

West Nile Virus: An integrated review of virology, epidemiology, clinical outcomes, and public health challenges

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ARTICLE INFO

Received: 01 July 2026

Accepted: 31 July 2026

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Keywords:

Arbovirus, Disease, Public health, Vector control, West Nile virus, Zoonosis.

ABSTRACT

West Nile virus (WNV), an arbovirus belonging to the *Flaviviridae* family, is the cause of West Nile Fever (WNF), a zoonotic illness that is mainly spread via the bite of *Culex* mosquitoes. WNF's wide geographic spread and intricate epidemiological dynamics have made it a global public health concern in recent decades. Humans and people are incidental hosts, but the virus's principal reservoir, birds, interacts with the mosquito vector to continue its transmission cycle. From asymptomatic infection to severe neuroinvasive forms such as encephalitis, meningitis, and paralytic syndrome, WNV infection has a wide range of clinical manifestations. Neurological complications can result in severe morbidity and mortality, particularly in high-risk groups, even though the majority of cases are minor. Because the disease's clinical symptoms are ambiguous and frequently match those of other arbovirus infections, laboratory confirmation is necessary for diagnosis. Since there is currently no human-specific antiviral medication or vaccination, supportive care is the main focus of management. Therefore, vector control, integrated surveillance, and a One Health strategy are very important prevention techniques for disease control. WNF has a substantial financial impact in addition to its negative effects on health because of treatment expenses, lost productivity, and control measures. This article aimed to comprehensively review various aspects of West Nile Fever, including its etiology, epidemiology, pathogenesis, clinical manifestations, diagnosis, and prevention and control strategies, to provide a deeper understanding of this disease.

Introduction

The West Nile virus (WNV), a member of the *Flaviviridae* family that may infect a variety of vertebrate animals, including people, horses, and birds, is the cause of West Nile Fever (WNF), a zoonotic disease (Pauli *et al.*, 2013). The genus *Culex* serves as the main vector in the transmission cycle of WNV, an arbovirus that is mostly spread by mosquito bites (Hamel *et al.*, 2024). Since its discovery in Uganda in 1937, the illness has grown to be one of the most prevalent arboviruses worldwide (Chancey *et al.*, 2015).

West Nile virus has grown in importance as a worldwide public health issue in recent decades (Gould and Fikrig, 2004). The virus's quick geographic spread, which included its arrival in the Americas in the late 20th century and subsequent rise in cases in other areas like Europe and Asia, is the main cause of this (Sejvar, 2003). Because birds are the virus's major reservoir and it can adapt to a variety of environmental situations, WNV is able to continue its effective cycle of transmission in the natural world (Taieb *et al.*, 2020). The virus's endemic area is dynamically expanded by wild bird migration, which also aids in the virus's regional expansion (Zerbato *et al.*, 2026).

West Nile virus infection has a very wide range of clinical manifestations. About 20% of infected people may have mild to moderate symptoms known as WNF, however the majority of infections are asymptomatic (Bruno *et al.*, 2025). Fever, headaches, aches in the muscles, and malaise are typical symptoms of this form (Marino *et al.*, 2025). The more severe type, West Nile neuroinvasive disease (WNND), which includes meningitis, encephalitis, and a paralytic condition that resembles poliomyelitis, can develop in a tiny proportion of cases (Sejvar, 2014). Higher rates of morbidity and mortality are associated with this neuroinvasive type, especially in vulnerable populations including the elderly and those with

weakened immune systems (Medić *et al.*, 2026).

From the standpoint of pathogenesis, WNV can multiply in a variety of cell types and, in some circumstances, cross the blood-brain barrier to infect the central nervous system (Winkelmann *et al.*, 2016). Disease severity is largely determined by the interplay between viral replication and the host immune response (Habarugira *et al.*, 2020). While a strong immune response can stop the spread of viruses, an overabundance of inflammation can cause tissue damage, especially to the neurological system (Lim *et al.*, 2011a).

West Nile virus's nonspecific clinical signs and resemblance to other arbovirus illnesses, like dengue and Japanese encephalitis, make diagnosis difficult (Marka *et al.*, 2013). To provide a precise diagnosis, laboratory confirmation using molecular and serological techniques is crucial (Sambri *et al.*, 2013). Since there isn't currently a specific antiviral treatment for WNV, supportive therapy and problem-solving are the mainstays of disease care (Asadi and Bunce, 2013).

Vector control is the main tactic used in prevention to lower the risk of transmission (Nasci and Mutebi, 2019). These initiatives include personal protection against mosquito bites, targeted insecticide usage, and environmental management to decrease mosquito habitats (Cagle *et al.*, 2025). Additionally, a One Health strategy that incorporates environmental, animal, and human health is becoming more widely acknowledged as being successful in halting the spread of WNV (Singh *et al.*, 2025).

West Nile virus continues to be a major worldwide health concern due to the intricacy of its epidemiology and effects. Therefore, this review aimed to comprehensively examine the etiology, epidemiology, pathogenesis, clinical manifestations, diagnosis, and control strategies of WNF to provide a deeper understanding and support future prevention and control efforts.

Etiology

West Nile virus, a positive-stranded, single-stranded RNA virus that is a member of the Flavivirus genus and family, is the cause of WNF (Saiz *et al.*, 2021). The single polyprotein that this virus's about 11 kb genome encodes is processed into seven non-structural proteins (NS1–NS5) and three structural proteins (capsid/C, premembrane/prM, and envelope/E) (Karim and Bai, 2023). The envelope (E) protein is the main focus of neutralizing immune response and is essential to the virus's attachment and entrance into host cells (Kocabiyik *et al.*, 2025).

Phylogenetically, WNV is separated into multiple lineages, the most linked to infections in humans and animals being lineages 1 and 2 (Lu *et al.*, 2024). Africa, Europe, Asia, and the Americas are among the regions where Lineage 1 is widely distributed (Chancey *et al.*, 2015). Originally limited to Africa, lineage 2 has recently moved to Europe, where it has contributed to the rise of cases (Hernández-Triana *et al.*, 2014). Virulence, transmissibility, and the virus's ability to adapt to hosts and vectors can all be impacted by genetic heterogeneity among lineages (Ciota and Kramer, 2013).

WNV is an arbovirus that is mainly spread via mosquito bites, especially those from the genus *Culex* (Jani *et al.*, 2022). Interactions between the mosquito vector and its main reservoir, birds, allow the virus to continue its life cycle (Geary *et al.*, 2026). Birds serve as amplification hosts in this cycle, generating high viremia that permits recurrent infections in the mosquito population (Pérez-Ramírez *et al.*, 2014). Because of their low viremia levels, humans and other mammals like horses typically function as dead-end hosts (Bruno *et al.*, 2025). The transmission cycle of WNV involves complex interactions among avian reservoirs, *Culex* mosquito vectors, and incidental mammalian hosts, as illustrated in Figure 1.

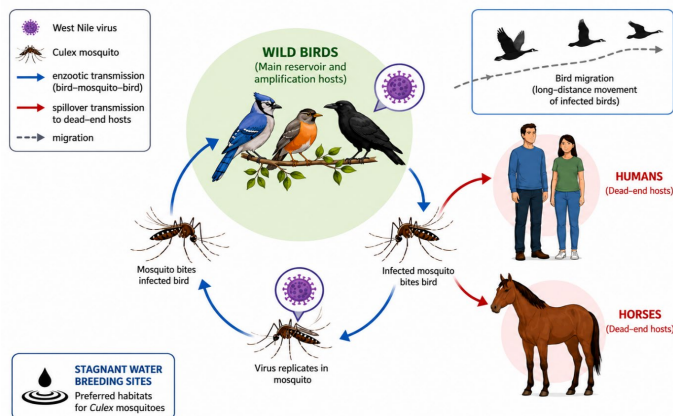


Figure 1. Transmission cycle of WNV involving avian reservoirs, mosquito vectors, and dead-end hosts.

Neurons, immunological cells, and epithelial cells are just a few of the many cell types that WNV can infect (Suen *et al.*, 2014). The range of clinical symptoms, from asymptomatic infection to severe neuroinvasive illness, is influenced by this wide tropism (Lee *et al.*, 2023). Additionally, the virus has ways to avoid the host immune response, such as altering the interferon pathway, which enables more efficient viral reproduction in the early stages of infection (Soraci *et al.*, 2026).

Temperature and humidity are examples of extrinsic factors that affect the relative stability of the virus in the environment and thus affect the effectiveness of vector-mediated transmission (Richards *et al.*, 2007). WNV is a disease with a high potential for worldwide expansion due to its tolerance to a variety of mosquito and avian species (Schwinn *et al.*, 2025).

Epidemiology

Since WNV infection was originally discovered in Uganda in 1937, its

geographic range has expanded (Chancey *et al.*, 2015). Due to its great tolerance to a variety of ecological and climatic settings, WNV, an arbovirus spread by mosquitoes, has now spread endemically throughout many parts of the world (Zerbato *et al.*, 2026).

In the past, WNV was only found in portions of Europe, the Middle East, and Africa (Sejvar, 2014). But the virus has significantly expanded geographically since the late 20th century, especially after it was brought to New York in 1999 (Hadfield *et al.*, 2019). This signaled the start of WNV's swift spread over the Americas, which subsequently extended into South America and North America, including Canada (Komar, 2003). WNV became endemic across the majority of the Americas in a comparatively short period of time, with seasonal case incidence (Ronca *et al.*, 2021).

Over the past 20 years, there has been a rise in WNV activity in Europe, with cases being reported more frequently and spreading into previously unaffected areas (Bakonyi and Haussig, 2020). Due to the favorable climate for vector populations, countries in Southern and Eastern Europe have become places with relatively high prevalence (Carrasco *et al.*, 2024). Additionally, the rise in cases in Europe has been attributed to the advent of lineage 2, which was formerly restricted to Africa (Hernández-Triana *et al.*, 2014).

Although its spread is typically more irregular than in the Americas and Europe, WNV has also been observed in Asia (Gould and Fikrig, 2004). Because the symptoms of WNV infections are similar to those of other arboviruses including dengue and Japanese encephalitis, they are frequently underdiagnosed in various Asian countries (Monyama *et al.*, 2025). In the meantime, the Kunjin virus, a closely related strain of the virus that causes comparable but often milder clinical signs, is found in Australia (Frost *et al.*, 2012).

The major vector, the *Culex* mosquito, and its natural reservoir, wild birds, have a significant impact on the global distribution of WNV (Campos *et al.*, 2025). Bird migration patterns are a major factor in the virus's ability to spread from one geographic area to another and into new ones (Swetnam *et al.*, 2018). Additionally, mosquito population dynamics and transmission rates are influenced by environmental conditions like temperature, humidity, and rainfall (Paz, 2015).

WNV's geographic proliferation has been found to be accelerated by urbanization and climate change (Patzina-Mehling *et al.*, 2026). The virus's incubation period in mosquitoes may be shortened by rising global temperatures, and the vector may find new homes as a result of changes in land use (Wang *et al.*, 2024). Consequently, formerly non-endemic regions become more susceptible to the virus's introduction and spread (Habarugira *et al.*, 2020).

According to epidemiology, WNV incidence is often seasonal, peaking in temperate regions between late summer and early fall (Barbić *et al.*, 2026). However, transmission can happen all year round in tropical areas, with variations impacted by rainfall patterns (Kioutsoukis and Stilianakis, 2019).

Pathogenesis

WNV infection starts when a mosquito, usually from the species *Culex*, bites the host and injects the virus into their skin (Karim and Bai, 2023). The virus first infects local cells like keratinocytes and skin dendritic cells after penetrating the dermal tissue (Lim *et al.*, 2011b). After that, infected dendritic cells go to local lymph nodes, which promotes primary viremia and more viral replication (Samuel and Diamond, 2006).

The spleen, liver, and kidneys are among the peripheral organs where the virus might spread due to viremia (Agliani *et al.*, 2023). Through the generation of type I interferon and the activation of immune cells including macrophages and natural killer cells, the innate immune response plays a critical role in regulating viral replication throughout this phase (Zimmerman *et al.*, 2019). However, the infection's progression to a more severe phase will depend on how well WNV avoids or suppresses this immune response (Gupta *et al.*, 2026).

The neuroinvasive type of the disease is characterized by the virus's ability to pass across the blood-brain barrier (BBB) and infect the central nervous system (CNS) in a tiny percentage of cases (Verma *et al.*, 2009). Increased BBB permeability brought on by a systemic inflammatory response, Trojan horse trafficking via infected immune cells, and maybe direct infection of vascular endothelial cells are all contributing factors to this penetration (Roe *et al.*, 2012). WNV shows neuronal tropism after it enters the central nervous system, especially in the brainstem, hippocampus, and spinal cord (Suen *et al.*, 2014). The progression from peripheral infection to central nervous system involvement is summarized in Figure 2.

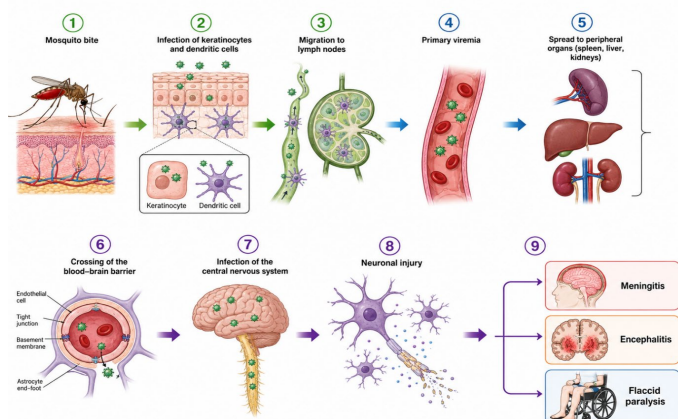


Figure 2. Pathogenesis of WNV infection from mosquito inoculation to neuroinvasive disease.

Apoptosis induction, oxidative stress, and direct cytopathic effects are some of the ways that viral replication in neurons damages cells (Medigeshi *et al.*, 2007). Additionally, pro-inflammatory cytokines are released, and microglia are activated as a result of an increased adaptive immune response, which damages brain tissue (Stonedahl *et al.*, 2020). Meningitis, encephalitis, and a paralytic state that resembles poliomyelitis are among the neurological clinical symptoms caused by this combination of direct viral effects and the host immunological response (Fulton *et al.*, 2020).

The severity of the pathogenesis is further influenced by host characteristics such as advanced age, immunological state, and comorbidities (Zerbato *et al.*, 2026). People with weakened immune systems typically have less efficient viral control, which raises the possibility of CNS invasion (Soraci *et al.*, 2026). Therefore, the dynamics of viral replication, immune evasion strategies, and the host immunological response—which is not necessarily protective—interact intricately to cause WNF (Kayesh *et al.*, 2025).

Immune response

Comprehensive immune response comprising both innate and adaptive immunological components is triggered by WNV infection, and these components cooperate to limit viral replication (Lim *et al.*, 2011a). The innate immune system mediates the first stage of protection and is essential in preventing the spread of viruses prior to the initiation of a particular immune response (Trobaugh and Green, 2015).

Pattern recognition receptors (PRRs) on dendritic cells and macrophages, such as Toll-like receptors (TLRs) and RIG-I-like receptors (RLRs), identify WNV after inoculation through a mosquito bite (Bai *et al.*, 2019). When these receptors are activated, type I interferons (IFN- α/β) are produced (Bourne *et al.*, 2007). These interferons impede viral replication and increase the expression of antiviral genes (interferon-stimulated genes/ISGs) (Lucas *et al.*, 2015). Additionally, natural killer (NK) cells use cytotoxic methods to help eradicate infected cells (Yao *et al.*, 2017).

WNV can, however, avoid the innate immune response by blocking the interferon signaling pathway (Guo *et al.*, 2005). This capacity increases the danger of severe viremia and systemic transmission by enabling the

virus to endure and multiply during the early stages of infection (Gack and Diamond, 2016).

Several days after infection, the adaptive immune response starts to take shape and is essential for getting rid of the virus (Mehlhof and Diamond, 2006). The creation of particular antibodies, mainly immunoglobulin M (IgM), which manifests during the acute phase, and immunoglobulin G (IgG), which offers long-term protection, is what defines humoral immunity (Papa *et al.*, 2015). Neutralizing antibodies prevents viruses from entering cells and identify viral particles so that the immune system can destroy them (Tsioris *et al.*, 2015).

On the other hand, CD4⁺ and CD8⁺ T cells are activated during the cellular immune response (Netland and Bevan, 2013). While CD8⁺ T cells contribute to the direct destruction of virus-infected cells, CD4⁺ T cells help activate B cells and bolster the immune response by secreting cytokines (Shrestha and Diamond, 2004). This cellular reaction is essential for managing infection, especially in the central nervous system and peripheral organs (Netland and Bevan, 2013).

However, pathogenesis can also be influenced by an overreaction of the immune system, especially in neuroinvasive instances (Chaillot *et al.*, 2025). Unchecked production of pro-inflammatory cytokines can worsen nerve tissue injury and make the blood-brain barrier more permeable (Constant *et al.*, 2022). Neurological dysfunction can be exacerbated by inflammation brought on by microglia activation and immune cell infiltration into the central nervous system (Stonedahl *et al.*, 2020).

The efficacy of the immune response to WNV is influenced by host variables, including advanced age and immunocompromised status (Prieto-Vega *et al.*, 2025). In these populations, a weakened immune system is frequently linked to a higher risk of serious illness and neurological issues (Bai *et al.*, 2019). Thus, the clinical outcome of WNF infection depends on striking a balance between a protective immune response and regulated inflammation (Suthar *et al.*, 2013).

Pathology

From minor lesions in peripheral tissues to serious harm to the central nervous system (CNS), especially in neuroinvasive cases, WNV infection causes a range of pathological alterations (Bruno *et al.*, 2025). The virus's preference for neurons and the interplay between viral replication and the host's immune response have a significant impact on histopathological symptoms (Chaillot *et al.*, 2025).

Pathological alterations in peripheral tissues are typically nonspecific. When the immune system is activated, organs including the spleen and lymph nodes may show signs of lymphoid hyperplasia (Piras *et al.*, 2025). Mononuclear inflammatory cells may infiltrate the portal and lobular regions of the liver along with modest to moderate hepatocyte damage (Mingo-Casas *et al.*, 2025). Except for severe systemic infections, kidney and other tissue lesions are typically modest (Sejvar, 2014).

The central nervous system is where the most noticeable pathological alterations take place (Winkelmann *et al.*, 2016). Macroscopically, the brain may exhibit mild to moderate edema, but there are frequently no noticeable alterations (Sampathkumar, 2003). Non-suppurative encephalitis with mononuclear cell infiltration, mostly lymphocytes and macrophages, around blood vessels (perivascular cuffing) is one of the primary microscopic features (Aglani *et al.*, 2023). Moreover, glial cell activation in reaction to nerve tissue damage results in diffuse gliosis (Chaillot *et al.*, 2025).

WNV has a strong affinity for neurons, leading to necrosis and neuronal degeneration, especially in the brainstem, hippocampus, cerebral cortex, and spinal cord (Shrestha *et al.*, 2003). Neuronophagy, or the phagocytosis of injured neurons by microglia, frequently occurs concurrently with this process (Chhatbar and Prinz, 2021). Flaccid paralysis, a disorder similar to poliomyelitis, is directly linked to spinal cord injuries, especially in the anterior horn (Sejvar *et al.*, 2005).

Immunopathological factors are important in addition to the di-

rect harm caused by viral replication (Donadieu *et al.*, 2013). Through secondary inflammatory pathways, the generation of pro-inflammatory cytokines and immune cell infiltration into the central nervous system can worsen tissue damage (Kumar *et al.*, 2010). In addition to increasing immune cell and inflammatory mediator infiltration, disruption of the blood-brain barrier exacerbates the neuropathological state (Roe *et al.*, 2012).

Non-suppurative encephalomyelitis predominates in CNS lesions in animals, especially horses, where the pathological picture is comparable to that in humans (Schwarz and Long, 2023). Lesions may be more widespread and affect several organs, including as the spleen, liver, and heart, with a greater degree of necrosis in sensitive birds (Vidaña *et al.*, 2020).

Clinical manifestations

Human WNV infections typically exhibit a wide range of clinical symptoms, from mild infection to serious central nervous system illness (Argirova *et al.*, 2024). 70–80% of infected people are thought to be asymptomatic, however some experience varied degrees of clinical illness (McDonald *et al.*, 2021).

Uncomplicated WNF, which has mild to moderate systemic symptoms, is the most prevalent clinical type (Sejvar, 2014). Acute fever, malaise, headache, myalgia, and arthralgia are among the first symptoms that usually show up after an incubation period of 2–14 days (Pauli *et al.*, 2013). A maculopapular rash, moderate lymphadenopathy, and gastrointestinal issues like nausea and vomiting may also be present in certain people (Najafi *et al.*, 2026). These symptoms usually go away on their own in a matter of days to weeks without causing any more issues (Zerbato *et al.*, 2026).

A tiny portion of instances progress to WNND, a neuroinvasive type (Chancey *et al.*, 2015). Meningitis, encephalitis, and poliomyelitis-like syndrome are the three primary syndromes associated with this illness (Debiasi and Tyler, 2006). The symptoms of WNV-induced meningitis include fever, stiff neck, photophobia, and excruciating headache (Madden, 2003). The more severe form, encephalitis, manifests as altered mental

status, confusion, tremors, seizures, and reduced awareness that eventually leads to coma (Habebe *et al.*, 2025). On the other hand, sudden, asymmetrical, flaccid muscular weakness is the hallmark of paralytic syndrome, which is comparable to poliomyelitis and frequently lacks noticeable sensory impairment (Kuo *et al.*, 2015).

Ataxia, decreased reflexes, and cranial nerve dysfunction are other neurologic symptoms that could be present (Madden, 2003). Myoclonus and tremors are very commonly observed, especially in older patients (Cooper and Said, 2014). Risk factors include advanced age, immunocompromised status, and comorbidities have a significant impact on the severity of neurologic symptoms (Sutinen *et al.*, 2022).

WNV infection frequently results in severe neurologic symptoms in animals, especially horses (Bertram *et al.*, 2020). Ataxia, limb weakness, hypersensitivity, and behavioral abnormalities are examples of clinical symptoms (Sampathkumar, 2003). Death and paralysis are possible in extreme situations (Petersen *et al.*, 2013). Infection can be lethal in birds, especially vulnerable species, with quickly progressing systemic symptoms (Gamino and Höfle, 2013).

Diagnosis

An integrated strategy that incorporates laboratory confirmation, epidemiological history, and clinical examination is necessary for the diagnosis of WNV infection (Gray and Webb, 2014). Laboratory-based diagnostic confirmation is crucial to making a diagnosis because of the nonspecific clinical signs and overlap with other arbovirus infections (Vanichanan *et al.*, 2016). Table 1 presents various diagnostic methods for West Nile virus infection, including clinical, serological, molecular, and ancillary tests.

Clinically, WNF is suspected in patients who have an acute fever, particularly if they also have neurological symptoms like meningitis or encephalitis, as well as a history of exposure to endemic areas or activities that raise the chance of coming into touch with mosquito vectors, especially those of the genus *Culex* (Sejvar, 2014). However, these symptoms need to be confirmed by additional testing because they are not specific

Table 1. Diagnostic methods for WNV infection.

Diagnostic category	Method / Examination	Principle / Parameters assessed	Advantages	Limitations	Clinical interpretation	References
Clinical and epidemiological assessment	Evaluation of clinical manifestations and exposure history	Acute febrile illness, meningitis/encephalitis, exposure to endemic areas, contact with mosquito vectors (especially <i>Culex</i> spp.)	Simple, rapid, and useful as an initial screening approach	Nonspecific findings; symptoms overlap with other arboviral infections	Raises initial suspicion of WNV infection and requires laboratory confirmation	Gray and Webb (2014); Vanichanan <i>et al.</i> (2016); Sejvar (2014); Bruno <i>et al.</i> (2025)
Serological	Detection of WNV-specific IgM and IgG antibodies (serum or CSF)	IgM indicates acute or recent infection; IgG reflects previous exposure or late-stage infection	Sensitive, widely used, and capable of detecting infection after symptom onset	Cross-reactivity with other flaviviruses may reduce specificity	Positive IgM supports recent infection; IgG requires cautious interpretation in clinical context	Sambri <i>et al.</i> (2013); Prince and Hogrefe (2003); Staples <i>et al.</i> (2022); Lustig <i>et al.</i> (2025)
Molecular	Reverse Transcription Polymerase Chain Reaction (RT-PCR)	Detection of viral RNA in blood, cerebrospinal fluid (CSF), or tissue samples	High specificity and direct detection of viral presence	Limited sensitivity due to short and low-level viremia; dependent on timing of sample collection	Positive results confirm active infection, particularly during the early phase or in immunocompromised patients	Vilibic-Cavlek <i>et al.</i> (2024); Simonin (2024); De Filette <i>et al.</i> (2012)
Confirmatory testing	Plaque Reduction Neutralization Test (PRNT)	Detection of WNV-specific neutralizing antibodies	High diagnostic accuracy and ability to distinguish closely related flaviviruses	Technically complex, expensive, time-consuming, and requires specialized laboratory facilities	Used as the definitive confirmatory test for WNV infection	Dewi <i>et al.</i> (2026); Sambri <i>et al.</i> (2013)
Cerebrospinal fluid (CSF) analysis	Cytological and biochemical examination of CSF	Lymphocytic pleocytosis, increased protein concentration, and relatively normal glucose levels	Supports diagnosis of neuroinvasive infection	Findings are nonspecific and insufficient for definitive diagnosis	Suggestive of viral infection involving the central nervous system (CNS)	Bakos <i>et al.</i> (2022); Debiasi and Tyler (2006)
Imaging	Brain Magnetic Resonance Imaging (MRI)	Detection of lesions involving the basal ganglia, thalamus, and brainstem	Useful for evaluating neurological complications and CNS involvement	Imaging abnormalities are not pathognomonic and may be absent	Supports assessment of central nervous system involvement	Petropoulou <i>et al.</i> (2005)

enough (Bruno *et al.*, 2025).

The identification of the viral genetic material and the detection of the humoral immune response are the main components of laboratory diagnosis (Sambri *et al.*, 2013). The most used technique is serological testing, which looks for WNV-specific immunoglobulin M (IgM) in serum or cerebrospinal fluid (CSF) as a sign of an acute infection (Prince and Hogrefe, 2003). IgM can last for weeks or months and is typically detectable within days of the onset of symptoms (Staples *et al.*, 2022). Due to the possibility of cross-reactivity with other flaviviruses, care must be taken when using immunoglobulin G (IgG) detection to evaluate past exposure or late-stage illness (Lustig *et al.*, 2025).

Viral RNA can be directly detected in blood, CSF, or tissue using molecular techniques such reverse transcription polymerase chain reaction (RT-PCR) (Vilibic-Cavlek *et al.*, 2024). Because the human viremia phase is often brief and low-level, this approach has a high specificity but a limited sensitivity (Simonin, 2024). As a result, RT-PCR is more helpful in the early phases of infection or in immunocompromised people who might have persistent viremia (De Filette *et al.*, 2012).

To distinguish WNV-specific antibodies from those of other antigenically identical flaviviruses, such dengue virus or Japanese encephalitis, additional confirmatory tests are employed, such as the plaque reduction neutralization test (PRNT) (Dewi *et al.*, 2026). Although this procedure is quite accurate, it takes longer to complete and requires specialist laboratory facilities (Sambri *et al.*, 2013).

Cerebrospinal fluid study usually reveals lymphocytic pleocytosis, increased protein levels, and relatively normal glucose levels in situations involving the central nervous system (Bakos *et al.*, 2022). The diagnosis of viral infection is supported by these nonspecific features (Debiasi and Tyler, 2006). Although the results are not always typical, imaging studies like Magnetic Resonance Imaging (MRI) can reveal lesions in specific brain areas, such as the brainstem, thalamus, and basal ganglia (Petropoulou *et al.*, 2005).

Differential diagnosis

Given its vague clinical symptoms and frequent overlap with numerous other viral disorders, especially those affecting the central nervous system, differential diagnosis of WNV infection is essential (Kemmerly, 2003). In both the febrile and neuroinvasive stages, a differential diagno-

sis approach is required to differentiate WNV from other viruses exhibiting comparable symptoms (Gallo *et al.*, 2025). Table 2 summarizes the differential diagnosis of West Nile virus infection based on the main clinical manifestation groups: the febrile, neurologic, and paralytic phases.

Early on, symptoms including fever, headache, myalgia, and malaise might mimic those of other arbovirus infections, such as the Zika and dengue viruses (Martins *et al.*, 2022). These two illnesses have a largely overlapping geographic range and are likewise spread via mosquito vectors (Hunsberger *et al.*, 2020). However, Zika infection is more commonly accompanied with skin rashes and congenital problems in pregnant women, whereas dengue is typically associated with conventional signs such as severe thrombocytopenia, retro-orbital discomfort, and possible bleeding (Gupta *et al.*, 2021).

WNV must be distinguished from other viral infections that produce meningitis or encephalitis in the context of neurologic illness, such as herpes simplex virus and Japanese encephalitis virus (Santini *et al.*, 2022). While herpes simplex encephalitis frequently exhibits a quick onset with distinctive temporal lobe involvement on brain imaging, Japanese encephalitis typically has a higher fatality rate and is highly prevalent in Asia (Kelly *et al.*, 2025). Additionally, rabies should be taken into account when neurologic symptoms worsen, particularly if there has been a history of animal bites (Han and Zunt, 2005).

Differentiating WNV infection from poliovirus and other non-polio enterovirus infections is also necessary for the poliomyelitis-like paralytic illness (Chan *et al.*, 2019). Specific virological testing is essential since both illnesses exhibit the distinctive acute flaccid weakness without sensory abnormalities (Sejvar, 2004).

Particularly in patients with a high temperature and nuchal stiffness, bacterial causes such bacterial meningitis should be taken into account in addition to viral etiologies (Burns *et al.*, 2024). In contrast to viral infections, bacterial infections typically exhibit a predominance of neutrophils, lower glucose levels, and noticeably higher protein levels in the cerebrospinal fluid profile (Arja *et al.*, 2025).

Transmission

A zoonotic cycle involving arthropod vectors and vertebrate reservoirs is the main way that WNV infection spreads (Habarugira *et al.*, 2020). Mosquito bites, especially those from the genus *Culex*, which serve as

Table 2. Differential diagnosis of WNV infection based on clinical manifestations.

Manifestation group	Differential diagnosis	Causative agent	Main clinical characteristics	Key distinguishing features from WNV	References
Febrile phase	Dengue fever	Dengue virus	High fever, retro-orbital pain, thrombocytopenia, and potential hemorrhagic manifestations	Severe thrombocytopenia and hemorrhagic manifestations are more characteristic	Martins <i>et al.</i> (2022); Hunsberger <i>et al.</i> (2020); Gupta <i>et al.</i> (2021)
Febrile phase	Zika virus infection	Zika virus	Mild fever, skin rash, conjunctivitis, and congenital complications	Skin rash predominance and association with fetal microcephaly	Martins <i>et al.</i> (2022); Hunsberger <i>et al.</i> (2020); Gupta <i>et al.</i> (2021)
Neurologic phase	Japanese encephalitis	Japanese encephalitis virus	Severe encephalitis, seizures, and high case fatality rate	More prevalent in Asia and generally associated with higher mortality	Santini <i>et al.</i> (2022); Kelly <i>et al.</i> (2025)
Neurologic phase	Herpes simplex encephalitis	Herpes simplex virus (HSV)	Rapid onset, behavioral changes, and seizures	Characteristic temporal lobe involvement on brain MRI	Santini <i>et al.</i> (2022); Kelly <i>et al.</i> (2025)
Neurologic phase	Rabies	Rabies virus	Progressive neurological symptoms, hydrophobia, and history of animal bite	History of animal exposure and typical hydrophobia	Han and Zunt (2005)
Paralytic phase	Poliomyelitis	Poliovirus	Acute flaccid paralysis without sensory impairment	Requires specific virological confirmation to differentiate from WNV-associated acute flaccid paralysis	Chan <i>et al.</i> (2019); Sejvar (2004)
Paralytic phase	Non-polio enterovirus infection	Non-polio enteroviruses	Acute muscle weakness that may clinically resemble poliomyelitis	Diagnosis relies on identification of the specific viral pathogen	Chan <i>et al.</i> (2019); Sejvar (2004)
Neurologic (bacterial)	Bacterial meningitis	Pathogenic bacteria (e.g., <i>Neisseria meningitidis</i>)	High fever, nuchal rigidity, and altered consciousness	CSF findings typically show neutrophilic predominance, decreased glucose, and elevated protein levels	Burns <i>et al.</i> (2024); Arja <i>et al.</i> (2025)

biological vectors, are the main method of transmission (Colpitts *et al.*, 2012). After consuming viremic birds, mosquitoes develop the infection (Pérez-Ramírez *et al.*, 2014). After that, the virus multiplies inside the mosquito and travels to its salivary glands, where it might spread to the subsequent victim while feeding (Hamel *et al.*, 2024).

In the WNV transmission cycle, birds are the main source of amplification (Vaughan *et al.*, 2022). Birds' high viremia levels enable effective mosquito infection, sustaining the virus's natural circulation (Wang *et al.*, 2026). On the other hand, because their viremia levels are typically too low to infect new mosquitoes and so do not significantly contribute to the transmission chain, people and horses are classified as dead-end hosts (Schwarz and Long, 2023).

There are non-vector transmission pathways that, despite being uncommon, have clinical and epidemiological significance in addition to vector-mediated transmission (Byas and Ebel, 2020). Blood transfusions, organ transplants, and perinatal exposure—including transplacental transmission and breast milk—can all result in transmission (Marnezi *et al.*, 2024). There have also been documented cases of infection brought on by laboratory exposure, especially in people who handle active viral specimens (Carrasco *et al.*, 2024).

The kinetics of WNV transmission are significantly influenced by environmental variables (Albrecht and Kaufeld, 2023). Climate factors that affect mosquito population density and speed up virus replication within the vector (extrinsic incubation period) include high temperatures and rainfall (Farooq *et al.*, 2023). Additionally, bird migration, urbanization, and environmental changes all contribute to the virus's global spread to new regions (Kirby *et al.*, 2025).

Transmission patterns are also influenced by differences in mosquito feeding habits (Llopis *et al.*, 2016). The enzootic cycle is maintained by ornithophilic mosquito species that prefer to bite birds, whilst opportunistic species that bite both humans and mammals serve as bridge vectors that link the cycle between humans and birds (Jansen *et al.*, 2013).

Risk factors

A complicated interplay between host traits, vector dynamics, and environmental factors affects the probability of contracting WNV (Giesen *et al.*, 2023). The likelihood of exposure, the severity of the condition, and the chance of experiencing neurological sequelae are all influenced by

variations in these parameters (Madran *et al.*, 2026). Table 3 summarizes the various risk factors contributing to West Nile virus infection, highlighting the interplay between the environment, ecology, host characteristics, behavior, and iatrogenic factors.

Exposure to vectors, especially *Culex* mosquitoes, is one important factor (Soh and Aik, 2021). People who live or work in locations with high mosquito concentrations are more likely to become infected, especially in the summer or during times of heavy rainfall, which encourage vector breeding (Montgomery and Murray, 2015). Mosquito populations can rise and virus transmission can be amplified in areas with stagnant water, inadequate drainage systems, and poorly managed urbanization (Campos *et al.*, 2025).

Birds are the main reservoir, thus ecological considerations are also important (Habarugira *et al.*, 2020). Viral circulation tends to be more intense in areas with large numbers of wild birds or along bird migratory routes (Dinu *et al.*, 2024). Rising global temperatures and other aspects of climate change can increase the geographic range of vectors and speed up viral replication in mosquitoes, raising the risk of outbreaks (Wang *et al.*, 2024).

Individual traits influence disease severity and susceptibility to infection in addition to environmental influences (Madran *et al.*, 2026). One of the biggest risk factors for the emergence of neuroinvasive forms is advanced age (Judson and Dowdy, 2025). The body's diminished capacity to regulate viral replication is a result of immunosenescence, or declining immunological function with age (Montgomery, 2017). Severe infection is also more likely to occur in those with immunocompromised circumstances, such as organ transplant recipients, patients with chronic illnesses, or those on immunosuppressive therapy (Mbonde *et al.*, 2024).

Increased clinical severity has been linked to comorbid conditions such diabetes mellitus, hypertension, and chronic renal disease (Badawi *et al.*, 2018). Viral invasion of the central nervous system can be facilitated by these conditions, which can worsen the inflammatory response and damage the blood-brain barrier (Cho and Diamond, 2012).

Additionally, behavioral aspects cannot be disregarded. The risk of exposure is increased while engaging in outside activities without wearing protective clothes or repellent to prevent mosquito bites (Loeb *et al.*, 2005). Additionally, the high risk of infection is exacerbated by a lack of public knowledge about vector management and personal safety measures (Fonzo *et al.*, 2024).

Table 3. Risk factors for WNV infection and determinants of clinical severity.

Factor category	Main determinants	Mechanism / Role in risk	Impact on infection and disease severity	References
Environmental factors	High mosquito density (<i>Culex</i> spp.), seasonal conditions (summer/heavy rainfall), stagnant water, poor drainage, and unmanaged urbanization	Increase vector abundance and activity, thereby enhancing opportunities for virus transmission	Increase the likelihood of exposure and incidence of WNV infection in human populations	Giesen <i>et al.</i> (2023); Soh and Aik (2021); Montgomery and Murray (2015); Campos <i>et al.</i> (2025)
Ecological factors	Presence of avian reservoirs, bird migratory routes, and climate change (increasing temperature)	Sustain and expand the natural transmission cycle and enhance viral replication efficiency within mosquito vectors	Broaden geographic distribution of disease and increase outbreak potential	Habarugira <i>et al.</i> (2020); Dinu <i>et al.</i> (2024); Wang <i>et al.</i> (2024)
Individual (host) factors	Advanced age, immunosenescence, and immunocompromised conditions	Reduce host capacity to control viral replication and weaken immune responses	Increase susceptibility to severe infection and neuroinvasive disease	Madran <i>et al.</i> (2026); Judson and Dowdy (2025); Montgomery (2017); Mbonde <i>et al.</i> (2024)
Comorbidities	Diabetes mellitus, hypertension, and chronic kidney disease	Exacerbate inflammatory responses and impair blood–brain barrier integrity, facilitating viral invasion of the central nervous system	Increase the risk of neurological complications and severe clinical outcomes	Badawi <i>et al.</i> (2018); Cho and Diamond (2012)
Behavioral factors	Outdoor activities without protective clothing, non-use of mosquito repellent, and limited awareness of vector control measures	Increase frequency of contact with infected mosquito vectors	Elevate the probability of exposure and infection	Loeb <i>et al.</i> (2005); Fonzo <i>et al.</i> (2024)
Iatrogenic (non-vector) factors	Blood transfusion and organ transplantation	Direct transmission of WNV through contaminated biological products	Rare but clinically significant route of infection, particularly in vulnerable individuals	Pisani <i>et al.</i> (2016); Orru' <i>et al.</i> (2025)

Although they are very uncommon, medical operations like organ transplants and blood transfusions can potentially be risk factors in non-vector scenarios (Pisani *et al.*, 2016). Therefore, one of the most important steps in lowering the risk of infection through this channel is donor screening in endemic areas (Orru' *et al.*, 2025).

Public health importance

Because WNV is a vector-borne zoonotic disease and can create outbreaks with erratic patterns, it is a worldwide significant public health concern (Klingelhöfer *et al.*, 2023). An integrated, cross-sectoral control strategy is required due to the intricate epidemiology of WNV, which involves interactions between bird reservoirs, mosquito vectors, and accidental hosts (Gray and Webb, 2014).

WNV is a problem from a surveillance standpoint since the majority of infections are moderate or subclinical and frequently go unreported (Lustig *et al.*, 2018). This makes it challenging to identify early increases in viral activity in a region and results in an overestimate of the actual illness burden (Gobbo *et al.*, 2025). Thus, monitoring vector populations, especially those of *Culex* mosquitoes—as well as natural reservoirs like wild birds are essential components of an efficient surveillance system in addition to reporting human cases (Abbas *et al.*, 2025).

The possibility of severe forms of illness, especially WNND, which is linked to increased hospitalization and fatality rates, also reflects the public health concern (Irekeola and Alshehri, 2025). Vulnerable groups, like the elderly and those with impaired immune systems, bear a significantly greater cost (Montgomery and Murray, 2015). Additionally, survivors with long-term neurological issues may require greater social support and assistance with rehabilitation (Maccarone *et al.*, 2024).

WNV has significant effects on organ transplantation and blood transfusion procedures in terms of medical safety (Pisani *et al.*, 2016). Laboratory screening has been implemented in several countries, especially during the active transmission season, due to the potential of transmission through infected but asymptomatic donors (Orru' *et al.*, 2025). Although this approach increases patient safety, it also makes managing the health system more difficult (Zerbato *et al.*, 2026).

The urgency of WNV as a public health issue is further increased by environmental variables and climate change (Singh *et al.*, 2025). The danger of exposure to human populations can be increased by expanding vector habitats and extending the transmission season due to rising temperatures and shifting rainfall patterns (Campos *et al.*, 2025). Additionally, uncontrolled urbanization might increase the likelihood of local transmission by providing mosquito breeding grounds (Ma *et al.*, 2025).

Because human, animal, and environmental health are closely related, a One Health strategy is essential for WNV control (Paternoster *et al.*, 2016). Early identification and quicker reaction to increased virus activity are made possible by integrating data from the ecological, veterinary, and human health sectors (Nistor *et al.*, 2026). Another essential element of public health policies is public education on environmental management and preventing mosquito bites (Marino *et al.*, 2025).

Economic impact

The human and animal health sectors, as well as the larger economic system, are significantly impacted by WNV infection, both directly and indirectly (Watts *et al.*, 2021). The degree of transmission, the health system's capabilities, and the success of control initiatives in a given area all have a significant impact on the size of the economic burden (Barrett, 2014).

The medical treatment of infection cases, especially neuroinvasive types that need critical care, is the main source of direct costs (Staples *et al.*, 2014). Long-term hospital stays, usage of intensive care units, and sophisticated diagnostic procedures including imaging and particular laboratory tests are frequently necessary for patients with encephalitis or

meningitis (Tetaj *et al.*, 2026). Additionally, patients with persistent neurological abnormalities require long-term rehabilitation, which adds to the cost of healthcare (Rao *et al.*, 2005). The healthcare system may be severely strained by these mounting expenses, especially during times of spikes in cases or epidemics (Zohrabian *et al.*, 2004).

Morbidity and mortality-related lost production are examples of indirect economic effects (Ouhoumane *et al.*, 2019). People with neurological issues may be less able to work or possibly permanently disabled, which would lower their own income and increase their social obligations (Fulton *et al.*, 2020). Economic losses at home and societal levels are also influenced by family members' caregiving responsibilities and missed work due to illness (Barrett, 2014).

The costs of prevention and control are also important factors in the field of public health (Kolimenakis *et al.*, 2016). Insecticide use, environmental management, and mosquito population observation (particularly of the species *Culex*) are examples of vector control programs that demand a substantial commitment of resources (Cholvi *et al.*, 2026). Additionally, the use of an integrated surveillance system increases operational expenses and complexity by tracking cases in human, animal, and avian reservoirs (Tamba *et al.*, 2024).

The veterinary industry, especially the equine sector, is also affected by WNV (Bosco-Lauth and Bowen, 2019). Horse infections can result in increased morbidity, decreased performance, and mortality, which can cost owners and industry money (Mongoh *et al.*, 2008). These effects are made worse by the expenses associated with vaccination, treating diseased animals, and losing economic value (Zohrabian *et al.*, 2006).

The expenses related to the safety of organ transplants and blood transfusions are another significant factor (Defilippo *et al.*, 2022). Healthcare facilities must implement donor screening for WNV in order to prevent iatrogenic transmission, although doing so raises operating costs (Zerbato *et al.*, 2026).

Treatment

Since there is currently no particular antiviral medication that has been shown to be clinically efficacious, treatment for WNV infection is still supportive (Tyler, 2014). Controlling symptoms, avoiding complications, and stabilizing the patient's health are the main goals of the treatment strategy, particularly in situations involving the central nervous system (Soraci *et al.*, 2026).

Therapy for mild cases (uncomplicated WNF) often consists of rest, proper hydration, and the use of analgesics and antipyretics to control pain and fever (Sampathkumar, 2003). In a matter of days to weeks, the majority of patients in this category recover on their own without the need for additional medical care (Najafi *et al.*, 2026).

Intensive supportive treatment is essential in cases that develop into WNND (Hiraldo *et al.*, 2023). In order to closely monitor neurological, respiratory, and hemodynamic function, patients with encephalitis or meningitis may need to be admitted to an intensive care unit (Taga *et al.*, 2024). Intravenous hydration therapy, mechanical ventilation support for respiratory failure, and anticonvulsant medicine for seizure control are examples of interventions (Maccarone *et al.*, 2024). Additionally, preventing secondary problems including thromboembolism and nosocomial infections is crucial to management (Marino *et al.*, 2025).

Intravenous immunoglobulin (IVIG) containing antibodies against WNV, interferon, and broad-spectrum antiviral medicines are among the experimental therapy strategies that have been studied (Ben-Nathan *et al.*, 2009). Nevertheless, the outcomes of current clinical trials are scant and have not consistently shown adequate efficacy to be suggested as conventional treatment (Sejvar, 2014). As a result, the application of these treatments is still under investigation and is typically taken into account in specific situations with stringent clinical considerations (Sampathkumar, 2003).

Some patients need long-term rehabilitation to address physical,

cognitive, or functional deficiencies during the healing phase, especially those with neurological involvement (Maccarone *et al.*, 2025). Post-infection patients' quality of life is greatly enhanced by a thorough rehabilitation program that includes occupational therapy and physical therapy (Maccarone *et al.*, 2024).

Treatment in the veterinary setting is also supportive, with an emphasis on neurological stabilization, fluid administration, and care to avoid harm from weakened muscles or decreased coordination, especially in horses (Nistor *et al.*, 2026). The intensity of symptoms at the time of initial diagnosis has a significant impact on an animal's prognosis (Yuseri *et al.*, 2019).

Vaccination

Veterinary and human health sectors have made different progress in their efforts to prevent WNV infection through vaccination (Bosco-Lauth and Bowen, 2019). While vaccines for humans are still in the research and development stage, effective, commercially available vaccines have been used extensively in animals, especially horses (Amanna and Slifka, 2014).

The main method for lowering morbidity and mortality from WNV infection in horses is vaccination (Cendejas and Goodman, 2024). Numerous vaccinations have been created, such as DNA vaccines, vector-based recombinant vaccines, and inactivated (dead) vaccines (Ulbert, 2019). By inducing a humoral immune response that generates neutralizing antibodies against the virus, inactivated vaccines prevent infection or lessen the severity of illness (Kayesh *et al.*, 2025). By producing WNV antigenic proteins in host cells, recombinant vaccines—such as those made with non-pathogenic viral vectors—are intended to increase immunogenicity (Taylor *et al.*, 2016). Regular horse vaccination programs have been shown to be successful in reducing illness incidence and protecting the community, especially in endemic areas (Naveed *et al.*, 2024).

There isn't a WNV vaccination that is currently licensed for use in humans, unlike in animals (Ulbert, 2019). Numerous vaccine candidates, including DNA vaccines, live-attenuated vaccines, inactivated vaccinations, and vaccines based on virus-like particles, have been produced (Gupta *et al.*, 2026). Human vaccine development has a number of obstacles, including safety concerns, long-term efficacy, and the low occurrence of severe cases, which hinders large-scale efficacy evaluation, despite early preclinical and clinical trial results showing encouraging immune responses (Nett *et al.*, 2025).

Additionally, vaccine design is complicated by immunological cross-reactivity among members of the Flavivirus genus, which can impact the immune response's specificity and possibly result in phenomena like antibody-dependent enhancement (ADE), though more research is needed in the case of WNV (Uhuami *et al.*, 2024).

Due to the scarcity of human vaccines, non-specific preventative measures like vector management, personal protection from mosquito bites, and improved surveillance systems are the main focus in public health (Fonzo *et al.*, 2024). However, the creation of human vaccines continues to be a top research goal, especially to safeguard vulnerable populations including the elderly and those with weakened immune systems (Soraci *et al.*, 2026).

Control

An integrated strategy that addresses the vector, reservoir, and environmental elements that promote transmission is necessary to control WNV infection (Campos *et al.*, 2025). Control techniques concentrate on avoiding exposure and breaking the cycle of transmission because there is no human vaccine or effective targeted antiviral medication (Cendejas and Goodman, 2024).

Controlling vectors, especially *Culex* mosquitoes, is a crucial part of WNV control (Fesce *et al.*, 2025). In order to reduce breeding habitats, waste management, drainage system improvement, and the removal of

stagnant water are all part of this effort (Zerbato *et al.*, 2026). Additionally, the results of mosquito population density tracking can be used to selectively apply pesticides, including larvicides and adulticides (Bellini *et al.*, 2014). To maximize efficacy while reducing environmental effects, this evidence-based strategy is crucial (Fesce *et al.*, 2025).

Another essential component of control systems is individual protection (Campos *et al.*, 2025). The danger of mosquito bites can be decreased by using repellents, wearing protective clothes, and installing mosquito nets or nets over home ventilation (Gould *et al.*, 2025). The success of community-based interventions is largely dependent on public education on exposure hazards and preventive behaviors (Marino *et al.*, 2025).

An essential component of early diagnosis and response to elevated viral activity is integrated epidemiological surveillance (Najafi *et al.*, 2026). This strategy includes tracking mosquito populations, keeping an eye on human cases, and identifying infections in reservoirs like wild birds (Bruce *et al.*, 2025). Targeted interventions are made possible by the data acquired, which enables the identification of high-risk locations and the timing of increased transmission (Habarugira *et al.*, 2020).

Horse vaccination is a useful preventive measure in the veterinary field to lessen the disease's effects (Naveed *et al.*, 2024). Additionally, early warning systems for human health can be strengthened by using animal health surveillance as an early indicator of virus activity in a region (Angelou *et al.*, 2025).

Given the intimate connection between environmental, animal, and human health, the One Health concept is an essential basis for WNV control (Bruno *et al.*, 2025). Faster information exchange and more efficient intervention coordination are made possible by cross-sector collaboration (Geffroy *et al.*, 2021). This entails combining information from research institutes, the agricultural, environmental, and health sectors. An integrated One Health framework for WNV control is presented in Figure 3.

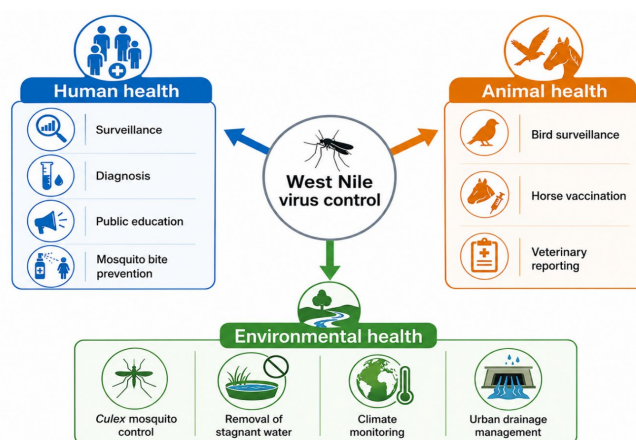


Figure 3. One Health-based integrated strategy for WNV surveillance, prevention, and control.

Long-term planning must also take environmental variables like urbanization and climate change into account (Singh *et al.*, 2025). Future risk reduction initiatives will include adjusting to shifting rainfall and temperature trends, which can affect vector dispersal (Paz, 2015).

Conclusion

West Nile virus is the cause of West Nile fever, a zoonotic illness that is spreading over the world and involves intricate relationships between vectors, reservoirs, and inadvertent hosts. This disease is difficult to diagnose, treat, and control due to its wide clinical spectrum, which ranges from asymptomatic infection to severe neuroinvasive forms.

The necessity of a preventive strategy, mainly through vector control and raised public awareness, is highlighted by the absence of particular antiviral medication and a human vaccine. Additionally, the epidemiological dynamics of this disease are influenced by environmental factors like

global movement and climate change.

In order to sustainably lessen the effects on health and the economy, West Nile fever control necessitates an integrated One Health approach that incorporates environmental measures, surveillance, and cross-sector cooperation.

Acknowledgement

The authors thank Badan Riset dan Inovasi Nasional for the funding support for this study.

Conflict of interest

The authors declare that there is no conflict of interest.

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