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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 Micco⁷

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

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.

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

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

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 viremia.^{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 viremia 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.

Zika 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 travel and travelers may make it easy to spread 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 modeling, 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.

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

| Feature | West Nile virus | Dengue virus | Malaria |
|-------------------------|---|---|---|
| Pathogen type | RNA virus (<i>Flavivirus</i> genus) | RNA virus (<i>Flavivirus</i> genus) | Protozoan (<i>Plasmodium</i> spp.) |
| Primary vector | <i>Culex pipiens</i> , <i>C. modestus</i> | <i>Aedes aegypti</i> , <i>A. albopictus</i> | <i>Anopheles</i> 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 <i>Aedes</i> breeding; increases human–vector contact |
| Global mobility and trade | Facilitates introduction of vectors and pathogens into new regions (e.g., <i>Aedes albopictus</i> 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 |

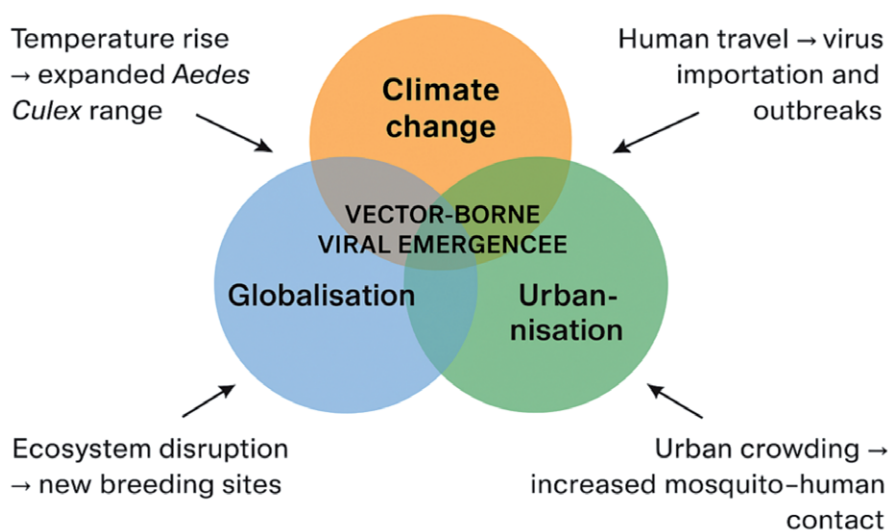


Figure 1. Global drivers and transmission pathways of West Nile, Dengue, and Zika viruses.

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, 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 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.

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