



## Comprehensive analysis of West Nile Virus transmission: Environmental, ecological, and individual factors. An umbrella review

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### ABSTRACT

**Background:** West Nile Virus (WNV) exemplifies the complexities of managing vector-borne diseases, expanding globally due to human activities and ecological changes. Originating from Africa and transmitted by *Culex* mosquitoes, WNV is now reported across multiple continents. The aim of this study was to identify the environmental, ecological, and individual factors influencing WNV transmission.

**Methods:** An umbrella review was conducted. Comprehensive searches were performed in PubMed, Scopus, Web of Science, Embase, and LILACS. Inclusion criteria were reviews involving WNV transmission agents (reservoirs, vectors, hosts) and associative analyses between environmental, ecological, or individual factors and WNV transmission. Data extraction and quality appraisal were performed using templates and the AMSTAR 2 tool.

**Results:** From 404 retrieved studies, 23 systematic reviews and meta-analyses were included. Almost 70 % were low or critically low quality. The co-occurrence network highlighted emerging research on climate change and environmental factors. Temperature, precipitation, and land use significantly influence WNV transmission. Warmer temperatures enhance mosquito populations and viral replication, while extreme weather events like droughts increase mosquito-human contact. Climate change significantly contributes to WNV dynamics by altering temperature and precipitation patterns, enhancing vector proliferation, and extending transmission seasons. Ecological factors such as higher avian diversity, vegetation indexes, and distribution of mosquito species can impact WNV transmission significantly. Education and income levels influence preventive behaviors and infection risk, with lower socioeconomic status linked to higher WNV risk. Certain occupational groups are also at elevated risk of WNV infection.

**Conclusion:** Environmental factors like temperature and precipitation critically affect WNV transmission by influencing mosquito behavior and avian reservoir dynamics. Socio-economic status and education levels significantly impact individual preventive behaviors and infection risk. Multifactorial influences on infection risk make necessary integrated surveillance systems and public health strategies. Longitudinal studies with One Health approaches are necessary to better understand WNV dynamics and reduce WNV transmission.

**Abbreviations:** AMSTAR, Assessing the Methodological Quality of Systematic Reviews; IVM, Integrated Vector Management; KAP, Knowledge, attitudes, and practices; NDVI, Normalized Difference Vegetation Index; ORadj, Adjusted Odds Ratio; PICO, Population, Intervention, Comparison, Outcome; PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses; RNA, Ribonucleic Acid; USA, United States of America; WNV, West Nile Virus.

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## 1. Introduction

West Nile Virus (WNV) exemplifies the complexities of managing vector-borne diseases globally, expanding beyond its origins due to human activities and ecological changes [1]. Originating from Africa and transmitted by *Culex* mosquitoes, this flavivirus is now reported across the Americas, Europe, Asia, and Australia, making it a key focus of epidemiological studies [2,3]. WNV transmission involves birds as reservoirs and mosquitoes as vectors. Humans and horses are dead-end hosts, with severe disease in a small percentage of cases [4]. The existence of different lineages of WNV is crucial for understanding its epidemiology and outbreak potential. WNV has up to seven distinct genetic lineages with unique origins and distributions, such as lineage 1a in the Mediterranean and lineage 2 in central Europe [5]. This genetic diversity affects the virus's spread, disease severity, and adaptability, highlighting the need for tailored surveillance and control strategies [5]. Clinically, WNV ranges from mild flu-like symptoms to severe neurological conditions, with about 80 % of infections asymptomatic, and about 19 % developing very mild and unspecific symptoms while approximately 1 % escalate to severe neurological diseases [6,7].

WNV incidence is increasing worldwide. Until 2000, WNV caused limited outbreaks, considered an African virus rarely introduced to Europe by migratory birds. It is now endemic in Europe, with 728 human infections in 2023, of which 709 were locally acquired [8]. Since its introduction into the United States of America (USA), WNV has caused thousands of cases annually, with transmission spikes correlating with suitable climatic conditions [9]. Climate change and habitat alterations driven by human activities facilitate the transmission of pathogens from wildlife to humans, thereby increasing risks to public and animal health [10]. These changes, along with human living conditions, lack of health education, and inadequate infrastructure, create environments conducive to the proliferation of vectors [11]. Non-human hosts, such as birds are the main reservoirs, while humans often become incidental hosts, increasing the exposure to pathogens through increased human-vector contact rates [12]. Researchers from the fields of virology, ecology, entomology, climate science, and public health have collaborated to uncover how environmental factors such as climate change influence the virus's transmission dynamics [13]. For instance, changes in temperature and precipitation significantly affect mosquito populations and virus replication rates, thus altering transmission patterns [14,15]. This multidisciplinary research underscores the necessity of a collaborative approach to effectively manage and anticipate the spread of vector-borne diseases like WNV.

Birds sometimes experiencing high mortality rates during outbreaks in the American continent, which can severely disrupt local ecosystems [16]. Mammals, including horses and other domestic animals, can also be infected [17]. This avian-mammal cross-species transmission highlights the importance of the One Health approach, which integrates human, animal, and environmental health strategies to manage zoonotic diseases effectively. One Health initiatives are essential for developing comprehensive surveillance and control measures that consider the ecological connections between human and animal health [18,19].

The surveillance and control of WNV require an understanding of multiple interlinked factors, including vector ecology, viral pathogenesis, environmental conditions and the social determinants of health [5]. Understanding these diverse factors is critical for the development of integrated strategies that can effectively reduce the incidence and impact of WNV [20,21].

In this umbrella review, we synthesize evidence from systematic reviews to delve deeper into how environmental, ecological and individual factors affect the transmission dynamics of WNV.

## 2. Methods

An umbrella review, defined as a review of reviews, was conducted to identify systematic reviews and meta-analysis that evidenced the

relationship between environmental, ecological and individual factors with WNV transmission and infection. This approach synthesizes evidence from various systematic reviews into a single article [22]. The study followed Joanna Briggs Institute guidelines and adhered to PRISMA [23,24]. It was registered in PROSPERO (CRD42024531438).

### 2.1. Search strategy

A comprehensive search was conducted in PubMed, Scopus, Web of Science, Embase, and LILACS up to March 13th, 2024. Snowball techniques and expert consultations were employed to capture all pertinent literature. A research librarian assisted with the search design and execution. No language restrictions were applied. The detailed search strategy is in Supplementary Material A.

### 2.2. Inclusion criteria

We included the following criteria: 1) Systematic reviews and meta-analyses, 2) studies involving agents of the WNV transmission cycle (reservoirs, vectors, hosts) presenting effect sizes influencing WNV transmission and 3) studies assessing association with any relevant transmission factor (environmental, ecological or human individual factors).

### 2.3. Exclusion criteria

We excluded the following the criteria: 1) Studies focusing on molecular mechanisms of WNV transmission and infection, not including a population-level of analysis and 2) intervention studies.

### 2.4. Screening

Bibliographic metadata was managed using Mendeley. A two-step screening process was conducted, reviewing titles and abstracts independently, followed by full-text screening. 20 % of the articles were assessed by two reviewers while the rest was divided between them. Kappa score measured the level of agreement between reviewers, and discrepancies were resolved by consensus with a third reviewer. Supplementary material B shows the list of excluded studies and the reason of exclusion.

### 2.5. Data extraction

Data was extracted using two standardized templates by two reviewers. Variables extracted included metadata such as year of publication, authors, and funding. Transmission factors, and study design were also extracted. Search-related information was captured through the data base number, search start date, and search ending date, as well as languages included. Geographical location of primary studies, total number of studies, studied actor, effect size measurements were retrieved when possible. Supplementary Material C contains the extraction template.

### 2.6. Quality appraisal and assessment of overlaps

Quality appraisal was conducted simultaneously by two reviewers using the AMSTAR 2 tool [25]. See supplementary material D for further details.

Primary studies were analyzed for overlaps using a citation matrix by Thomson et al. [26]. In this process, we identified the proportion of primary studies focused on WNV transmission, while primary studies related to other vector-borne diseases were not considered. Details are provided in Supplementary material E.

2.7. Data synthesis

Data was narratively synthesized by the review team, with descriptive analysis assessing main characteristics. Information was synthesized by variable categories (environmental, ecological, individual factors) detailing WNV transmission influences (reservoir, vector, host). Contradictory findings were discussed considering review quality and study characteristics.

A co-occurrence network was designed to study the factor studied over the time based on the keywords. Nodes correspond to the number of times a keyword is used and edges the times they are used in the same review. VOSviewer software was used.

3. Results

3.1. Overview of studies included

The PRISMA flowchart (Fig. 1) shows 404 studies retrieved, with 244 remaining after duplicates were removed. After screening titles and abstracts, 151 articles were excluded, leaving 93 for full-text review. Twelve articles were scored by two researchers with 92 % agreement ( $\kappa = 0.63$ ). Finally, 23 systematic reviews and meta-analyses were retained for data extraction (Table 1).

The selected reviews included 1998 primary studies, with 519 (25.97 %) focused on WNV transmission. Four systematic reviews focused entirely on WNV transmission [12,27–29]. Of the 519 WNV-focused studies, 54 (10.4 %) overlapped, with 44 shared between two studies and ten among three. Fig. 2 represents the total of the 1027 geographical study locations reported along 16 reviews [12,28–42], while 7 remaining reviews did not provide the information [27,43–48]. USA led with 255 studies (24.8 %). European contributions were from Italy (81 studies, 7.9 %), Spain (47, 4.6 %), France (41, 4.0 %), Germany (29, 2.8 %), and the UK (27, 2.6 %). In Asia, contributors included India (33, 3.2 %), China (27, 2.6 %), and Japan (9, 0.9 %). Africa’s representation was led by Kenya (14, 1.4 %) and South Africa (11, 1.1 %). Latin America included Brazil (49, 4.8 %), Mexico (12, 1.2 %), and

Argentina (6, 0.6 %). Oceania’s contributions came from Australia (21, 2.0 %) and New Zealand (7, 0.7 %).

Fig. 4 represents the visualization of the co-occurrence network. A chronological order was applied through colors gradient. Minimum number of occurrences were established to 3, from which 62 out of 500 met the threshold. Fourteen keywords met were included to analyze.

3.2. Risk of bias and study quality

The review revealed substantial heterogeneity among studies, with varying effect sizes and biases stemming from methodological differences, leading to inconsistent results across geographic and environmental contexts.

Given the characteristics of this study, a significant level of heterogeneity was present in this study and within each individual article. Such conditions were narratively addressed by a high number of studies [12,31–33,43,44,46,49], while others used a statistical approach to analyze heterogeneity [30,34,35,38,40,42,45].

Within the retrieved articles bias was addressed in a variety of ways, from simple acknowledgment of conditions such as geographical location and language retrieved [12,30,31,43], to the use of quality assessment tools [12,28–30,33,35,36,45], and statistical approaches [30,38,40,42,46].

Applying AMSTAR 2 tool, two reviews were rated high quality, two as moderate, and almost 19 as low or critically low. Fig. 3 shows the occurrence of weaknesses across the included studies. Low scores were due to two main critical domains: providing a list of excluded studies and assessing the risk of bias. The domain on reporting funding sources was negative for all studies. See the entire assessment in Supplementary Material E.

3.3. Transmission factors

About 80 % of the reviews analyze the roles of hosts, reservoirs, and vectors in WNV transmission. Table 2 summarizes the main factors identified and their association with WNV transmission. The 23 reviews

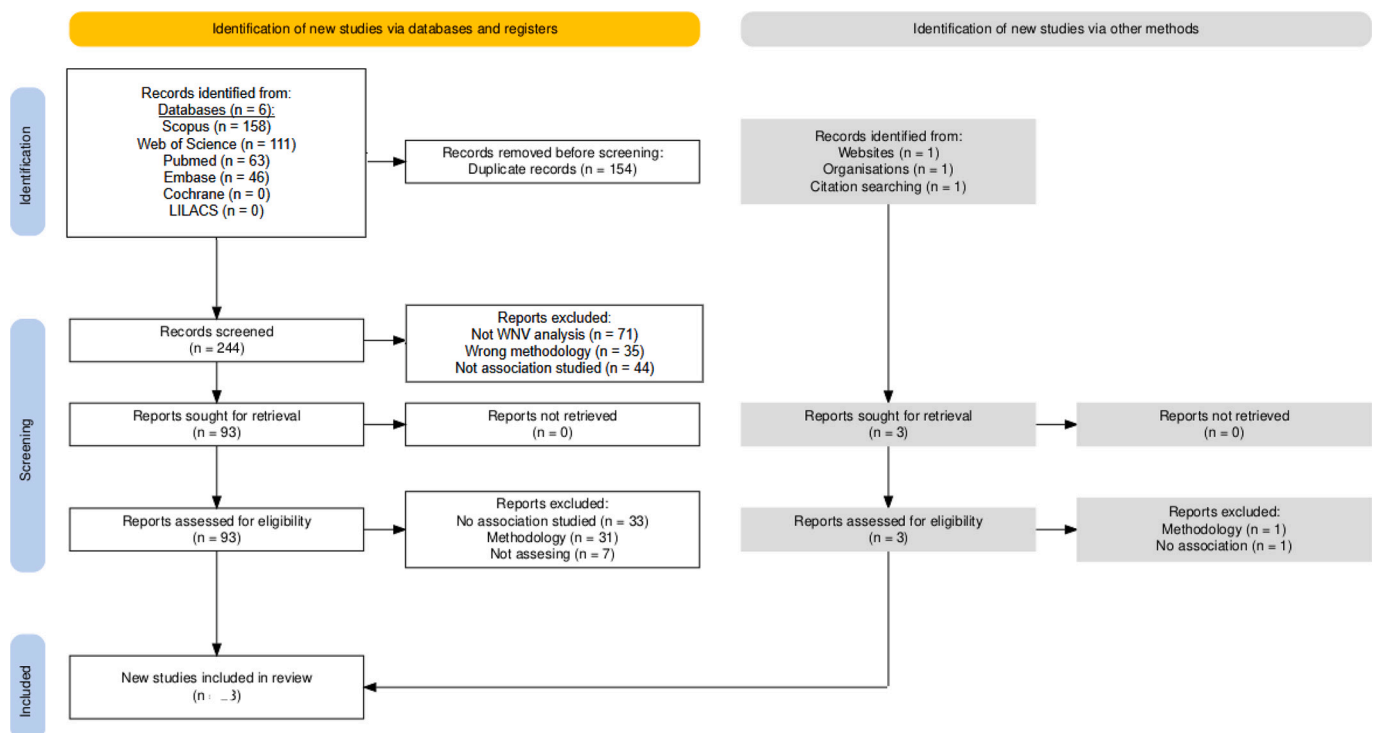


Fig. 1. PRISMA flowchart.

**Table 1**  
Overview of the main characteristics of the studies included.

No. [Ref.]	Author(s) and Year	Type of Review	Search time	No. of primary studies	WNV primary studies	Language restriction	Subject of study	Main variables studied
1. [45]	Agunos, A. et al., 2016	SR and MA	Up to 01/03/2015	156	2	English	Human	Occupational
2. [44]	Brown, L. et al., 2014	SR	01/01/1990–30/11/2021	38	16	English	Reservoir, and vector	Environmental and ecological (drought)
3. [33]	Brugueras, S. et al., 2020	SR	01/01/2000–30/09/2017	61	20	English, Spanish, French, Italian, and Portuguese	Reservoir, vector, human/equine	Environmental and ecological
4. [32]	Chakrabortyid, S. et al., 2023	SR	30/09/2019–08/06/2020	127	3	English	Human	Landuse (cattle)
5. [48]	Counotte, M. J. et al., 2018	SR and MA	Up to 15/04/2018	128	3	None	Human	Alternative transmission path (Sexual)
6. [27]	D'amore, C. et al., 2023	SR	Up to 01/01/2023	26	26	English	Reservoir, vector, and human	Environmental and ecological
7. [46]	Esser, H. J. et al., 2019	SR	01/01/1980–07/01/2016	183	55	English	Reservoir, vector, and human/equine	Environmental and ecological
8. [42]	Ferraguti, M. et al., 2023	SR and MA	Up to 28/10/2019	162	11	English	Vector and human	Land-use
9. [29]	Fonzo, M. et al., 2024	SR	Up to 04/05/2023	17	17	English	Human	Sociodemographic (knowledge and practices)
10. [31]	García-Romero, C. et al., 2023	SR and MA	Up to 31/07/2021	43	10	Spanish, Portuguese, and English	Human and non-human	Vegetation
11. [12]	Giesen, C. et al., 2023	SR	01/01/2000–31/12/2020	65	65	English, French, Portuguese, German, Italian and Spanish	Reservoir, vector, and human/equine	Environmental and ecological
12. [36]	Giménez-Richarte, Á. et al., 2022	SR	Up to 10/11/2021	29	11	English, Spanish	Human	Transplant/transfusion
13. [43]	Mann, T. Z. et al., 2018	SR	01/01/1910–12/06/2017	17	5	English, Spanish, Portuguese	Human	Alternative transmission path (Breast milk)
14. [28]	Odigie, A. E. et al., 2024	SR	Up to 01/09/2023	21	21	English	Human	Occupational
15. [38]	Perrin, A. et al., 2022	MA	Up to 01/06/2021	107	35	English	Vector	Land-use
16. [35]	Power, G. M. et al., 2022	SR and MA	01/01/1980–30/06/2020	36	1	English, Portuguese, Spanish, French	Human	Sociodemographic
17. [30]	Priyadarshana, T. S. et al., 2023	SR and MA	Up to 30/11/2021	31	16	Not mentioned	Vector	Predation
18. [34]	Rudolph, K. E. et al., 2014	SR and MA	15/04/2010–06/01/2011	60	5	English	Human	Alternative transmission path (transplant/transfusion)
19. [47]	Sack, A. et al., 2020	SR	Up to 01/12/2016	233	14	English	Human	Occupational
20. [40]	Salkeld, D. J. et al., 2013	MA	Not mentioned	16	3	English	Reservoir, vector, human	Ecological (Biodiversity)
21. [37]	Shingde, R. et al., 2018	SR and MA	Up to 01/06/2017	119	8	None	Human	Alternative transmission path (Transplant/transfusion)
22. [39]	Tolsá-García, M. J. et al., 2023	SR and MA	Up to 04/10/2020	234	162	English	Vector	Environmental and ecological
23. [41]	Vonesch, N. et al., 2019	SR	01/01/2007–01/10/2018	89	10	English	Human	Occupational

SR: Systematic review, MA: Meta-analysis.

covered various focus areas: environmental and ecological factors (39 %), alternative transmission pathways (22 %), occupational exposure (17 %), land use changes (13 %), and socio-demographic factors (9 %).

### 3.4. Environmental factors

#### 3.4.1. Temperature

Temperature significantly affects WNV avian reservoir behavior. Warmer conditions lead to increased WNV circulation as birds congregate around water bodies, heightening their exposure to vector [12,44].

Temperature fluctuations impact mosquito populations, particularly *Culex pipiens*. An increase in average, maximum, and minimum daily,

weekly, biweekly, monthly, or annual temperature is associated with larger adult mosquito populations, with temperature increases of 1.5–2.5 °C from April to June being particularly impactful. However, the direction and strength of correlations vary, as laboratory studies indicate that while some mosquito habitats show increased WNV infection and transmission rates with rising temperatures, others do not [12,46].

Temperature anomalies, or significant deviations from historical averages, have a direct correlation with West Nile Disease (WND) cases in Europe. For instance, higher monthly mean and minimum temperatures have been linked to increased WND incidences in Israel, Greece, and Italy. Similarly, unusually warm summers in Spain have led to more human cases, attributed to increased vector exposure during outdoor

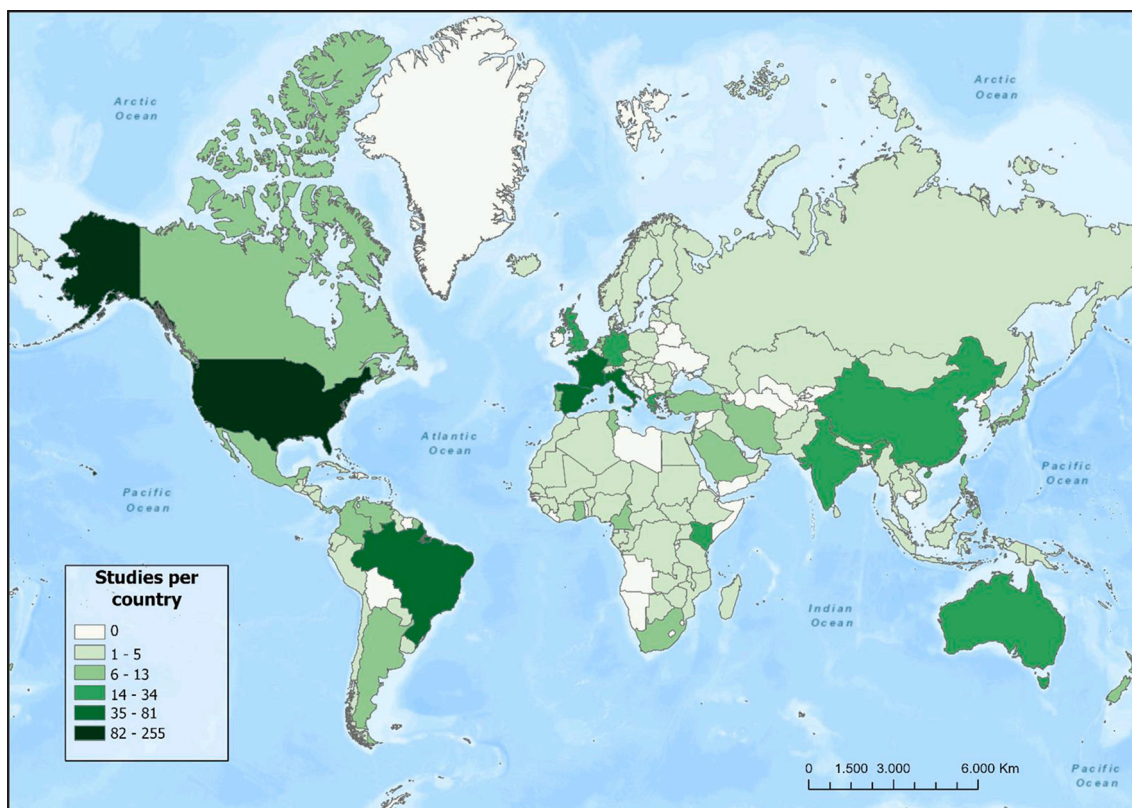


Fig. 2. Primary studies geographic distribution. Represented by colors the number of each study location. Some primary studies focused on more than one geographic location.

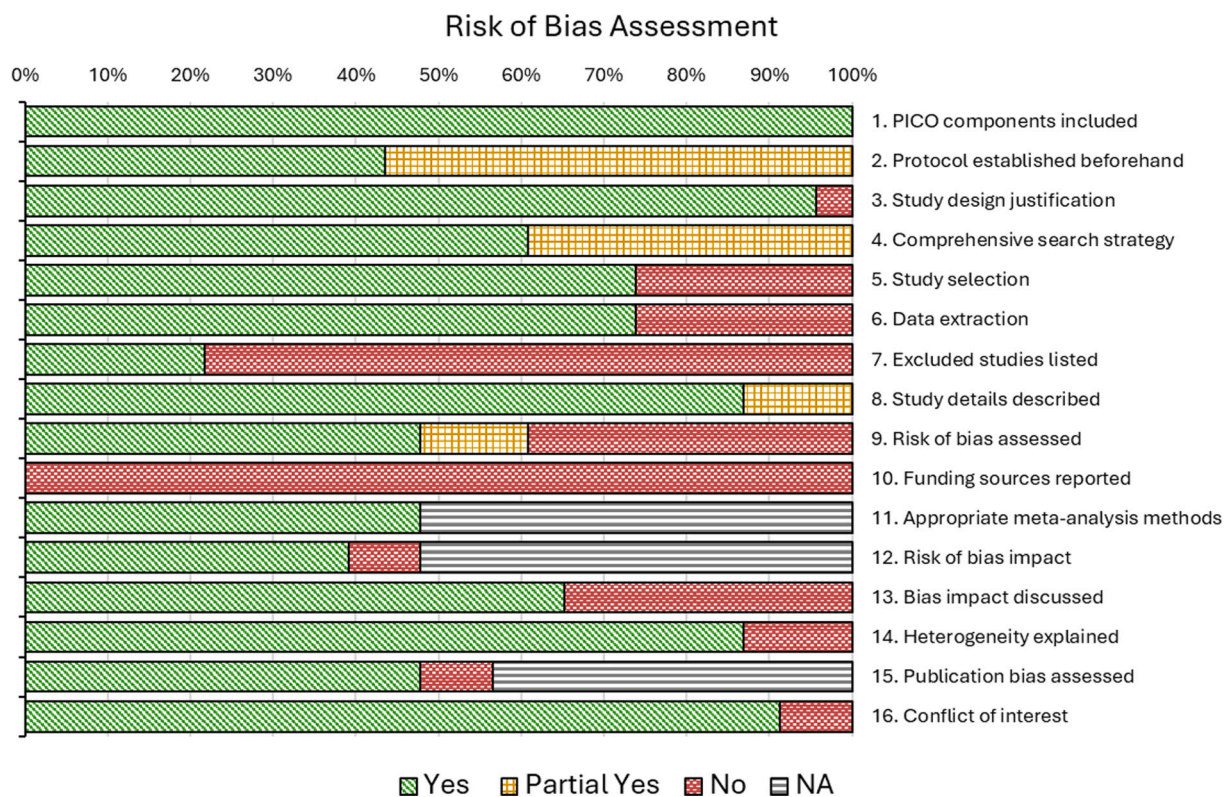


Fig. 3. This graph displays the AMSTAR 2 assessment results, where each bar represents one question. The colors indicate the proportion of systematic reviews rated as Yes (green), Partial Yes (yellow), No (red), and not applicable (gray) for each question. The number in each bar represents the references of Table 1.

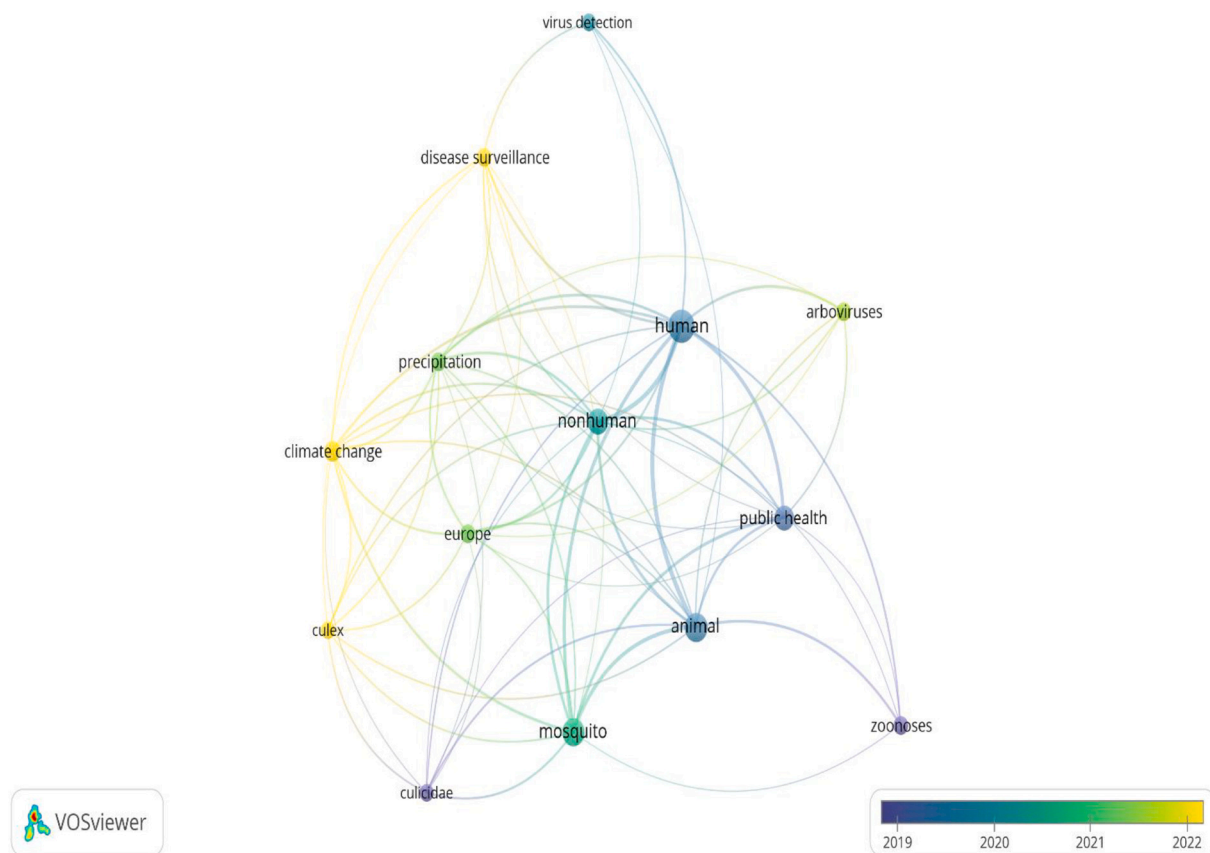


Fig. 4. Co-currence network visualization. Nodes represent the keywords included, edges the amount of times references are shared between included studies.

activities [12]. A meta-analysis found no significant effect of viral titer, temperature, or days post-infection on transmission efficiency but reported that the extrinsic incubation period was shorter at higher temperatures [39]. Additionally, high temperatures specifically during the summer of 1998 in Israel correlated with an uptick in WNV cases by 2000 [12]. In Volgograd, Russia, high temperatures from July to September were linked to an increase in WNV cases from 2000 to 2007 [27]. In the USA, a 5 °C increase in weekly maximum temperature corresponded with a 32–50 % increase in WNV infections from 2001 to 2005 [12,27].

Finally, the impact of temperature on mammal hosts, other than humans, is also relevant. In Israel, a study documented that increased daily land surface temperatures from 2001 to 2010 were associated with more WNV cases in equines. Additionally, higher daily mean temperatures during July and August in Germany and elevated spring and summer temperatures across southern Europe were linked to a greater presence of seropositive horses, camels, donkeys, goats, mules, and sheep [12].

#### 3.4.2. Precipitation, humidity, and waterbodies

In the USA, a study spanning 2001–2005 demonstrated that a 20-mm increase in cumulative weekly precipitation led to a 4–8 % rise in WNV infection rates in humans, with heavy rainfall periods (>50 mm per day) triggering a 33 % increase in cases, though this relationship weakened during summer months [27]. In contrast, a study in the Danube Delta showed a negative correlation between precipitation and mosquito infection rates after a 30-day lag, without directly impacting mosquito densities [46]. Drought conditions transform flowing waters into stagnant pools, ideal for mosquito breeding, and prompt birds to congregate around limited water sources, increasing WNV transmission [44,46]. Higher incidences of WNV are observed during high temperatures, summer droughts, and significant late winter/early spring precipitation

[46].

The correlation between precipitation and human WNV incidence is complex. Studies in Italy and Greece indicated a positive association with increased mean and minimum monthly precipitation, while another study found a negative correlation in the same regions and Israel [12]. Nevertheless, five other studies reported no significant relationships between rainfall patterns and WNV incidence in humans [12]. Two reviews noted that increased relative humidity correlates with higher human cases [12,27]. Studies on evapotranspiration found positive associations with mosquito density, highlighting the role of hydroclimatic conditions in vector behavior [27,33].

Temperature extremes and hydrological features significantly influence WNV risks. Maximum temperatures between June and October, coupled with the presence of wetlands, have been identified as positive predictors of WNV risk in southern Spain, particularly affecting bird populations [12]. Wetlands within 500 m are associated with higher horse WNV incidence in France and Spain [12]. Lower altitude areas in Israel are associated with higher WNV risk [12]. In urban settings within the USA, more extensive water bodies contribute to increased mosquito populations due to favorable breeding conditions, thereby enhancing WNV transmission [46].

### 3.5. Biotic and ecological factors

#### 3.5.1. Land-use related factors

Land-use patterns significantly influence the distribution and abundance of vector populations, as well as the transmission dynamics of vector-borne diseases such as WNV.

The percentage of irrigated crop lands and fragmented forests were positively related to WNV incidence across Europe [46].

Proximity to urban areas, higher human population density, and nearby livestock farms positively correlate with *Culex pipiens* abundance

Table 2

Association of the main variables related to West Nile Virus transmission among the reviewed studies.

Variable	Reservoir (Birds)	Vector (Mosquitoes)	Human Host	Non-Human Host
Ecological factors				
Temperature	+ (Increased WNV circulation) [12,44]	+ (Greater mosquito abundance) [12,46]	+/- (Increased cases in some areas but no significant relationship in others) [12,27,39]	+ (Greater presence of seropositive animals) [12]
Humidity	NE	+ (Associated with increased mosquito density) [12]	+ (Increased relative humidity linked to higher human cases) [12]	NE
Precipitation	+ (Enhanced bird-mosquito interactions during drought) [46]	+/- (Positive impact on mosquito breeding but negative correlation with infection rates after lag in some areas) [27,46]	+/- (Both positive and negative associations with WNV incidence) [12]	+ (Increased presence of wetlands linked to higher WNV risk) [12]
Water Bodies	NE	+ (Increased mosquito populations near water bodies) [46]	NE	+ (Wetlands associated with higher WNV incidence in horses) [12]
Land Use	NE	+ (Urbanization increases breeding sites) [38]	NE	NE
Vegetation (NDVI)	NE	+ (Higher NDVI associated to larger mosquito populations) [33]	+ (Increased NDVI linked to higher human WNV incidence) [12]	NE
Biodiversity	+/- (Higher avian diversity reduces WNV spread) [40,46]	- (Dispersion of blood meals across diverse bird species reduces infection rates and Predation on mosquito larvae reduces vector populations) [30,31,46]	+ (Higher avian diversity linked to lower human WNV incidence) [40]	NE
Migration Routes	NE	NE	NE	+ (Migratory birds contribute to WNV spread) [46]
Wind	NE	+/- (Can influence mosquito flight and dispersal patterns) [27,46]	NE	NE
Population Density	NE	+ (Higher human density increases exposition risk) [12,33]	+ (Higher risk in densely populated areas) [12,33]	NE
Individual human factors				
Age	NE	NE	- (Older adults less likely to use preventive measures) [29]	NE
Occupation	NE	NE	+ (Certain occupational groups face higher risk due to exposure) [28,41,45,47]	NE
Education	NE	NE	- (Less education linked to higher risk) [35]	NE
Blood Transfusion	NE	NE	+ (Risk of WNV transmission via transfusions) [34,36]	NE
Organ Transplants	NE	NE	+ (Risk of WNV transmission via organ transplants) [34,37]	NE
Sexual Transmission	NE	NE	Possible (Potential for sexual transmission of WNV) [48]	NE
Mother-to-Child Transmission	NE	NE	Possible (Limited evidence of transmission via breast milk) [43]	NE

NE: Not specified.

[12]. Urban expansion generally reduces *Culex* spp. populations, but *Cx. pipiens* adapts to urban settings, maintaining significant populations [12]. Notably, the impact of urban versus rural environments on mosquito dynamics are poorly known [12]. Additionally, a systematic review suggested that cattle near urban areas can increase WNV risk by increasing vector populations [12,32].

A systematic review and meta-analysis found that medium land-use intensity is associated with higher infection prevalence among hosts [42]. The same review highlighted that urbanization creates ideal breeding sites for the vector *Cx. quinquefasciatus*, such as man-made containers and stable water sources, while agricultural development promotes them due to higher sedimentation and warmer temperatures. The analysis of Perrin et al. [38]. highlights that landscape anthropization (urbanization, deforestation, and agricultural development) has a significant negative effect on overall mosquito diversity ( $r = -0.25$ ,  $p = 0.03$ ) and abundance ( $r = -0.13$ ,  $p = 0.006$ ). However, these impacts vary across mosquito species. While the abundance of some species decreases, others, particularly those associated with transmitting multiple vector-borne diseases (VBDs), show an increase [38]. Tolsá-García et al. [39]. also identified that the mosquito species with highest standardized minimum infection rate (SMIR) were *Cx. restuans* in North America (SMIR = 56.01) and *Cx. pipiens* in Africa and Europe (SMIR = 20.45 and 29.25, respectively) [39].

Some studies from USA have provided support for a potential role of avian diversity reducing WNV transmission. According to Esser et al.

[46]., these studies have found negative correlations between avian diversity and different components of WNV epidemiology, namely the prevalence of pathogens in mosquitoes, the density of infected mosquitoes and the incidence of WNV [46]. However, other studies in USA or Europe have not found any relationship between avian diversity and WNV transmission, or even positive relationships between avian diversity and WNV incidence in birds [46,50]. Some studies emphasize the relative significance of other factors like mosquito host preference, host reservoir competence, temperature, and precipitation in influencing local WNV transmission dynamics [31,46], and frequent differences in the factors driving WNV outbreaks in the Old and the New World [46].

A meta-analysis highlighted dragonfly and damselfly naiads as effective biological control agents against mosquito populations, including *Culex* species. On average, a single dragonfly/damselfly naiad consumed 40 mosquito larvae per day (95 % CI: 20, 60), corresponding to a 45 % reduction in larval populations (95 % CI: 30 %, 59 %) within experimental containers [30].

The influence of vegetation on WNV was synthesized by three reviews [12,33,46]. The Normalized Difference Vegetation Index (NDVI) [43], a measure of vegetation photosynthetic activity, quantity, and density of plants, positively correlates with both the presence and abundance of *Culex* spp., suggesting that areas with higher vegetation productivity support larger mosquito populations, potentially enhancing WNV transmission [33,46]. Drought conditions intensify this

effect by reducing water availability and vegetation cover, leading to smaller temporal water pools that favor mosquito breeding by diminishing natural predator presence [33]. Increased NDVI and relative humidity have been linked to higher human WNV incidence, while factors such as lower altitude and land use heterogeneity act as negative predictors, leading to larger vector populations and higher availability of breeding sites [12]. Habitat loss and deforestation increased the odds of mammalian exposure to arboviruses by 46 % (Odds Ratio: 1.46; 95 % CI: 1.34–1.59;  $p < 0.0001$ ) compared to vegetated areas [31].

The proximity to migratory routes correlates directly with an increase in WNV cases [12]. Differences in antibodies prevalence and mass mortality events could explain, at least in part, differences in the epidemiology between Europe and America according to Esser et al. [46]. Migratory birds, especially those traveling from Africa—where WNV is more prevalent—to northern Europe, play a pivotal role in disseminating WNV. Once introduced, WNV can maintain itself within local bird communities and mosquito populations [46].

### 3.5.2. Population density

Despite human density has been associated to higher WNV incidence in humans [12], that study was done at provincial resolution across Europe [51], and consequently it is difficult to understand at what scale is this factor operating. More densely human-populated areas may have an increased density of areas where mosquitoes may get in contact with humans, or areas with a higher probability of interaction between birds, humans and infected mosquitoes [12,33].

## 3.6. Individual human factors

### 3.6.1. Socio-economic status and education

A systematic review found that lower socioeconomic status, indicated by reduced household income, is associated with higher WNV infection risk [35]. The relationship between education level and vector-borne infection risk was assessed in 25 studies across 18 countries. A meta-analysis of 17 studies showed that lack of education correlates with a combined relative risk (RR) of 1.5 (95 % CI 1.3 to 1.9) for vector-borne infection, including WNV [35].

Another review on knowledge, attitudes, and practices (KAP) regarding WNV revealed demographic disparities in preventive behaviors. Older adults (aged >50) were less likely to use insect repellents compared to younger individuals, with an Adjusted Odds Ratio (ORadj) of 0.4, which quantifies the strength of association between an exposure and an outcome, accounting for potential confounding variables. Women were more likely to wear long clothing (ORadj = 1.4) and use repellents (ORadj = 1.3) than men. Higher education levels were associated with better knowledge and more consistent preventive practices (ORadj = 3.5). Income and urban/rural residence varied in impact, while higher concern and risk perception significantly increased preventive actions [29].

### 3.6.2. Occupational risk

Certain occupational groups face higher WNV infection risks. Military personnel in endemic areas show high seroprevalence due to outdoor activities and communal living in vector exposed areas. Veterinarians are at high risk through contact with infected animals' blood and mosquitoes (seroprevalence up to 23.0 %) [28]. Agricultural workers and farmers also have increased seroprevalence due to outdoor work during peak mosquito activity [28]. Laboratory workers handling WNV specimens are at risk of accidental inoculation, with a notable case of infection via needlestick injury [41,47].

Furthermore, reviews have identified WNV as a zoonotic pathogen potentially transmittable from horses to humans, especially during activities like horse necropsies. In addition, poultry workers in the USA, exposed to WNV-infected turkeys have presented symptoms of infection. None the less in these studies the mechanism of transmission is poorly understood [45].

## 3.7. Alternative pathways of transmission

### 3.7.1. Blood transfusions

The risk associated with blood transfusions is notable, with 42 reported cases predominantly involving red blood cells. These instances show that about 73.8 % of recipients displayed symptoms post-transmission, and notably, about 31.0 % of these cases resulted in fatalities. This data underscores the critical need for vigilant screening and preventive measures in blood transfusion services to prevent WNV transmission [36].

### 3.7.2. Organ transplants

WNV transmission through kidney transplants presents a severe risk, with a 38.5 % mortality rate among recipients. The median time from transplantation to symptom onset is 0.6 months, with diagnosis occurring at around 0.4 months. The one-year survival rate for infected patients is 69 %, highlighting the serious risk. The incubation period ranges from median incubation period for WNV to be 2.6 days (95 % CI: 1.6–3.5) in transplanted patients, compared to 2.9 days (95 % CI: 0.5–3.1), with a dispersion of 1.04 (95 % CI: 1.04–1.29) for mosquito-human transmission [34].

### 3.7.3. Sexual transmission

There is emerging evidence suggesting the potential for WNV sexual transmission, detected in the prostate and testis postmortem in a male, and causing systemic illness following experimental intravaginal inoculation in mice. While there is no detailed information on the natural occurrence of sexual transmission of WNV in humans, these findings indicate a possible, yet under-explored, pathway for WNV spread [48].

### 3.7.4. Mother-to-child transmission

The possibility of mother-to-child transmission of WNV through breast milk has been supported by limited evidence. Several studies have detected WNV RNA (Ribonucleic Acid) in human milk, but these findings are inconclusive regarding the actual risk of transmission. For example, a case report identified WNV RNA in a milk sample six days post-onset of maternal symptoms, but subsequent samples were negative and non-culturable [43]. Animal studies suggest the potential for transmission through breastfeeding, yet distinguishing this from other transmission routes remains challenging. Despite these uncertainties, the health benefits of breastfeeding outweigh the potential risks, and current guidelines recommend that mothers with possible or confirmed WNV infection continue to breastfeed [43].

## 4. Discussion

This umbrella review synthesizes evidence from systematic reviews and meta-analyses to elucidate the complex interplay of environmental, ecological, and human factors in WNV transmission. Our study provides a comprehensive summary of evidence on the effects of climatic variables, land use patterns, and socio-economic conditions in shaping WNV transmission dynamics.

The co-occurrence network demonstrates the trends of new research frontiers in the understanding of WNV such as climate change and environmental factors as precipitation. The key-word Europe is relatively new, consistent with the endemicity of WNV in the continent [8].

Risk of bias assessment revealed significant variability in methodological rigor. Common shortcomings included inadequate assessment of publication bias, limited search strategy comprehensiveness, and failure to report funding sources, crucial for assessing conflicts of interest [52]. Underreporting of occupational WNV infections due to the lack of awareness among health professionals can lead to a misrepresentation of prevalence among certain populations [28,41]. Authors also reported a geographical bias towards Europe and North America, with a lack of studies in Africa, South America, and Asia [29,42]. Heterogeneity on the results evidenced the complexity of studying WNV due to the

geographical, ecological and environmental diversity in which this pathogen thrives.

Higher temperatures facilitate mosquito proliferation and viral replication [12,46], while extreme weather events, such as droughts, can increase mosquito-human contact by driving bird reservoirs closer to human settlements [44]. However, such effects do not need to be linear, and this may contribute to explain the apparently contradictory results reported in different countries. Higher temperatures are associated with increased WNV cases due to accelerated mosquito development and enhanced viral replication rates. For example, Magallanes et al. [53] found that warm winters in southern Spain are linked to more intense WNV circulation, highlighting the impact of seasonal temperature variations on virus dynamics [53]. Higher temperatures, particularly in winter and spring, correlate with increased WNV transmission [39].

Our review highlights how climatic conditions influence vector ecology and WNV transmission, with specific environmental factors affecting different regions and populations. Some studies reported a positive correlation between precipitation and WNV incidence, while others found a negative or no significant relationship, suggesting local ecological contexts critically modulate these effects [39,46]. Discrepancies align with prior research on the heterogeneity of vector-borne disease dynamics, where low temperatures may limit WNV transmission in higher latitudes/altitudes, and high temperatures may limit it in lower latitudes with hot, dry climates [54]. Recent research by Erazo et al. [13] indicates that climate change has significantly contributed to the spatial expansion of WNV in Europe. The study shows that rising summer and winter temperatures have increased the ecological suitability for WNV in regions like northern Italy, the Carpathian Mountains, and parts of Greece [13]. Similarly, another study highlights how climatic changes, such as increased temperatures and altered precipitation patterns, create favorable conditions for mosquito vectors, enhancing the risk of WNV transmission [55]. It is also remarkable the role of avian diversity and the different evidence found about its relationship with WNV transmission. Some studies have shown that migratory birds can be at higher exposure to WNV circulation [56].

Socio-economic factors, particularly education and income levels, significantly influence preventive behaviors and infection risk [29,35]. Harrigan et al. describe this phenomenon due to the geographic location of low-income communities, older infrastructure, and inefficient drainage systems [11]. Socio-economic disparities, particularly in education, impact individuals' awareness and adoption of preventive measures like mosquito nets or air conditioning, influencing infection rates [35]. The observed occupational risks for groups such as military personnel and veterinarians underscore the importance of targeted preventive strategies for high-risk populations [28,41,45,47].

Our findings highlight the need for integrated surveillance systems monitoring environmental conditions, vector populations, and human cases [5]. Public health strategies should prioritize educational campaigns in low-income, less-educated communities. Integrated vector management (IVM) approaches, combining chemical and non-chemical methods with community engagement, significantly reduce vector breeding sites and transmission risk. Sustainability of vector control programs relies on community capacity building, collaboration, and institutional support, reinforcing the need to integrate IVM principles [57].

A major strength of this review is its comprehensive approach, synthesizing a wide range of systematic reviews and meta-analyses, allowing for a robust understanding of WNV transmission's multifactorial nature. However, the review is limited by the heterogeneity of included studies, complicating the synthesis of quantitative data. Potential publication bias and exclusion of molecular and intervention studies may have constrained our findings. Umbrella reviews depend heavily on the quality and reporting of primary studies, potentially leading to selection and lost-to-follow-up biases, especially in meta-analyses of observational studies. Additionally, umbrella reviews

exclude the latest evidence from newer studies not yet reviewed [58].

Gaps identified in our study are the reduced number of longitudinal studies to understand WNV transmission dynamics. In addition, studies identifying the direct and indirect effects of climatic dynamics on the different actors involved in WNV amplification and transmission to humans are urgently needed. Furthermore, improving our knowledge of the environmental effects on the diversity and dynamics of WNV lineages and viral variants can elucidate the process involved in the introduction, establishment, spreading and overwintering of WNV [59]. In addition, it is necessary to integrate the study providing information of the main actors of the transmission, including mosquitoes, avian reservoirs and humans. [12]. Studies have evidenced the need for a quantitative approach to measure anthropization and land-use change [38]. Setting research priorities through an interdisciplinary process is essential, involving diverse stakeholders to identify key areas such as equity, technology, and surveillance [60]. Efficient surveillance and screening protocols are necessary to comprehend the direct transmissions through organ and blood transplant, as well for occupational transmission [45]. An evident gap found by our study was the analysis of socioeconomic factors and its relationship with WNV transmission, which was not sufficiently studied [35]. Additionally, studies need to evaluate the effectiveness of integrated One Health approaches that consider human, animal, and environmental health in managing WNV and other zoonotic diseases and improve the surveillance and control of mosquito-borne pathogens [61].

## 5. Conclusion

This review highlights the critical role of environmental, ecological, and individual human factors in WNV transmission. The findings underscore the necessity of a multidisciplinary approach and integrated public health strategies to effectively manage and mitigate the spread of WNV. By addressing the complex interplay of these factors, we can develop more effective surveillance, prevention, and control measures to reduce the burden of WNV globally.

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## Author contributions: CRediT

The conceptualization of this study was carried out by B-TC. Data curation was managed by V-CCA and G-PS. Formal analysis was conducted by B-TC and V-CCA. Funding acquisition was secured by P-SI and R-dFB. The investigation was led by CB-T and V-CCA. The methodology was developed by V-CCA, G-PS, FJ, MdIPJ, and B-TC. Project administration was overseen by B-TC, who also supervised the study. Visualization was executed by V-CCA. The original draft was written by V-CCA, while the review and editing were collaboratively done by V-CCA, FJ, MdIPJ, F-AS, GFV, MdIRM, PI, R-dFB, LM, B-TC.

## CRediT authorship contribution statement

**Carlos Adrian Vargas Campos:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation. **Selene García-Pérez:** Methodology, Data curation. **Jordi Figuerola:** Writing – review & editing, Methodology. **Josué Martínez-de la Puente:** Writing – review & editing, Methodology. **Irene Polo:** Writing – review & editing, Validation, Funding acquisition. **Belén Rodríguez-de-Fonseca:** Writing – review & editing, Validation, Funding acquisition. **Sofía Fernández-Álvarez:** Writing – review & editing. **Victor Galván Fraile:** Writing – review & editing. **Marta Martín-Rey:**

Writing – review & editing. **Marina Lacasaña**: Writing – review & editing. **Clara Bermúdez-Tamayo**: Writing – review & editing, Writing – original draft, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### Data availability

No data was used for the research described in the article.

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### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.onehlt.2025.100984>.

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