Italian Journal of Medicine

https://www.italjmed.org/ijm

eISSN 1877-9352

Publisher's Disclaimer. E-publishing ahead of print is increasingly important for the rapid dissemination of science. The Early Access service lets users access peer-reviewed articles well before print/regular issue publication, significantly reducing the time it takes for critical findings to reach the research community.
These articles are searchable and citable by their DOI (Digital Object Identifier).

The **Italian Journal of Medicine** is, therefore, E-publishing PDF files of an early version of manuscripts that have undergone a regular peer review and have been accepted for publication, but have not been through the copyediting, typesetting, pagination, and proofreading processes, which may lead to differences between this version and the final one.

The final version of the manuscript will then appear in a regular issue of the journal.

The E-publishing of this PDF file has been approved by the authors.

Ital J Med 2025 [Online ahead of print]

Please cite this article as:

Siniscalchi C, Coppola MG, Cardillo G, et al. **Globalization, climate change, and the re-emergence of West Nile, Dengue, and Zika viruses**. *Ital J Med* doi: 10.4081/itjm.2025.2404

Submitted: 13-11-2025
Accepted: 01-12-2025

© the Author(s), 2025
Licensee PAGEPress, Italy

Note: The publisher is not responsible for the content or functionality of any supporting information supplied by the authors. Any queries should be directed to the corresponding author for the article.
All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Globalization, climate change, and the re-emergence of West Nile, Dengue, and Zika viruses

Carmine Siniscalchi,[1] Maria Gabriella Coppola,[2] Giuseppe Cardillo,[3] Egidio Imbalzano,[4] Manuela Basaglia,[1] Rodolfo Nasti,[5] Vincenzo Russo,[6] Pierpaolo Di Micco[7]

[1]Internal Medicine Department, Parma University Hospital; [2]Internal Medicine Department, San Pio Hospital, Benevento; [3]MedyLab SRL, Bologna; [4]Department of Clinical and Experimental Medicine, University of Messina; [5]Internal Medicine Unit, Ospedale Evangelico Villa Betania, Naples; [6]Department of Translational Science, Vanvitelli University, Caserta; [7]Internal Medicine Ward, Department of Internal Medicine, Santa Maria delle Grazie Hospital, Naples, Italy

Correspondence: Pierpaolo Di Micco, Department of Internal Medicine, Internal Medicine Ward, Santa Maria delle Grazie Hospital, Naples, Italy.
E-mail: pdimicco@libero.it

Key words: West Nile virus, Dengue virus, Zika virus, globalization, climate change.

Contributions: CS, conceptualization, methodology, validation; CS, PDM, formal analysis, investigation, resources; CS, MGC, GC, EI, MB, PDM, data curation, writing—original draft preparation, writing—review and editing, visualization, supervision, project administration. All authors have read and agreed to the published version of the manuscript.

Conflict of interest: the authors declare that they have no competing interests and all authors confirm accuracy.

Ethics approval and consent to participate: not applicable.

Informed consent: not applicable.

Patient consent for publication: not applicable.

Availability of data and materials: no new data were created or analyzed in this study. Data sharing is not applicable to this article.

Funding: none.

AI use statement: Artificial intelligence-assisted text generation software (ChatGPT, OpenAI, San Francisco, CA, USA) was employed to aid in language editing and organization of the manuscript. The tool was used solely to enhance clarity and style. All content, interpretations, and conclusions were conceived, written, and critically reviewed by the authors, who revised every part of the text to ensure its accuracy, originality, and scientific quality. The authors have reviewed and edited the output and take full responsibility for the content of this publication.

Abstract

Vector-borne viral infections such as West Nile virus (WNV), Dengue virus (DENV), and Zika virus (ZIKV) exemplify how globalization, climate change, and ecological disruption are reshaping the geography of infectious diseases. These flaviviruses, transmitted primarily by *Culex* and *Aedes* mosquitoes, have expanded their range beyond traditional tropical and subtropical boundaries, establishing endemic and epidemic cycles in temperate regions. Rising global temperatures, altered rainfall patterns, and urbanization enhance vector breeding, accelerate viral replication, and prolong transmission seasons. Clinically, WNV typically causes asymptomatic or mild febrile illness, though a minority of infections progress to severe neuroinvasive disease, especially in older or immunocompromised individuals. DENV, characterized by four antigenically distinct serotypes, can result in severe DENV due to antibody-dependent enhancement and immune dysregulation. ZIKV infection, often mild or asymptomatic, has revealed serious neurotropic potential, being associated with congenital Zika syndrome and Guillain-Barré syndrome during major outbreaks in the Americas and Pacific Islands. Diagnosis relies on molecular and serological assays, though cross-reactivity between flaviviruses remains a challenge. No specific antiviral therapies are currently available, and prevention depends on integrated vector management, personal protection, and surveillance. Vaccines for DENV are available with serostatus-dependent indications, while those for WNV and ZIKV are under investigation. Understanding the shared ecological and epidemiological determinants of these infections within a One Health framework is crucial to strengthening surveillance, guiding vaccine implementation, and building resilience against future arboviral threats intensified by climate and environmental change.

Introduction

Vector-borne diseases (VBDs) remain a major global health burden, accounting for over 17% of all infectious diseases and causing more than 700,000 deaths each year. Their transmission dynamics reflect a complex interplay between biological, environmental, and social determinants. Among them, West Nile virus (WNV),[1] Dengue virus (DENV), and Zika Virus (ZIKV) represent three paradigmatic mosquito-borne infections that exemplify the growing impact of climate change, globalization, and vector adaptation on emerging and re-emerging pathogens.[2]

Over the last two decades, these diseases have undergone substantial epidemiological shifts. WNV, once confined to Africa and the Middle East, has established endemic transmission across Europe and the Americas, becoming a key public health concern in temperate regions.[3] DENV, historically restricted to tropical and subtropical zones, now affects more than 120 countries and has recently produced autochthonous outbreaks in southern Europe, reflecting the expanding range of *Aedes albopictus*.

Climate change is a crucial driver of these trends. Rising global temperatures, irregular precipitation, and prolonged humid seasons enhance mosquito breeding, accelerate pathogen replication within vectors, and extend the transmission period.[4] These climatic changes, coupled with urbanization, deforestation, and increased human mobility, have facilitated the northward expansion of mosquitoes into previously non-endemic regions.

While biologically distinct, WNV, DENV, and ZIKV, being flaviviruses, these infections share common determinants of vulnerability: poverty, inadequate sanitation, limited healthcare access, and disrupted vector control programs. The COVID-19 pandemic further exacerbated these vulnerabilities by diverting resources from surveillance and prevention, leading to resurgent vector populations and delayed case detection in several countries.[4] In this context, traditional disease-specific control strategies are insufficient. The One Health approach, integrating human, animal, and environmental surveillance, has become essential for early outbreak detection, risk assessment, and coordinated interventions. Understanding the overlapping ecological and epidemiological mechanisms of these diseases is vital to guide integrated prevention policies, strengthen health systems, and mitigate the global impact of vector-borne infections.

This review aims to provide a concise comparative overview of WNV, DENV, and ZIKV, focusing on their epidemiological characteristics, clinical manifestations, and preventive strategies, while highlighting shared determinants and future public health challenges.

Overview of major arboviruses: West Nile, Dengue, and Zika viruses

West Nile virus

The WNV is a single-stranded, positive-sense RNA virus belonging to the *Flavivirus* genus within the *Flaviviridae* family.[5,6] It is maintained in a bird-mosquito transmission cycle, primarily involving *Culex pipiens* and *Culex modestus* species, with humans and other mammals acting as incidental “dead-end” hosts due to their low-level viraemia.[5,6] Since its initial isolation in Uganda in 1937, WNV has evolved into one of the most widespread arboviruses globally, with endemic transmission documented across Africa, the Middle East, Europe, and the Americas.[5,6]

In Europe, WNV infection has transitioned from sporadic to endemic circulation over the last 2 decades.[7] Italy, Greece, and Hungary are among the most affected European countries, with recurrent outbreaks since the late 2000s. Climatic factors, such as milder winters and increased rainfall, have prolonged mosquito breeding seasons and facilitated viral overwintering. Furthermore, migratory bird routes contribute to interregional dissemination, supporting the persistence of multiple viral lineages.[7] Clinically, approximately 80% of human infections are asymptomatic. Around 20% present with a self-limiting febrile illness, often referred to as “West Nile fever”, characterized by fever, headache, myalgia, and occasionally rash. Less than 1% of infections progress to neuroinvasive disease, which includes meningitis, encephalitis, or acute flaccid paralysis. Neuroinvasive disease predominantly affects older adults and immunocompromised individuals and is associated with high morbidity and mortality.[8]

Diagnosis relies on detection of WNV-specific IgM in serum or cerebrospinal fluid, confirmed by neutralization assays, or by reverse transcription polymerase chain reaction (RT-PCR) when viraemia is present. No specific antiviral therapy has been approved. Management remains supportive, though experimental and compassionate use of antivirals such as remdesivir has been reported. Prevention focuses on integrated vector control, mosquito surveillance, public education, and blood donor screening.

Dengue virus

DENV is a single-stranded, positive-sense RNA virus belonging to the *Flavivirus* genus, closely related to other arboviruses such as WNV, ZIKV, and yellow fever viruses. It is transmitted primarily by *Aedes aegypti* and, to a lesser extent, *Aedes albopictus* mosquitoes. DENV is now endemic in more than 120 countries and represents the most prevalent arboviral infection worldwide, with an estimated 390 million infections annually, of which approximately 100 million are symptomatic.

The global expansion of DENV is attributed to urbanization, globalization, increased air travel, and climate variability. *Aedes albopictus*, originally confined to Southeast Asia, has spread to temperate regions, including southern Europe, facilitated by rising temperatures and adaptability to peridomestic breeding sites.[9]

DENV exists as four antigenically distinct serotypes (DENV-1 to DENV-4), each capable of causing disease. Infection with one serotype confers lifelong immunity to that serotype but only transient protection against others. Sequential infection with a different serotype increases the risk of severe disease due to antibody-dependent enhancement.[10] Severe DENV manifests with plasma leakage, coagulopathy, and multiorgan involvement. There is no specific antiviral therapy; management is primarily supportive.

Zica virus

ZIKV is a mosquito-borne flavivirus closely related to DENV, WNV, and yellow fever viruses. It was first identified in Uganda in 1947 in *Aedes africanus* mosquitoes, but remained neglected until the large outbreaks in the Pacific Islands (2013-2014) and the Americas (2015-2016). The principal vectors are *Aedes aegypti* and *Aedes albopictus*, which also transmit DENV and chikungunya viruses. Transmission occurs primarily via mosquito bites, but vertical, sexual, and transfusion-related routes have also been documented, highlighting its unique epidemiological profile among arboviruses.[11]

Most ZIKV infections are asymptomatic or present as a mild, self-limiting febrile illness characterized by rash, arthralgia, myalgia, and conjunctivitis. However, the 2015-2016 epidemic revealed the virus’s neurotropic potential, notably its association with congenital Zika syndrome, featuring microcephaly and other severe neurological malformations in fetuses of infected pregnant women. In adults, post-infectious complications such as Guillain-Barré syndrome have also been observed.[12,13]

Diagnosis relies on RT-PCR for viral RNA in serum, urine, or saliva during the acute phase, and on serological assays in later stages. Cross-reactivity with other flaviviruses, especially DENV, poses a diagnostic challenge in endemic regions. No specific antiviral therapy is available, and management remains supportive. Prevention focuses on mosquito control, personal protection, and pregnancy-related travel advisories. Research into ZIKV vaccines is ongoing, with several DNA, mRNA, and inactivated vaccine candidates in various stages of clinical trials.[14]

The resurgence risk of ZIKV in tropical and subtropical regions underscores how climate change and *Aedes* vector expansion continue to threaten global health security. The silent re-emergence potential of ZIKV demands sustained surveillance, integrated vector management (IVM), and prioritization of maternal-fetal health monitoring within the One Health framework

Shared epidemiological drivers and prevention strategies

WNV, DENV and ZIKV share fundamental ecological and epidemiological determinants that transcend their biological differences. All three diseases depend on mosquito vectors whose life cycles are profoundly influenced by climatic, environmental, and anthropogenic factors. Rising global temperatures, irregular precipitation, and increased humidity extend mosquito breeding seasons, accelerate larval development, and shorten incubation periods.[15,16]

Urbanization and globalization have further accelerated disease spread. Rapid, unplanned urban growth often creates ideal breeding habitats for *Aedes* mosquitoes through stagnant water in discarded containers and poorly managed drainage systems. Similarly, increased international mobility and trade facilitate the movement of infected humans and vectors, contributing to local transmission in temperate regions. Socio-economic vulnerability remains a central driver. Limited access to clean water, inadequate sanitation, and insufficient healthcare infrastructure hinder prevention and early diagnosis, particularly in low- and middle-income countries. Together, with a clear correlation with environmental, ecological, climatic and socio-economic factors, in these recent years in which globalization is present and the number of travelers is increasing around the world, as well as the number of migrants from disadvantaged countries to western countries for any reason, an associated increased risk of having small outbreaks of these vector-related diseases is present. International travels and travelers may make it easy to spread of vector-related diseases, and for this reason, the prevention and control programs to limit this risk should be applied as soon as possible.

IVM represents the cornerstone of prevention across these infections. Surveillance systems increasingly incorporate molecular and entomological data, enabling early detection of viral circulation or insecticide resistance. Moreover, the One Health approach, linking human, animal, and environmental health, has become critical for WNV control, where birds serve as amplifying hosts.[17,18]

Future perspectives and global health preparedness

The convergence of climate change, globalization, and ecological disruption has transformed the epidemiology of mosquito-borne viral infections, necessitating a paradigm shift in public health preparedness. The future of WNV, DENV, and ZIKV control depends on a dynamic integration of surveillance, predictive modelling, vaccine innovation, and community engagement within a sustainable One Health framework. Climate projections indicate that by 2050, nearly half of the world's population could be at risk of DENV infection due to the continued expansion of *Aedes aegypti* and *Aedes albopictus* into temperate zones.[19] Similarly, WNV is likely to become a recurrent seasonal infection in southern and central Europe, driven by warmer winters, increased vector survival, and migratory bird routes serving as viral reservoirs.[20] These evolving patterns underscore that the traditional concept of "tropical diseases" is no longer valid; vector-borne viruses are becoming truly global health concerns.[21]

A key future challenge lies in the development and implementation of predictive surveillance systems that integrate climate, entomological, and genomic data. Advances in artificial intelligence and machine learning have enabled early-warning models capable of forecasting outbreak probability based on temperature, precipitation, and vegetation indices.[20,21] However, the translation of these models into public health action remains limited by fragmented governance and insufficient intersectoral coordination. Strengthening real-time data sharing between meteorological, environmental, and health institutions will be crucial to anticipate and mitigate outbreaks rather than merely responding to them.

Another pressing issue is the emergence of insecticide resistance, which threatens the efficacy of current vector control measures. Novel strategies offer promising avenues but raise ethical, ecological, and regulatory questions that require global consensus.[22] At the same time, vaccine development for flaviviruses must adapt to evolving epidemiological realities. For DENV, achieving safe and effective immunization across serotypes remains complex due to antibody-dependent enhancement, while ZIKV and WNV vaccines are still in experimental phases.[19,22] Global partnerships and equitable access will determine whether these tools can reach populations at greatest risk.[20,23]

Furthermore, global health preparedness must extend beyond biomedical innovation to address social vulnerability. Urban overcrowding, inadequate housing, poor waste management, and health inequity continue to fuel transmission cycles.[23] Strengthening community-based surveillance and public awareness is therefore essential. The COVID-19 pandemic demonstrated both the fragility and resilience of health systems: while it disrupted vector control programs, it also accelerated digital health integration, telemedicine, and genomic surveillance, all of which can be leveraged for arboviral preparedness.[21,23]

In the coming decades, success in controlling WNV, DENV, and ZIKV will depend on sustained international cooperation, data-driven policy-making, and investment in adaptive public health infrastructure.[22] The global nature of these infections demands collective accountability, transcending geopolitical boundaries. Ultimately, embracing an anticipatory, interdisciplinary, and equitable approach will be the cornerstone of resilience against the next generation of vector-borne viral threats.[19,20]

Table 1 summarizes the principal epidemiological, clinical, and preventive features of three major mosquito-borne flaviviruses, WNV, DENV, and ZIKV. Although these viruses differ in geographic distribution and clinical spectrum, they share similar transmission dynamics, with *Aedes* and *Culex* mosquitoes acting as vectors. While WNV is mainly associated with neuroinvasive disease in elderly or immunocompromised patients, DENV and ZIKV predominantly cause febrile illnesses with possible severe complications such as plasma leakage or neurological involvement. No specific antiviral therapy is currently available for any of these infections; prevention relies on vector control and, in selected cases, vaccination or travel precautions.

Table 2 highlights the common ecological and socioeconomic determinants influencing the transmission of WNV, DENV, and ZIKV, as well as key preventive and control strategies. Factors such as climate change, urbanization, and global mobility contribute to the expansion of mosquito habitats and the emergence of arboviral outbreaks in temperate regions. IVM, the One Health approach, vaccination, and data-driven surveillance represent essential pillars for long-term prevention and global preparedness.

Figure 1 shows the conceptual representation of the main environmental and socio-ecological drivers contributing to the re-emergence and geographic expansion of mosquito-borne flaviviruses. The intersection of climate change, globalization, and urbanization illustrates how rising temperatures, human mobility, and ecosystem disruption interact to facilitate vector proliferation, viral amplification, and transmission in both tropical and temperate regions. This framework highlights the importance of an integrated One Health approach to anticipate and mitigate future arboviral threats.

Discussion

The growing global burden of VBDs, such as WNV, DENV, and ZIKV, reflects a complex interaction between climate, ecology, and human behavior. These infections, despite their different etiological agents and clinical presentations, share convergent epidemiological patterns that highlight the fragility of current public health systems. Their spread into temperate regions demonstrates how global warming, urban expansion, and increased international mobility have reshaped the geographic range of vector species and the pathogens they transmit.[24]

A central challenge lies in the adaptive capacity of mosquito vectors. *Aedes albopictus*, once limited to tropical Asia, now thrives in southern and central Europe, acting as a competent vector for DENV and potentially other arboviruses. These ecological shifts indicate that climate mitigation alone is insufficient; instead, integrated and anticipatory surveillance is required to detect and contain outbreaks before they become established.[25,26]

From a clinical perspective, the overlapping symptomatology of these infections, fever, malaise, and neurological or systemic complications, creates diagnostic uncertainty, particularly in resource-limited settings. Laboratory confirmation often depends on specialized assays, including RT-PCR and serology, which may be unavailable during peak transmission seasons. Consequently, underdiagnosis and misclassification persist, obscuring the true epidemiological burden.[27]

Preventive strategies must therefore extend beyond reactive responses. IVM (IVM), combining environmental control, biological larvicides, and community engagement, remains the cornerstone of mosquito-borne disease prevention. However, insecticide resistance among *Anopheles* and *Aedes* populations threatens the effectiveness of traditional interventions.

Ultimately, these diseases underscore the necessity of a One Health approach, recognizing that human health is inseparable from that of animals and ecosystems. Coordinated surveillance integrating veterinary, entomological, and environmental data is critical to detect zoonotic amplification and vector dynamics in real time. Furthermore, socioeconomic inequities, limited access to healthcare, inadequate housing, and poor sanitation continue to amplify vulnerability to infection and must be addressed through cross-sectoral investment.

In summary, the persistence and expansion of WNV, DENV, and ZIKV exemplify how environmental disruption and globalization are transforming infectious disease landscapes. Sustained surveillance, equitable access to prevention tools, and long-term adaptation strategies are imperative to mitigate the next wave of VBDs emergence.

Conclusions

VBDs s such as WNV infection, DENV, and ZIKV exemplify the intersection between human, environmental, and ecological health. Despite their different etiologies, these infections share determinants of emergence climate change, urbanization, and inequality that drive their persistence in both endemic and temperate regions.

References

1. Carrasco L, Utrilla MJ, Fuentes-Romero B, et al. West nile virus: an update focusing on southern Europe. Microorganisms 2024;12:2623.
2. Young JJ, Haussig JM, Aberle SW, et al. Epidemiology of human West Nile virus infections in the European Union and European Union enlargement countries, 2010 to 2018. Euro Surveill 2021;26:2001095.
3. Brady OJ, Hay SI. The Global Expansion of Dengue: how *Aedes aegypti* mosquitoes enabled the first pandemic arbovirus. Annu Rev Entomol 2020;65:191-208.
4. Ryan SJ, Carlson CJ, Mordecai EA, Johnson LR. Global expansion and redistribution of Aedes-borne virus transmission risk with climate change. PLoS Negl Trop Dis 2019;13:e0007213.
5. Colpitts TM, Conway MJ, Montgomery RR, Fikrig E. West nile virus: biology, transmission, and human infection. Clin Microbiol Rev 2012;25:635-48.
6. van den Elsen K, Quek JP, Luo D. Molecular insights into the flavivirus replication complex. Viruses 2021;13:956.
7. Sewgobind S, McCracken F, Schilling M. JMM Profile: West Nile virus. J Med Microbiol. 2023 Jul;72(7). doi: 10.1099/jmm.0.001730.
8. Sejvar JJ. Clinical manifestations and outcomes of West Nile virus infection. Viruses 2014;6:606-23.
9. Oliveira S, Rocha J, Sousa CA, Capinha C. Wide and increasing suitability for Aedes albopictus in Europe is congruent across distribution models. Sci Rep 2021;11:9916.
10. Guzman MG, Vazquez S. The complexity of antibody-dependent enhancement of dengue virus infection. Viruses 2010;2:2649-62.
11. Musso D, Gubler DJ. Zika Virus. Clin Microbiol Rev 2016;29:487-524.
12. Mlakar J, Korva M, Tul N, et al. Zika virus associated with microcephaly. N Engl J Med 2016;374:951-8.
13. Cao-Lormeau VM, Blake A, Mons S, et al. Guillain-Barré syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study. Lancet 2016;387:1531-9.
14. Modjarrad K, Lin L, George SL, et al. Preliminary aggregate safety and immunogenicity results from three trials of a purified inactivated Zika virus vaccine candidate: phase 1, randomised, double-blind, placebo-controlled clinical trials. Lancet 2018;391:563-71.
15. Lowe R, Barcellos C, Brasil P, et al. The Zika virus epidemic in Brazil: from discovery to future implications. Int J Environ Res Public Health 2018;15:96.

16. Caminade C, McIntyre KM, Jones AE. Impact of recent and future climate change on vector-borne diseases. Ann N Y Acad Sci 2019;1436:157-73.

17. Lizzi KM, Qualls WA, Brown SC, Beier JC. Expanding integrated vector management to promote healthy environments. Trends Parasitol 2014;30:394-400.

18. Robbiati C, Milano A, Declich S, Dente MG. One Health prevention and preparedness to vector-borne diseases: how should we deal with a multisectoral, multilevel and multigroup governance? One Health Outlook 2024;6:21.

19. Thomson MC, Stanberry LR. Climate change and vectorborne diseases. N Engl J Med 2022;387:1969-78.

20. Colón-González FJ, Sewe MO, Tompkins AM, et al. Projecting the risk of mosquito-borne diseases in a warmer and more populated world: a multi-model, multi-scenario intercomparison modelling study. Lancet Planet Health 2021;5:e404-14.

21. Islam J, Frentiu FD, Devine GJ, et al. A state-of-the-science review of long-term predictions of climate change impacts on Dengue transmission risk. Environ Health Perspect 2025;133:56002.

22. Abbasi E. The impact of climate change on travel-related vector-borne diseases: a case study on dengue virus transmission. Travel Med Infect Dis 2025;65:102841.

23. Sambado S, Sparkman A, Swei A, et al. Climate-driven variation in the phenology of juvenile Ixodes pacificus on lizard hosts. Parasit Vectors 2025;18:141.

24. Sibani M, Mazzaferri F, Carrara E, et al. White paper: bridging the gap between surveillance data and antimicrobial stewardship in long-term care facilities-practical guidance from the JPIAMR ARCH and COMBACTE-MAGNET EPI-Net networks. J Antimicrob Chemother 2020;75:ii33-41.

25. Medlock JM, Hansford KM, Schaffner F, et al. A review of the invasive mosquitoes in Europe: ecology, public health risks, and control options. Vector Borne Zoonotic Dis 2012;12:435-47.

26. D'Amore C, Grimaldi P, Ascione T, et al. West Nile Virus diffusion in temperate regions and climate change. A systematic review. Infez Med 2023;31:20-30.

27. Peper ST, Jones AC, Webb CR, et al. Consideration of vector-borne and zoonotic diseases during differential diagnosis. South Med J 2021;114:277-82.

Table 1. Epidemiological and clinical comparison of West Nile Virus, Dengue, and malaria.

Feature	West Nile virus	Dengue virus	Malaria
Pathogen type	RNA virus (*Flavivirus* genus)	RNA virus (*Flavivirus* genus)	Protozoan (*Plasmodium* spp.)
Primary vector	*Culex pipiens*, *C. modestus*	*Aedes aegypti*, *A. albopictus*	*Anopheles* spp.
Geographic distribution	Africa, Middle East, Europe, Americas	>120 tropical and subtropical countries	Sub-Saharan Africa, Asia, Latin America
Reservoir hosts	Birds (amplifying hosts)	Humans	Humans (primary), some primates
Incubation period	2-14 days	4-10 days	7-30 days
Clinical spectrum	Mostly asymptomatic; <1% neuroinvasive (encephalitis, meningitis)	Febrile illness → severe dengue with plasma leakage, hemorrhage	Febrile illness → severe malaria (anemia, cerebral malaria, multiorgan failure)
High-risk groups	Elderly, immunocompromised	Children, secondary infection cases	Children, pregnant women
Case fatality rate	4–10% in neuroinvasive disease	<1% (higher in severe dengue)	0.3–2% (up to 20% in severe malaria)
Diagnosis	IgM/IgG ELISA, RT-PCR, CSF testing	NS1 antigen, RT-PCR, serology	Microscopy, rapid antigen test, PCR
Specific therapy	None (supportive only)	None (supportive only)	Artemisinin-based combination therapy
Vaccine availability	Under development	CYD-TDV, TAK-003	RTS,S/AS01, R21/Matrix-M
Main prevention	Vector control, donor screening	Vector control, vaccination	Bed nets, spraying, vaccination

IgM/IgG ELISA, immunoglobulin M/immunoglobulin G enzyme-linked immunosorbent assay; RT-PCR, reverse transcription polymerase chain reaction; CSF, cerebrospinal fluid.

Table 2. Shared drivers and integrated prevention strategies in vector-borne diseases

Determinant/Strategy	Impact across West Nile virus, Dengue virus, and malaria
Climate change	Expands mosquito habitats through increased temperature, rainfall, and humidity; prolongs breeding and transmission seasons
Urbanization	Creates stagnant water and poor waste management environments ideal for Aedes breeding; increases human–vector contact
Global mobility and trade	Facilitates introduction of vectors and pathogens into new regions (e.g., Aedes albopictus in Europe)
Socioeconomic inequality	Limits access to clean water, sanitation, and healthcare, amplifying vulnerability in low- and middle-income countries
Vector adaptation	Mosquito species adapt to cooler climates, increasing transmission potential in temperate regions
Integrated vector management	Combines environmental management, biological control, insecticides, and community participation for sustainable control
One Health approach	Integrates human, animal, and environmental surveillance—critical for zoonotic pathogens such as West Nile virus
Vaccination	Dengue virus (CYD-TDV, TAK-003) and malaria (RTS,S/AS01, R21/Matrix-M) represent milestones; West Nile virus vaccines under investigation
Data-driven surveillance	Incorporates molecular and entomological monitoring for early outbreak detection and insecticide resistance tracking
Public education	Promotes awareness on personal protection and early medical consultation

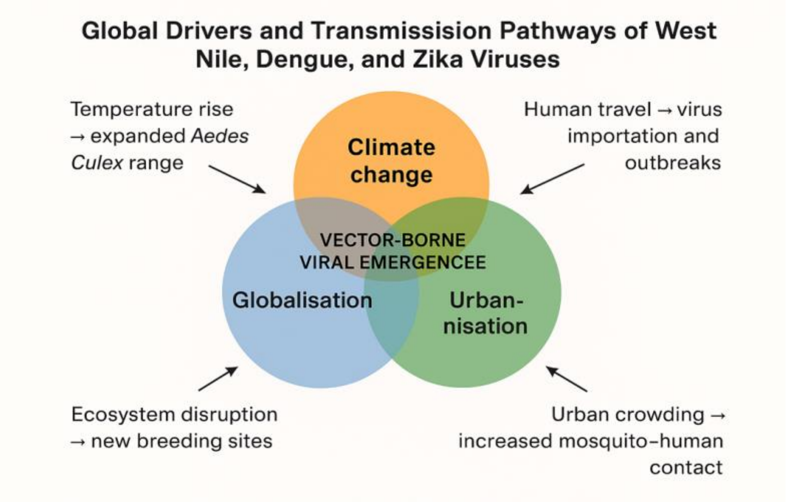

Figure 1. Global drivers and transmission pathways of West Nile, Dengue, and Zika viruses.