Recent studies have explored the potential of targeting *Leishmania* exosomes as a novel control strategy. For example, blocking exosome production or delivery could reduce parasite survival in the sandfly and interrupt transmission (Rogers et al., 2022). However, the feasibility of this approach in field settings remains a subject of debate.

2.2.2 Vector Immune Evasion

Mosquitoes:

The mosquito immune system plays a critical role in controlling *Plasmodium* infection. The thioester-containing protein 1 (TEP1) is a key component of the mosquito’s complement-like system, binding to *Plasmodium ookinetes* and marking them for destruction. However, *Plasmodium* has evolved countermeasures, such as the production of *Pfs47*, which inhibits TEP1 binding and prevents immune recognition (Molina-Cruz et al., 2023).

Mosquitoes also produce antimicrobial peptides (AMPs) such as defensins and cecropins, which target *Plasmodium* parasites. However, *Plasmodium* can suppress the expression of these AMPs by modulating the mosquito’s immune signaling pathways, such as the IMD (Immune Deficiency) pathway (Smith et al., 2022).

Mechanistic Depth: *Pfs47* achieves immune evasion by binding to TEP1 and preventing its activation. This interaction is mediated by specific amino acid residues in the *Pfs47* protein, which have been identified through structural studies (Molina-Cruz et al., 2023). A proposed pathway for *Pfs47*-mediated immune evasion is illustrated in Table 4.

Table 4: Pathway for Pfs47-Mediated Immune Evasion in Mosquitoes

Step	Mechanism	Outcome
Pfs47 Expression	<i>Plasmodium falciparum</i> expresses Pfs47 on the surface of ookinetes.	Pfs47 interacts with mosquito TEP1 protein.
TEP1 Inhibition	Pfs47 binds to TEP1, preventing its activation and binding to ookinetes.	Inhibition of mosquito complement-like system.
Immune Evasion	Reduced TEP1 activity allows ookinetes to evade immune destruction.	Enhanced survival and development of <i>Plasmodium</i> in the mosquito.

Key Insight: Pfs47 enables *Plasmodium* to evade mosquito immune responses by inhibiting TEP1-mediated destruction (Molina-Cruz *et al.*, 2023; Hammond *et al.*, 2022).

Emerging Research: Recent studies have highlighted the potential of targeting Pfs47 as a novel control strategy. For example, CRISPR-based gene editing could be used to disrupt the *Pfs47* gene in *Plasmodium*, rendering the parasite susceptible to mosquito immune responses (Hammond *et al.*, 2022). However, the ethical and ecological implications of such an approach remain controversial.

Triatomines:

Trypanosoma cruzi, the causative agent of Chagas disease, employs multiple strategies to evade the immune response of its triatomine vector. One such mechanism involves the suppression of nitric oxide synthase (NOS), an enzyme that produces nitric oxide (NO), a potent antimicrobial agent. By reducing NO production, *T. cruzi* minimizes oxidative stress and enhances its survival in the bug's midgut (López *et al.*, 2021). *T. cruzi* also secretes proteases that degrade antimicrobial peptides produced by the triatomine, further facilitating its persistence in the vector (Garcia *et al.*, 2023).

Mechanistic Depth: *T. cruzi* achieves NO suppression by secreting proteases that degrade NOS or by modulating the expression of NOS-related genes in the triatomine midgut (Garcia *et al.*, 2023). A proposed pathway for NO suppression is illustrated in Table 5.

Table 5: Pathway for NO Suppression by *T. cruzi* in Triatomines

Step	Mechanism	Outcome
NOS Suppression	<i>Trypanosoma cruzi</i> secretes proteases that degrade nitric oxide synthase (NOS).	Reduced production of nitric oxide (NO), a potent antimicrobial agent.
Oxidative Stress Reduction	Lower NO levels minimize oxidative stress in the triatomine midgut.	Enhanced survival of <i>T. cruzi</i> in the vector.
Immune Evasion	Reduced NO production weakens the triatomine immune response to <i>T. cruzi</i> .	Increased transmission efficiency to humans.

Key Insight: *T. cruzi* enhances its survival in triatomines by suppressing NO production, a key component of the vector's immune response (López *et al.*, 2021; Garcia *et al.*, 2023).

Emerging Research: Recent studies have explored the role of triatomine microbiota in shaping *T. cruzi* transmission. For example, certain bacterial species in the triatomine gut have been shown to enhance or inhibit *T. cruzi* survival, suggesting that microbiota manipulation could be a novel control strategy (López *et al.*, 2021). However, the feasibility of this approach in field settings remains a subject of debate.

2.2.3 Climate-Driven Transmission Shifts

Temperature Effects:

Rising global temperatures are accelerating the life cycles of many vector species. For example, *Aedes aegypti*, the primary vector of dengue and Zika viruses, develops 10% faster with every 1°C increase in temperature. This acceleration increases the vector's reproductive rate and expands its geographic range, potentially introducing protozoan diseases into new regions (Rocklöv and Dubrow, 2024).

Similarly, warmer temperatures enhance the development of *Plasmodium* parasites within *Anopheles* mosquitoes, increasing the likelihood of malaria transmission. Studies predict that a 2°C rise in global temperatures could expand malaria-endemic areas by 15%, exposing an additional 500 million people to the disease (Ryan *et al.*, 2023).

Deforestation and Habitat Change:

Deforestation in Brazil has been linked to a 30% increase in the abundance of *Lutzomyia* sandflies, the vectors of *Leishmania* parasites. The destruction of natural habitats forces sandflies to seek new breeding sites in peri-urban areas, bringing them into closer contact with human populations. This ecological shift has contributed to a rise in *Visceral leishmaniasis* (VL) cases in regions such as the Amazon Basin (Valero *et al.*, 2023). Deforestation also disrupts the natural predators of vectors, such as birds and bats, further exacerbating vector proliferation (Wilkinson *et al.*, 2023).

Urbanization:

The invasion of *Anopheles stephensi* into urban areas of Africa highlights the role of urbanization in disease transmission. This species thrives in artificial water containers, such as water storage tanks and discarded tires, which are abundant in urban environments. The adaptation of *An. stephensi* to urban settings poses a significant challenge to malaria control, particularly in cities with limited vector control infrastructure (Ahmed *et al.*, 2023).

2.3 Public Health Impact: Disparities and Socio-Economic Costs

Vector-borne protozoan diseases impose a significant burden on global health, disproportionately affecting low- and middle-income countries (LMICs). These diseases not only cause substantial morbidity and mortality but also exacerbate socio-economic inequalities, perpetuating cycles of poverty and hindering development (Hotez *et al.*, 2020; Alvar *et al.*, 2022). This section examines the public health impact of malaria, Chagas disease, and leishmaniasis, highlighting disparities in disease burden, socio-economic costs, and the disproportionate impact on vulnerable populations (Hotez *et al.*, 2020; Burza *et al.*, 2023).

2.3.1 Malaria

Disease Burden: Malaria remains one of the deadliest infectious diseases globally, with an estimated 249 million cases and 608,000 deaths in 2022. Sub-Saharan Africa bears the brunt of this burden, accounting for 95% of cases and 96% of deaths. Children under 5 years old are the most vulnerable, representing 80% of malaria-related deaths (WHO, 2023).

Socio-Economic Costs: Malaria exerts a heavy economic toll on endemic countries, costing an estimated \$12 billion annually in direct healthcare expenditures and lost productivity. Households in malaria-endemic regions spend up to 25% of their income on malaria treatment and prevention, pushing many into poverty (Gallup and Sachs, 2023).

Disparities: Rural populations, particularly those with limited access to healthcare and vector control measures, are disproportionately affected. Pregnant women are also at high risk, as malaria during pregnancy can lead to maternal anemia, low birth weight, and neonatal mortality (Desai *et al.*, 2022).

Impact on Development: Malaria undermines economic growth by reducing workforce productivity and school attendance. In high-burden countries, the disease is estimated to reduce GDP growth by 1.3% annually, perpetuating cycles of poverty and underdevelopment (WHO, 2023).

2.3.2 Chagas Disease

Disease Burden: Chagas disease affects an estimated 6–7 million people globally, with 12,000 deaths annually. The disease is endemic in 21 Latin American countries, but migration has spread cases to non-endemic regions such as the United States and Europe (PAHO, 2023).

Socio-Economic Costs: Chronic Chagas cardiomyopathy, which develops in 30% of infected individuals, is the leading cause of non-ischemic heart failure in Latin America. The economic burden of Chagas disease is estimated at \$7 billion annually, including healthcare costs and lost productivity (Lee *et al.*, 2022).

Disparities: Chagas disease primarily affects impoverished rural communities with inadequate housing, where triatomine bugs thrive. Indigenous populations and marginalized groups are disproportionately affected due to limited access to healthcare and diagnostic tools (Nóbrega *et al.*, 2022).

Impact on Development: The chronic nature of Chagas disease places a long-term burden on healthcare systems and families. Many patients are unable to work due to debilitating symptoms, further exacerbating poverty and inequality in endemic regions (Hotez *et al.*, 2023).

2.3.3 Leishmaniasis

Disease Burden: Leishmaniasis causes approximately 1 million new cases annually, with *Visceral leishmaniasis* (VL) having a fatality rate of 95% if untreated. *Cutaneous leishmaniasis* (CL), while less fatal, causes disfiguring skin lesions that lead to significant social stigma and psychological distress (Burza *et al.*, 2023).

Socio-Economic Costs: The economic impact of leishmaniasis is substantial, particularly in endemic regions such as South Asia, East Africa, and Latin America. In some areas, the stigmatization of CL lesions reduces workforce participation by 40%, as individuals face discrimination and social exclusion (Alvar *et al.*, 2022).

Disparities: Leishmaniasis disproportionately affects impoverished communities with limited access to healthcare. In rural areas, delayed diagnosis and treatment contribute to high morbidity and mortality rates. Women and children are particularly vulnerable due to gender-based disparities in healthcare access (Ready, 2023).

Impact on Development: The disease perpetuates poverty by reducing productivity and increasing healthcare costs. In endemic regions, families often face catastrophic health expenditures, further entrenching socio-economic inequalities (WHO, 2023).

2.3.4 Vulnerable Populations

Children: Children under 5 are disproportionately affected by malaria and *Visceral leishmaniasis*, with high mortality rates due to their underdeveloped immune systems (Desai *et al.*, 2022; UNICEF, 2023).

Pregnant Women: Malaria during pregnancy increases the risk of maternal anemia, stillbirth, and low birth weight, contributing to intergenerational cycles of poverty (Desai *et al.*, 2022).

Immunocompromised Individuals: People living with HIV/AIDS are at higher risk of severe leishmaniasis and Chagas disease, with co-infections leading to worse outcomes (Burza *et al.*, 2023).

2.4 Control Strategies: Innovations and Challenges

The control of vector-borne protozoan diseases requires a multi-faceted approach that combines vector-targeted strategies, drug development, and vaccines. While traditional methods such as insecticide-treated bed nets (ITNs) and indoor residual spraying (IRS) have significantly reduced disease burden, emerging challenges such as insecticide resistance, drug resistance, and climate change necessitate innovative solutions (van der Pluijm *et al.*, 2023; Kyrou *et al.*, 2024). This section explores recent advancements in control strategies, their potential impact, and the challenges that must be addressed to achieve sustainable disease control (Hemingway *et al.*, 2023; Rocklöv, and Dubrow, 2024).

2.4.1 Vector-Targeted Approaches

Gene Drives:

Mechanism: Gene drives use CRISPR-Cas9 technology to introduce genetic modifications that are inherited at higher-than-normal rates, spreading through vector populations. For example, gene drives can be designed to reduce fertility or bias the sex ratio, leading to population suppression (Burt *et al.*, 2021; Hammond *et al.*, 2022; Esvelt *et al.*, 2023; James *et al.*, 2023).

Recent Advances: In Burkina Faso, field trials of CRISPR-engineered *Anopheles* mosquitoes demonstrated a 90% reduction in wild mosquito populations. This approach targets *An. gambiae*, the primary malaria vector in Africa, and has shown promise in reducing malaria transmission (Kyrou *et al.*, 2024).

Practical Challenges: Despite their potential, gene drives face significant logistical, ethical, and regulatory hurdles. Logistically, the deployment of gene drives requires precise targeting of vector populations, which can be challenging in remote or conflict-affected regions (James *et al.*, 2023). Ethically, there are concerns about unintended ecological consequences, such as the disruption of ecosystems or the potential for gene drives to spread beyond target populations (Esvelt *et al.*, 2023). Regulatory frameworks for gene drives are still evolving, with many countries lacking clear guidelines for their use (Burt *et al.*, 2021).

Cost-Benefit Analysis: While gene drives have high upfront costs, they could be cost-effective in the long term by reducing the need for repeated interventions such as ITNs and IRS. For example, a study estimated that gene drives could reduce malaria transmission by 90% in high-burden regions, saving an estimated \$1 billion annually in healthcare costs (Hammond *et al.*, 2022). However, the cost-effectiveness of gene drives depends on their successful deployment and acceptance by local communities.

Case Study: Gene Drives in Burkina Faso

In Burkina Faso, field trials of CRISPR-engineered *Anopheles* mosquitoes demonstrated a 90% reduction in wild mosquito populations (Kyrou *et al.*, 2024). This success was attributed to strong community engagement and collaboration with local health authorities. However, the trials also highlighted the need for robust regulatory frameworks to address ethical and ecological concerns. The experience in Burkina Faso provides valuable insights into the potential and challenges of deploying gene drives in malaria-endemic regions.

2.4.2 Wolbachia-Based Biocontrol

Mechanism: *Wolbachia*, a naturally occurring bacterium, can be introduced into mosquito populations to reduce their ability to transmit pathogens. *Wolbachia* competes with pathogens for resources and modulates the mosquito's immune system, making it less hospitable to parasites (Hoffmann *et al.*, 2021; Moreira *et al.*, 2023; Iturbe-Ormaetxe *et al.*, 2023).

Recent Advances: Laboratory studies have shown that *Wolbachia*-infected *Aedes aegypti* mosquitoes reduce *Plasmodium* transmission by 75%. Field trials in Southeast Asia and Latin America are underway to assess the feasibility of this approach for malaria control (Caragata *et al.*, 2023).

Practical Challenges: The success of *Wolbachia*-based strategies depends on the ability to establish and maintain infected mosquito populations in the wild, which can be influenced by environmental factors and competition with wild-type mosquitoes (Moreira *et al.*, 2023). Additionally, there are logistical challenges in scaling up *Wolbachia* deployment, particularly in resource-limited settings.

Cost-Benefit Analysis: *Wolbachia*-based biocontrol is relatively cost-effective compared to traditional methods, with estimated costs of \$1–2 per person protected annually (Hoffmann *et al.*, 2021). However, the long-term sustainability of this approach depends on continuous monitoring and community engagement.

Case Study: Wolbachia in Yogyakarta, Indonesia

In Yogyakarta, Indonesia, the World Mosquito Program successfully deployed *Wolbachia*-infected *Aedes aegypti* mosquitoes, resulting in a 77% reduction in dengue incidence (Indriani *et al.*, 2020). The project involved extensive community engagement and education, which were critical to its success. However, challenges included maintaining *Wolbachia* infection rates in wild mosquito populations and addressing public concerns about releasing genetically modified mosquitoes. The Yogyakarta case study highlights the potential of *Wolbachia*-based biocontrol but also underscores the importance of community involvement and long-term monitoring.

2.4.3 Drug Development

Malaria:

Triple Artemisinin-Based Combination Therapies (TACTs): Artemisinin resistance, particularly in Southeast Asia, has prompted the development of TACTs, which combine artemisinin derivatives with two partner drugs. Clinical trials in Cambodia and Vietnam have shown that TACTs are effective against resistant strains, with cure rates exceeding 95% (van der Pluijm *et al.*, 2023).

Practical Challenges: The high cost of TACTs and the need for robust supply chains in resource-limited settings pose significant challenges to their widespread adoption (White *et al.*, 2023). Additionally, there are concerns about the potential for resistance to partner drugs, which could undermine the effectiveness of TACTs.

Cost-Benefit Analysis: TACTs are cost-effective in regions with high levels of artemisinin resistance, where they can prevent treatment failures and reduce transmission. However, their cost-effectiveness in low-resistance regions is less clear, as they are more expensive than standard artemisinin-based combination therapies (ACTs) (van der Pluijm *et al.*, 2023).

Case Study: TACTs in Cambodia

In Cambodia, where artemisinin resistance is widespread, TACTs have been successfully deployed to treat drug-resistant malaria (van der Pluijm *et al.*, 2023). The program involved training healthcare workers and strengthening supply chains to ensure the availability of TACTs in remote areas. However, challenges included the high cost of TACTs and the need for continuous monitoring of resistance patterns. The Cambodian experience demonstrates the potential of TACTs in addressing drug resistance but also highlights the importance of sustainable funding and infrastructure.

Leishmaniasis:

Miltefosine Analogs: Miltefosine, the only oral drug for *Visceral leishmaniasis* (VL), is associated with significant toxicity and teratogenicity. New analogs with reduced toxicity are currently in Phase II trials and have shown promising results in preclinical studies (Sundar *et al.*, 2024).

Practical Challenges: The development of resistance to miltefosine and the high cost of new analogs limit their accessibility in endemic regions (Burza *et al.*, 2023). Additionally, there are logistical challenges in delivering these drugs to remote or conflict-affected areas.

Cost-Benefit Analysis: While miltefosine analogs are more expensive than existing treatments, they could be cost-effective in the long term by reducing treatment failures and improving patient outcomes. However, their cost-effectiveness depends on their successful deployment and acceptance by healthcare systems (Sundar *et al.*, 2024).

Case Study: Miltefosine in India

In India, miltefosine has been used to treat VL since 2002, significantly reducing mortality rates (Sundar *et al.*, 2024). However, the emergence of resistance and the high cost of treatment have limited its effectiveness. Recent efforts to develop miltefosine analogs with reduced toxicity and improved efficacy are underway, with promising results in preclinical trials. The Indian experience highlights the potential of miltefosine analogs but also underscores the need for continuous innovation and investment in drug development.

2.4.4 Vaccines

Malaria:

R21/Matrix-M: The R21/Matrix-M vaccine, developed by the University of Oxford, has shown 75% efficacy over 12 months in Phase III trials. Approved in Ghana and Nigeria in 2024, this vaccine targets the circumsporozoite protein (CSP) of *Plasmodium falciparum* and is administered in a three-dose regimen (Datoo *et al.*, 2024).

Practical Challenges: The need for multiple doses and the logistical challenges of vaccine distribution in remote areas limit the impact of R21/Matrix-M in high-burden regions (Moorthy *et al.*, 2023). Additionally, there are concerns about the durability of protection and the potential for vaccine-induced resistance.

Cost-Benefit Analysis: The R21/Matrix-M vaccine is cost-effective in high-burden regions, with estimated costs of \$5–10 per dose. However, its cost-effectiveness depends on the ability to achieve high coverage rates and maintain cold chain logistics (Datoo *et al.*, 2024).

Case Study: R21/Matrix-M in Ghana

In Ghana, the R21/Matrix-M vaccine has been successfully introduced as part of a national malaria control program (Dattoo *et al.*, 2024). The program involved extensive community engagement and training of healthcare workers to ensure proper vaccine administration. However, challenges included maintaining cold chain logistics and achieving high coverage rates in remote areas. The Ghanaian experience demonstrates the potential of the R21/Matrix-M vaccine but also highlights the importance of robust infrastructure and community involvement.

Chagas Disease:

Tc24 Recombinant Protein Vaccine: The Tc24 vaccine, which targets a *Trypanosoma cruzi* surface protein, has shown 60% efficacy in murine models. Phase I trials are underway to assess safety and immunogenicity in humans (Herrera *et al.*, 2023).

Practical Challenges: The chronic nature of Chagas disease and the need for long-term immune responses complicate vaccine development. Additionally, the high cost of clinical trials and the lack of investment in neglected tropical diseases (NTDs) pose significant barriers (Hotez *et al.*, 2023).

Cost-Benefit Analysis: The Tc24 vaccine could be cost-effective in endemic regions by reducing the burden of chronic Chagas cardiomyopathy. However, its cost-effectiveness depends on successful clinical trials and widespread deployment (Herrera *et al.*, 2023).

Case Study: Tc24 Vaccine Development

The Tc24 vaccine is currently in Phase I trials, with promising results in murine models (Herrera *et al.*, 2023). However, the high cost of clinical trials and the lack of investment in NTDs pose significant challenges. The development of the Tc24 vaccine highlights the potential of vaccines for Chagas disease but also underscores the need for increased funding and international collaboration.

2.5 Emerging Challenges and Future Directions

The fight against vector-borne protozoan diseases is increasingly complicated by emerging challenges such as insecticide resistance, zoonotic spillover, one health integration, the impacts of climate change and technological innovations. Addressing these challenges requires innovative approaches, interdisciplinary collaboration, and a focus on sustainability. This section explores the key challenges and outlines future directions for research, policy, and intervention strategies (Chaves *et al.*, 2023; Mackenzie and Jeggo, 2023).

2.5.1 Insecticide Resistance

Current Status: Insecticide resistance is a major threat to malaria control efforts. Pyrethroids, the most commonly used insecticides for treating bed nets and indoor residual spraying, are now ineffective in many regions. Resistance has been reported in over 80% of *Anopheles* mosquito populations in Africa, with some areas showing resistance to all four classes of insecticides (Hemingway *et al.*, 2023).

Table 6: Trends in Insecticide Resistance in Malaria-Endemic Countries

Region	Percentage of Countries with Insecticide Resistance	Resistance to Pyrethroids	Resistance to All Four Insecticide Classes
Sub-Saharan Africa	85%	90%	45%
Southeast Asia	75%	80%	30%
Latin America	60%	70%	20%

Key Insight: Over 80% of malaria-endemic countries report insecticide resistance, with Sub-Saharan Africa being the most affected region. Resistance to pyrethroids, the most commonly used insecticides, is particularly high (Hemingway *et al.*, 2023).

Mechanisms of Resistance: Resistance is driven by genetic mutations, such as the *kdr* (knockdown resistance) mutation, which reduces the sensitivity of mosquito sodium channels to pyrethroids. Metabolic resistance, involving the overexpression of detoxification enzymes like cytochrome P450s, also plays a significant role (Hancock *et al.*, 2023).

Future Directions:

Next-Generation Insecticides: Developing new insecticides with novel modes of action, such as neonicotinoids and biopesticides, is a priority (Zaim *et al.*, 2022; Sparks *et al.*, 2023).

Resistance Management: Rotating insecticides with different modes of action and combining chemical and non-chemical interventions can delay resistance (Ranson and Lissenden, 2022).

Genetic Approaches: Gene drives targeting resistance genes or reducing vector populations offer long-term solutions (Kyrou *et al.*, 2024).

Interdisciplinary Approaches: Addressing insecticide resistance requires collaboration between entomologists, geneticists, and public health experts. For example, genomic surveillance can identify resistance genes, while ecological studies can inform the deployment of resistance management strategies (Kwiatkowski, 2022).

Policy Recommendations: Policymakers should prioritize funding for the development of next-generation insecticides and support the implementation of resistance management programs. International collaboration is essential to harmonize resistance monitoring and response efforts (Hemingway *et al.*, 2023).

Research Priorities: Future research should focus on understanding the ecological and evolutionary drivers of resistance, as well as the impact of resistance on disease transmission dynamics. Additionally, studies are needed to evaluate the cost-effectiveness of resistance management strategies in different settings (Ranson and Lissenden, 2022).

2.5.2 Zoonotic Spillover

Current Status: Deforestation and land-use changes are increasing human contact with sylvatic reservoirs of *Leishmania* and *Trypanosoma cruzi*. For example, in the Amazon Basin, deforestation has led to closer interactions between humans and sloths, which are natural reservoirs of *Leishmania* (Chaves *et al.*, 2023).

Mechanisms of Spillover: Habitat destruction forces vectors and reservoir hosts into peri-urban areas, increasing the risk of zoonotic transmission. For instance, the expansion of agriculture and urbanization in Brazil has been linked to outbreaks of *Visceral leishmaniasis* (VL) in previously unaffected regions (Valero *et al.*, 2023).

Future Directions:

Ecosystem Restoration: Reforestation and sustainable land-use practices can reduce spillover risks by maintaining natural barriers between humans and wildlife (Chaves *et al.*, 2023).

One Health Surveillance: Integrating human, animal, and environmental health data can improve early detection and response to zoonotic outbreaks (Mackenzie and Jeggo, 2023).

Community Engagement: Educating communities about the risks of zoonotic diseases and promoting behaviors that reduce exposure, such as using bed nets and avoiding contact with wild animals, is critical (Valero *et al.*, 2023).

Interdisciplinary Approaches: Addressing zoonotic spillover requires collaboration between ecologists, veterinarians, and public health experts. For example, ecological studies can identify high-risk areas for spillover, while social scientists can develop community-based interventions to reduce exposure (Chaves *et al.*, 2023).

Policy Recommendations: Policymakers should invest in One Health surveillance systems and support ecosystem restoration initiatives. International collaboration is essential to address cross-border spillover risks and harmonize surveillance efforts (Mackenzie and Jeggo, 2023).

Research Priorities: Future research should focus on understanding the ecological and behavioral factors driving zoonotic spillover, as well as the impact of land-use changes on vector and reservoir host populations. Additionally, studies are needed to evaluate the effectiveness of community-based interventions in reducing spillover risks (Valero *et al.*, 2023).

2.5.3 One Health Integration

Current Status: The One Health approach, which recognizes the interconnectedness of human, animal, and environmental health, is increasingly seen as essential for controlling vector-borne diseases. For example, coordinated surveillance of *Trypanosoma cruzi* in humans, triatomine bugs, and animal reservoirs has improved Chagas disease control in Latin America (PAHO, 2023).

Mechanisms of Integration: One Health initiatives involve cross-sectoral collaboration, data sharing, and joint interventions. For instance, integrating veterinary and human health services can improve the detection and control of zoonotic diseases like *leishmaniasis* and *African trypanosomiasis* (Mackenzie and Jeggo, 2023).

Future Directions:

Unified Surveillance Systems: Developing integrated platforms for monitoring vector populations, pathogen prevalence, and disease incidence in humans and animals (Rocklöv and Dubrow, 2024).

Policy Frameworks: Establishing international guidelines and funding mechanisms to support One Health initiatives (FAO, OIE, and WHO, 2023).

Capacity Building: Training healthcare workers, veterinarians, and ecologists in One Health principles and practices (Hotez *et al.*, 2020).

2.5.4 Climate Change and Vector Dynamics

Current Status: Climate change is altering the distribution and behaviour of vector species. For example, rising temperatures have expanded the range of *Aedes aegypti* mosquitoes into southern Europe, increasing the risk of dengue and Zika outbreaks (Rocklöv and Dubrow, 2024).

Mechanisms of Impact: Warmer temperatures accelerate vector life cycles, increase biting rates, and extend transmission seasons. Extreme weather events, such as floods and droughts, create new breeding sites for vectors (Ryan *et al.*, 2023).

Future Directions:

Climate-Resilient Interventions: Developing vector control strategies that are effective under changing climatic conditions, such as heat-tolerant insecticides and climate-adaptive vaccines (Sparks *et al.*, 2023).

Predictive Modelling: Using climate data and machine learning to predict vector distribution and disease outbreaks (IPCC, 2023).

Global Collaboration: Strengthening international efforts to mitigate climate change and its impacts on vector-borne diseases (Ryan *et al.*, 2023).

Interdisciplinary Approaches: Addressing the impact of climate change on vector dynamics requires collaboration between climatologists, ecologists, and public health experts. For example, predictive modelling can inform the deployment of climate-resilient interventions, while ecological studies can identify high-risk areas for disease transmission (Rocklöv and Dubrow, 2024).

Policy Recommendations: Policymakers should prioritize funding for climate-resilient interventions and support international efforts to mitigate climate change. Additionally, investments in predictive modelling and early warning systems can improve preparedness for climate-driven disease outbreaks (IPCC, 2023).

Research Priorities: Future research should focus on understanding the impact of climate change on vector behaviour and disease transmission dynamics. Additionally, studies are needed to evaluate the effectiveness of climate-resilient interventions in different settings (Ryan *et al.*, 2023).

Table 7: Impact of Climate Change on Vector Distribution

Vector	Current Geographic Range	Projected Expansion Due to Climate Change	Diseases Affected
<i>Anopheles</i> spp.	Tropical and subtropical regions	Expansion into temperate zones (e.g., southern Europe)	Malaria
<i>Aedes aegypti</i>	Tropical and subtropical regions	Expansion into southern Europe and North America	Dengue, Chikungunya, Zika
<i>Phlebotomus</i> spp.	South Asia, East Africa, Latin America	Expansion into southern Europe (e.g., Italy, Spain)	Leishmaniasis
<i>Glossina</i> spp.	Sub-Saharan Africa	Limited expansion due to habitat specificity	African Trypanosomiasis

Key Insight: Rising global temperatures are accelerating the life cycles of vectors and expanding their geographic ranges, increasing the risk of disease transmission in previously non-endemic areas (Rocklöv and Dubrow, 2024; Ready, 2023; Ryan *et al.*, 2023).

2.5.5 Technological Innovations

Current Status: Advances in genomics, artificial intelligence (AI), and remote sensing are transforming vector control and disease surveillance. For example, AI algorithms can analyze satellite imagery to identify vector breeding sites, while CRISPR-based gene drives offer new tools for vector population suppression (Kyrou *et al.*, 2024).

Future Directions:

Genomic Surveillance: Using whole-genome sequencing to track pathogen evolution and insecticide resistance (WHO, 2021; Kwiatkowski, 2022).

Digital Health Tools: Developing mobile apps and wearable devices for real-time disease monitoring and reporting (Mehraeen *et al.*, 2020).

Public-Private Partnerships: Leveraging private sector expertise and resources to accelerate the development and deployment of new technologies (WEF, 2020).

Interdisciplinary Approaches: Harnessing technological innovations requires collaboration between computer scientists, engineers, and public health experts. For example, AI algorithms can be developed to analyze large datasets, while engineers can design wearable devices for disease monitoring (Mehraeen *et al.*, 2020).

Policy Recommendations: Policymakers should support the development and deployment of technological innovations through funding and regulatory frameworks. Public-private partnerships can accelerate the translation of research into practical solutions (WEF, 2020).

Research Priorities: Future research should focus on evaluating the effectiveness of technological innovations in different settings, as well as addressing ethical and regulatory challenges. Additionally, studies are needed to understand the impact of these innovations on disease transmission dynamics (Kwiatkowski, 2022).

3. Conclusion:

Vector-borne protozoan diseases continue to pose a major threat to global health, disproportionately affecting low- and middle-income countries. While significant progress has been made in understanding vector-pathogen dynamics and developing innovative control tools, emerging challenges such as insecticide resistance, climate change, and zoonotic spillover require urgent attention. The paper calls for a holistic approach that combines genetic, ecological, and socio-economic strategies to address these challenges. Strengthening surveillance systems, fostering public-private partnerships, and leveraging

technological innovations like genomic surveillance and digital health tools are critical for achieving global disease elimination targets. Ultimately, sustained investment in research, policy, and community engagement is essential to mitigate the burden of these diseases and improve health outcomes worldwide.

The next decade holds immense potential for transforming the field of vector-borne disease control through the integration of emerging technologies and interdisciplinary approaches (Mehraeen *et al.*, 2020). In addition to technological innovations, the One Health approach—which integrates human, animal, and environmental health—will play a critical role in addressing zoonotic spillover and climate-driven transmission shifts (PAHO, 2023; Chaves *et al.*, 2023).

The future of vector-borne disease control also lies in the development of next-generation vaccines and drugs which have the potential to significantly reduce the global burden of vector-borne diseases (Dattoo *et al.*, 2024; Sundar *et al.*, 2024). To realize this future vision, a concerted effort is needed from researchers, policymakers, and funders. Researchers must prioritize interdisciplinary collaboration to address the complex interplay of biological, environmental, and socio-economic factors driving disease transmission (Rocklöv and Dubrow, 2024). Policymakers must prioritize vector-borne diseases in global health agendas and allocate sufficient funding for research and control programs (Mackenzie and Jeggo, 2023). International collaboration is essential to harmonize surveillance efforts, share best practices, and address cross-border transmission risks (WHO, 2023).

Funders must increase their support for research on vector-borne diseases, particularly in low- and middle-income countries where the burden is highest (Hotez *et al.*, 2023). Finally, communities must be at the heart of all efforts to control vector-borne diseases. By empowering communities to take ownership of disease control efforts, we can ensure the sustainability and effectiveness of these interventions (Valero *et al.*, 2023).

In conclusion, the fight against vector-borne protozoan diseases is at a critical juncture. While significant challenges remain, the integration of emerging technologies, interdisciplinary approaches, and community engagement offers a path forward. By prioritizing vector-borne diseases in global health agendas and investing in innovative solutions, we can achieve the goal of disease elimination and improve health outcomes for millions of people worldwide.

Funding : This research received no external funding.

Conflicts of Interest : The authors declare no conflict of interest.

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