

Impact of climate change on West Nile virus distribution in South America

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Background: West Nile virus (WNV) is a vector-borne pathogen of global relevance and is currently the most widely distributed flavivirus causing encephalitis worldwide. Climate conditions have direct and indirect impacts on vector abundance and virus dynamics within the mosquito. The significance of environmental variables as drivers in WNV epidemiology is increasing under the current climate change scenario. In this study we used a machine learning algorithm to model WNV distributions in South America.

Methods: Our model evaluated eight environmental variables for their contribution to the occurrence of WNV since its introduction in South America in 2004.

Results: Our results showed that environmental variables can directly alter the occurrence of WNV, with lower precipitation and higher temperatures associated with increased virus incidence. High-risk areas may be modified in the coming years, becoming more evident with high greenhouse gas emission levels. Countries such as Bolivia, Paraguay and several Brazilian areas, mainly in the northeast and midwest regions and the Pantanal biome, will be greatly affected, drastically changing the current WNV distribution.

Conclusions: Understanding the linkages between climatological and ecological change as determinants of disease emergence and redistribution will help optimize preventive strategies. Increased virus surveillance, integrated modelling and the use of geographically based data systems will provide more anticipatory measures by the scientific community.

Keywords: climate change, epidemiology, South America, temperature, West Nile virus

Abbreviations

IPCC Intergovernmental Panel on Climate Change
GCM global climate model
GGE greenhouse gas emission
MIROC-5 Model for Interdisciplinary Research On Climate
PCA principal component analysis
RCP Representative Concentration Pathway
WNV West Nile virus

Introduction

Currently, West Nile virus (WNV) is considered the most widely spread arbovirus on the planet.¹ It is the aetiological agent that

causes West Nile fever, which is commonly asymptomatic or mild, but nearly 1 in 150 cases becomes neuroinvasive, inducing encephalitis or even death.² Although mosquito bites are responsible for almost all human infections, WNV transmission can also occur through organ transplantation, blood transfusion, intrauterine transmission and possible transmission through breastfeeding.³

Since its appearance on the American continent in 1999, WNV caused approximately 48 000 reported cases, with 24 000 reported neuroinvasive cases, >2300 deaths² and an estimated 7 million total human infections in the USA alone.⁴ At present, WNV is considered one of the most relevant viruses to cause zoonotic diseases in the US population.² WNV is also an important animal pathogen, as it results in a reported equine incidence of >28 000 cases and mortality in >300 bird species,⁵

causing substantial population declines among approximately 23 bird species.⁶ For example, in the last 20 y the American crow (*Corvus brachyrhynchos*) population in North America declined by 45% after the introduction of WNV.⁶ The negative impact of this virus has not been restricted to the USA, as >5000 human cases have been reported in Canada, and WNV is currently recognized as an emerging threat for America.⁷ WNV recently also became established in southeastern Europe, with a large outbreak in the summer of 2010 and recurrent outbreaks in 2011 and 2012.⁸

In its natural cycle, WNV is maintained in birds and mosquitoes, although several wild vertebrates and domestic animals such as horses, cats and dogs can be natural reservoirs for the virus.⁹ Although WNV has been isolated in 65 different mosquito species and 326 bird species, only a few *Culex* mosquito species, including *Culex pipiens*, *Culex quinquefasciatus* and *Culex nigripalpus*, drive the transmission of WNV in nature and the subsequent spread to humans.³ Migratory birds are often naturally infected intermediate hosts for WNV and likely carry the virus when they migrate. The virus they carry is most likely spread by the bite of an infected mosquito. This confirms the significance of migratory birds in WNV spread between two areas.¹⁰

The development and expansion of WNV is extremely divergent in each season, with periodic outbreak years combined with low levels of viral transmission, and climate is one of the central elements driving these trends.¹¹ For example, higher air temperatures influence vector population growth rates and its competence, accelerate virus replication in mosquitoes (extrinsic incubation period), prolong the breeding season and increase the viral transmission to birds.¹⁰ Changes in climatic conditions have been hypothesized to play a central role in increasing the number of WNV outbreaks reported worldwide in the last few decades. Viral transmission occurs when competent vectors are abundant and active. In addition, precipitation is another climatic factor that plays a crucial role in mosquito productivity and abundance,¹² thus precipitation also impacts WNV distribution and transmission.

The recent Intergovernmental Panel on Climate Change (IPCC) report¹³ revealed an overall increase in warm days and heat waves in South America, and several other regions with more precipitation increases than decreases were observed, with heterogeneous spatial trends. To date, there are few studies about the impact of climate change on WNV dissemination in South America. Although large scale, the spread of this virus has not been followed by noticeable bird mortality or disease in horses or humans in Latin America and the Caribbean¹⁴; the main concern is the absence of data on the West Nile fever burden in its hosts. Despite several studies and records in epidemiological bulletins,^{15–18} to the best of our knowledge, no predictive models for WNV have been developed in this context, especially for South America. In this study we analysed and showed how WNV could increase its relevance by exploring future climate scenarios. We addressed these questions by searching for evidence of virus circulation in human patients, mosquitoes, equids and birds throughout South America during the last 15 y and developing a predictive model considering environmental variables that directly affect WNV transmission dynamics and distribution.

Methods

Data acquisition

The approximate locations of WNV records (human cases, detection in any non-human host or infected mosquito) were defined using locations described in the literature between 2004 (first record in South America) and 2020 (Table 1). Data were collected through the PubMed and Google Scholar databases. We included all records of WNV in South American regions registered in epidemiological bulletins since the very first record (2004) through 2020. The criterion for inclusion of a region in our analysis was the presence of one or more WNV case recorded. We included here any human case, infected non-human host or mosquito.

The procedures followed in our study were based on Lorenz et al.¹⁹ To verify the ecological and climatic variables associated with the presence of WNV, we explored the associations between the locations of the records and eight variables: annual rainfall (mm), annual temperature (°C), elevation (m), type of biome, seasonality of temperature, seasonality of precipitation, thermal amplitude and daytime temperature variation. Biome is a qualitative variable that represents a biological unit or geographic space whose specific characteristics are defined by macroclimate, phytophysiology, soil and elevation. The corresponding values in our model were Amazonian rainforest, savannah, Caatinga, Atlantic rainforest, Pantanal (wetlands), prairies, Chaco, mangrove, desert, elevation fields, temperate forests and veld. The seasonality of the temperature value was calculated as the standard deviation (SD) of the average monthly temperature. The thermal amplitude value was calculated by subtracting the minimum temperature during the coldest month from the maximum temperature during the hottest month. The seasonality of the precipitation value was calculated as the coefficient of variation for the average monthly precipitation. The mean daytime temperature variation was calculated by subtracting the mean minimum temperature from the mean maximum temperature. These variables were selected because they were assumed to have a possible effect on life cycles and biological conditions of mosquitoes, humans and non-human hosts or to be at least correlated with more proximal causal factors.²⁰ All weather data were obtained from the WorldClim – Global Climate Data database,²¹ which contains representative observational data for 1950–2000 that were interpolated to a resolution of 30 arc seconds (approximately 1 km).

Data analysis

We performed principal component analysis (PCA) using XLSTAT software version 2021.3.1 (Addinsoft, New York, NY, USA) to preselect the environmental variables that were used in the WNV modelling. After performing the PCA, we choose the four most representative eigenvectors of the variables, which were employed for Maxent analysis (version 3.3.3k; a machine learning algorithm for modelling species distributions based on existing data and environmental variables).²² The principle of maximum entropy was used in data selection, with the original variables that reached maximum and minimum values within the ordered

Table 1. South American areas that have presented WNV detection in the 2004–2020 period. We considered all human cases, any non-human host and infected mosquito detection (Data from Google Scholar and PubMed databases).

COUNTRY	REGION	YEAR	RECORD TYPE	REFERENCE	COORDS
COLOMBIA	Córdoba	2004	Horse	32	9.195296, –76.010268
COLOMBIA	Sucre	2004	Horse	32	8.844197, –74.745573
ARGENTINA	Córdoba	2005	Bird	33	–31.760224, –63.560619
COLOMBIA	El Meta	2005	Horse	34	3.828449, –73.898221
ARGENTINA	San Antonio de Areco	2006	Horse	35	–34.246975, –59.457666
ARGENTINA	Victoria - Entre Rios Province	2006	Horse	35	–32.624022, –60.150743
ARGENTINA	Mar Chiquita - Córdoba	2006	Bird	33	–30.810762, –62.862172
ARGENTINA	Chaco	2006	Bird	33	–26.162497, –60.722666
ARGENTINA	Tucumán	2006	Bird	33	–26.819668, –65.216417
ARGENTINA	Monte Cristo - Córdoba	2006	Bird	33	–31.339957, –63.945559
ARGENTINA	Monte Alto	2006	Bird	33	–26.955432, –62.814174
COLOMBIA	Atlántico - coast	2006	Horse	36	10.912077, –74.991247
COLOMBIA	Bolívar - coast	2006	Horse	36	10.313668, –75.300519
COLOMBIA	Magdalena - coast	2006	Horse	36	11.149139, –73.982325
VENEZUELA	Laguna de los Patos - Sucre	2007	Mosquito	37	10.423033, –64.201746
COLOMBIA	Medellín	2008	Bird	9	6.222606, –75.580183
BRAZIL	Nhecolândia/MS	2009	Horse	15, 38	–18.33861111, –57.24861111
BRAZIL	Aquidauana/MS	2009	Horse	39	–20.457118, –55.777345
BRAZIL	Bonito/MS	2009	Horse	39	–21.120316, –56.487325
BRAZIL	Anastácio/MS	2009	Horse	39	–20.487545, –55.811486
BRAZIL	Bodoquena/MS	2009	Horse	39	–20.551787, –56.678702
BRAZIL	São José da Cruz do Brejo/PB	2009	Horse	39	–6.229616, –37.342943
BRAZIL	Nova Brasilândia/MT	2009	Horse	16	–14.773138, –55.060898
BRAZIL	Lagoa do Peixe National Park/RS	2009	Bird	7, 16	–31.253750, –50.969954
BRAZIL	Ilha da Canela/PA	2009	Bird	7, 16	–0.784771, –46.723208
BRAZIL	Nabuleque/MS	2010	Horse	15	–20.863440, –57.836708
BRAZIL	Porto Jofre/MT	2010	Horse / chicken	40	–16.248888, –56.858888
BRAZIL	Poconé/MT	2010	Horse / chicken	40	–16.665, –56.793888
BRAZIL	Pinheiro/MA	2010	Bird	7, 16	–2.528208, –45.089733
COLOMBIA	Córdoba	2012	Mosquito	41	9.358333, –75.976944
BRAZIL	Aroeiras do Itaim/PI	2014	Human	42	–7.245577, –41.582601
BRAZIL	Picos/PI	2017	Human	42	–7.066997, –41.427460
BRAZIL	Piripiri/PI	2017	Human	42	–4.275203, –41.771882
BRAZIL	São Mateus/ES	2018	Horse	43	–18.721112, –39.847865
BRAZIL	Baixo Guandu/ES	2018	Donkey	44	–18.6883713, –40.4082043
BRAZIL	Nova Venécia/ES	2018	Horse	44	–18.702494, –40.329336

Table 1. Continued

COUNTRY	REGION	YEAR	RECORD TYPE	REFERENCE	COORDS
BRAZIL	Logoa Alegre/PI	2019	Human	42	-4.513817, -42.621034
BRAZIL	Teresina/PI	2019	Human	42	-5.044479, -42.754136
BRAZIL	Amarante/PI	2019	Human	42	-6.238821, -42.840200
BRAZIL	Água Branca/PI	2020	Human	42	-5.905901, -42.628846
VENEZUELA	Barinas	2004-2006	Horse / birds	45	8.691259, -70.183141
VENEZUELA	Zulia	2004-2006	Horse / birds	45	10.481874, -71.794726
VENEZUELA	Zulia	2004-2006	Horse	45	10.589885, -72.256152
VENEZUELA	Zulia	2004-2006	Horse	45	8.944228, -71.618945
VENEZUELA	Yaracuy	2004-2006	Horse	45	10.495604, -68.827474
VENEZUELA	Yaracuy	2004-2006	Horse	45	10.006410, -68.563802
VENEZUELA	Carabobo	2004-2006	Horse	45	10.249961, -68.071230
VENEZUELA	Guarico	2004-2006	Horse	45	9.784117, -66.051638
VENEZUELA	Guarico	2004-2006	Horse	45	9.193557, -65.425417
VENEZUELA	Guarico	2004-2006	Horse	45	9.144750, -65.700075
VENEZUELA	Guarico	2004-2006	Horse	45	8.830059, -67.089846
VENEZUELA	Guarico	2004-2006	Horse	45	8.547693, -66.650393
VENEZUELA	Anzoategui	2004-2006	Bird	45	8.762900, -64.179341
VENEZUELA	Sucre	2004-2006	Bird	45	10.301206, -64.183431
COLOMBIA	Turbo - Antioquia	2006-2008	Horse	34	8.094207, -76.731325
COLOMBIA	Chigorodó - Antioquia	2006-2008	Horse	34	7.633846, -76.620891
COLOMBIA	Bolombolo - Antioquia	2006-2008	Horse	34	5.970876, -75.838147

ranking of each principal component, as they describe the full range of data variation. The Maxent model may be expressed as:

$$p[f_i] = \frac{1}{N} \sum_{i=1}^N f_i(x_i),$$

where x^* =the geographical region of interest; $x=\{x_1, \dots, x_N\}$ with $x \in x^*$; $x \rightarrow$ observed points at x^* ; $f_i=f_{i1}, f_{i2}, \dots, f_{im}$ (environmental variables); N =the number of observed records and p =the probability of WNV occurrence. The model was run 25 times, with a difference of 10% of the localities for each run to estimate the parameters and their precision. Potential distribution maps were generated by interpolating the occurrence points and the similarity measures of the environmental variables in each pixel.

Future climate data were integrated using the Model for Interdisciplinary Research on Climate (MIROC-5)²³ global climate model (GCM). The spatial resolution of the GCM was the same as that of the environmental layers (30 arc seconds, approximately 1 km). The comparison method was the same as for the Maxent model, although the probability calculation for the GCMs incorporated a comparison of the present and future environmental conditions. To obtain future climate scenarios using GCMs, it is also necessary to choose a condition for the evolution of greenhouse gas emissions (GGEs) during the period when the future climate is projected. In our prediction, we used two different scenarios: low emissions (Representative Concentration Pathway [RCP] 2.6) and very high emissions (RCP 8.5), detailed in the Special Report on Emissions Scenarios by the IPCC.¹³ In the first case, the global temperature tends to increase by 1.0°C and can reach a temperature anomaly ranging from 0.4 to 1.6°C and 0.3 to 1.7°C for 2046–2065 and 2081–2100, respectively. In the second scenario, with high GGEs, the global temperature tends to increase 2.0 to 3.7°C and can reach a thermal anomaly ranging from 1.4 to 2.6°C and 2.6 to 4.8°C for 2046–2065 and 2081–2100, respectively.

Results

Regarding PCA, the first two components (F_1 and F_2) accounted for 66.04% of the variation (Figure 1). According to this analysis, it was possible to perceive that the most representative variables of PCA were associated with precipitation (annual rainfall and precipitation seasonality) and temperature (annual temperature average and thermal amplitude) (Table 2).

After selecting the four most important variables, we constructed a Maxent model (Figure 2B) to determine the areas where WNV will most likely be observed in South America. We observed that there is a concentration of WNV in the northern region of South America, including Venezuela and Colombia, eastern Brazil and Paraguay, Bolivia and southern Argentina. The contribution of each variable to the final model in Maxent was annual rainfall 51.6%, annual temperature 36.3%, precipitation seasonality 6.5% and thermal amplitude 5.5%. The average training area under the curve (AUC) for the final model is 0.85 and the SD is 0.028, which was significantly better than the random prediction ($p=0.001$), indicating good performance of the model (Figure 3). The behaviour of each variable in the model is shown in Figure 3. These curves show how each environmental variable affects the Maxent prediction. The curves show how

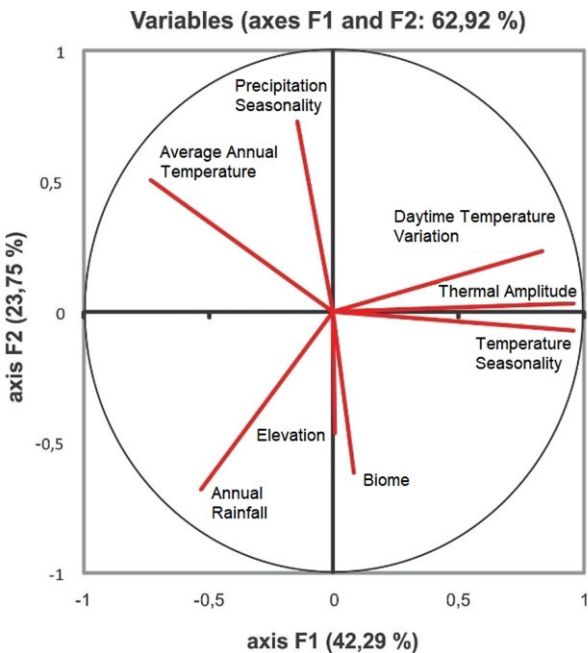


Figure 1. PCA showing the most representative environmental variables for our WNV model. The first two components (F_1 and F_2) accounted for 66.04% of the variation. We choose the four most representative eigenvectors of the variables, which were employed for Maxent analysis.

Table 2. Environmental variables used in the analysis and model selection.

Variables	Eigenvectors	
	F ₁	F ₂
Biome	0.043	−0.447
Elevation	0.003	−0.335
Annual rainfall	−0.287	−0.492
Daytime temperature variation	0.454	0.171
Average annual temperature	−0.399	0.366
Precipitation seasonality	−0.078	0.529
Thermal amplitude	0.523	0.027
Temperature seasonality	0.520	−0.050

Variables included in the final model are indicated in bold.

the logistic prediction changes as each environmental variable is varied, keeping all other environmental variables at their average sample value. In other words, the curves show the marginal effect of changing exactly one variable, whereas the model may take advantage of sets of variables changing together.

Probability maps were generated using two different future climate projections (Figure 4). The results reveal progressively expanding areas with an increased likelihood of WNV distribution, especially in areas with high GGE levels. Countries such as Bolivia and Paraguay will be greatly affected, drastically changing their current WNV distribution. Several Brazilian areas will also increase the likelihood of presenting WNV, mainly in the northeast and midwest regions. It is worth highlighting the possible change in

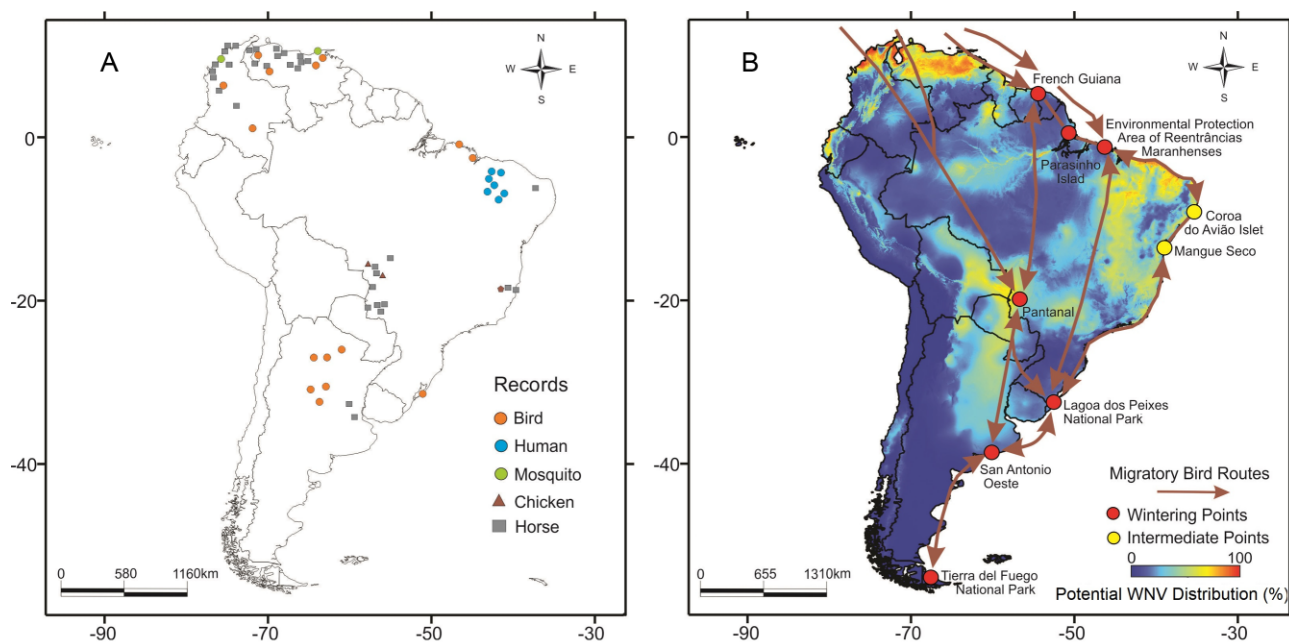


Figure 2. Occurrence of WNV in South America during the last 15 y. **(A)** Records by host type. **(B)** Maxent model showing the probable current distribution and bird migration routes. The maps were built using QGIS version 2.10.1.

the distribution of WNV on the Galapagos Islands in the following years (Figure 5).

Discussion

Predicting at-risk locations for WNV is important for targeting vector control and public health resources. According to the reviewed literature, there are several records of WNV distribution in South America detected in different types of hosts, but our Maxent model showed that the distribution area of this virus can be significantly larger than observed. It is possible that there may be a significantly larger number of infected mosquitoes, horses and birds, but the lack of adequate testing and serological surveys among populations may underestimate this number. The incongruence between the actual cases and the reported cases is mainly due to the similarity of the clinical symptoms among many arboviruses, underestimating the occurrence of WNV in South America. This issue is enhanced by the lack of correct diagnostic techniques for identifying the virus. Considering that several countries in South America have reported outbreaks of dengue, Zika and chikungunya in recent decades,²⁴ it is possible that other arboviruses with related symptoms have been confused with WNV. Despite information regarding high circulation of WNV in some areas, several cases remain undiagnosed, probably due to mild and self-limited clinical manifestations. Commonly, patients fully recover after a few days. Nevertheless, more serious cases may remain undiagnosed, principally due to lack of health-care facilities nearby, difficulties in sample transport and a lack of laboratories qualified to perform diagnostic tests.¹⁴

WNV dissemination in South America possibly behaves distinctively from that reported in North America and Europe, and

some hypotheses relate this fact to the higher level of genetic resistance in South America due to the large variety of circulating flaviviruses. Perhaps WNV could circulate similar to other flaviviruses, such as ilheus or Saint Louis,¹⁵ which infect equids but do not produce severe clinical symptoms that are applicable to health surveillance. The main difference between WNV and other viruses is that humans do not have enough viremia to infect mosquito vector species with WNV, which makes a great difference in the epidemiology of WNV. South American countries appear to have provided a method of coexistence with WNV in which the virus can circulate at a low level of pathogenicity without causing major issues.¹⁷ Since the introduction of WNV in South America in 2004, only seven human cases have been recorded in Brazil, with only one death reported.²⁵ Brazil is a tropical country with one of the most diverse fauna populations in the world. This could be a protective factor against an outbreak because every small part of the ecosystem needs to be taken into consideration in the complex WNV transmission network to reduce viral activity.²⁶

Our results confirm the associations between the increased WNV incidence with higher temperatures and lower precipitation.¹⁵ Higher temperatures increase fecundity and blood meal intake in *Culex* mosquitoes that transmit WNV and decrease its time to development.²⁷ A large population of mosquitoes combined with aggressive feeding behaviour in reservoir species enhances the probability of detecting WNV in a specific region. Precipitation quantity was inversely associated with WNV incidence, confirming the result of a study conducted in Illinois.²⁴ Immature forms of *Culex* are especially vulnerable to being flushed out of the containers they occupy and are probably killed by rainfall events.²⁸ Heavy rainfall might also dilute the nutrients for larvae, thus decreasing their development rate. We found

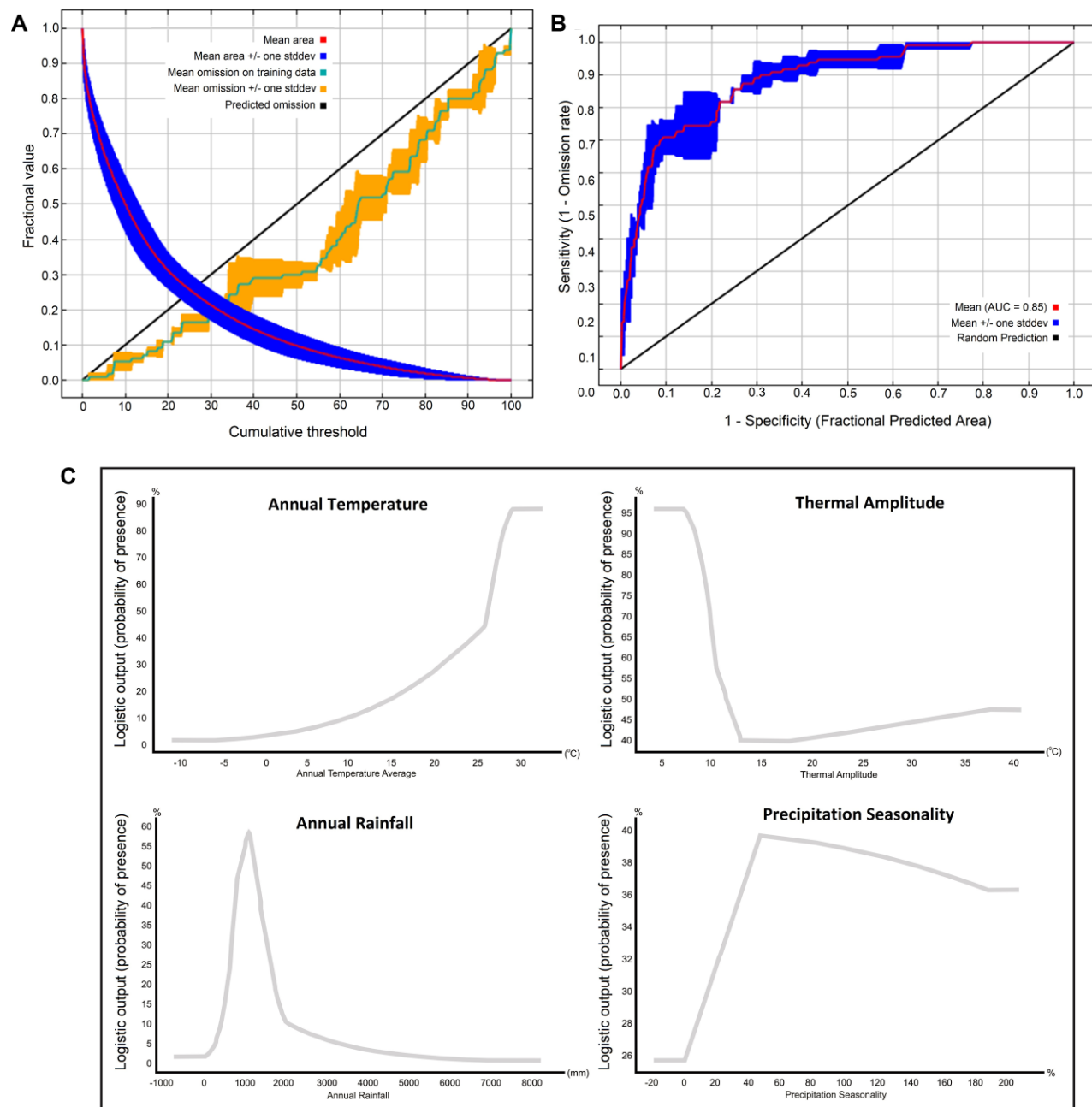


Figure 3. (A) Training omission rate and predicted area as a function of the cumulative threshold, averaged over the replicate runs. (B) Receiver operating characteristics curve for the same data, again averaged over the replicate runs. The average training area under the curve for the replicate runs is 0.85 and the SD is 0.028. (C) Behaviour of each selected variable in the Maxent model according to the logistic output (probability of presence of WNV).

that approximately 1200 mm of annual rainfall was the optimal value for maximizing the potential distribution of WNV in our predicted conditions. A possible explanation is that drought events cause proximity between birds and mosquitoes around residual water sources, thereby accelerating the epizootic cycling and dissemination of WNV within these populations. Also, during drought conditions, permanent water pools become rich in

organic materials that mosquitoes need to develop. These water areas might also be attractive for several avian species, thus favouring the bird-mosquito interaction.²⁶ Seasonality is when an event that occurs at a certain time of the year. The *Culex* mosquito has a very fast population growth, as it is a species that colonizes unstable habitats, with high fecundity and a short biological cycle, with records of >10 generations per year. The

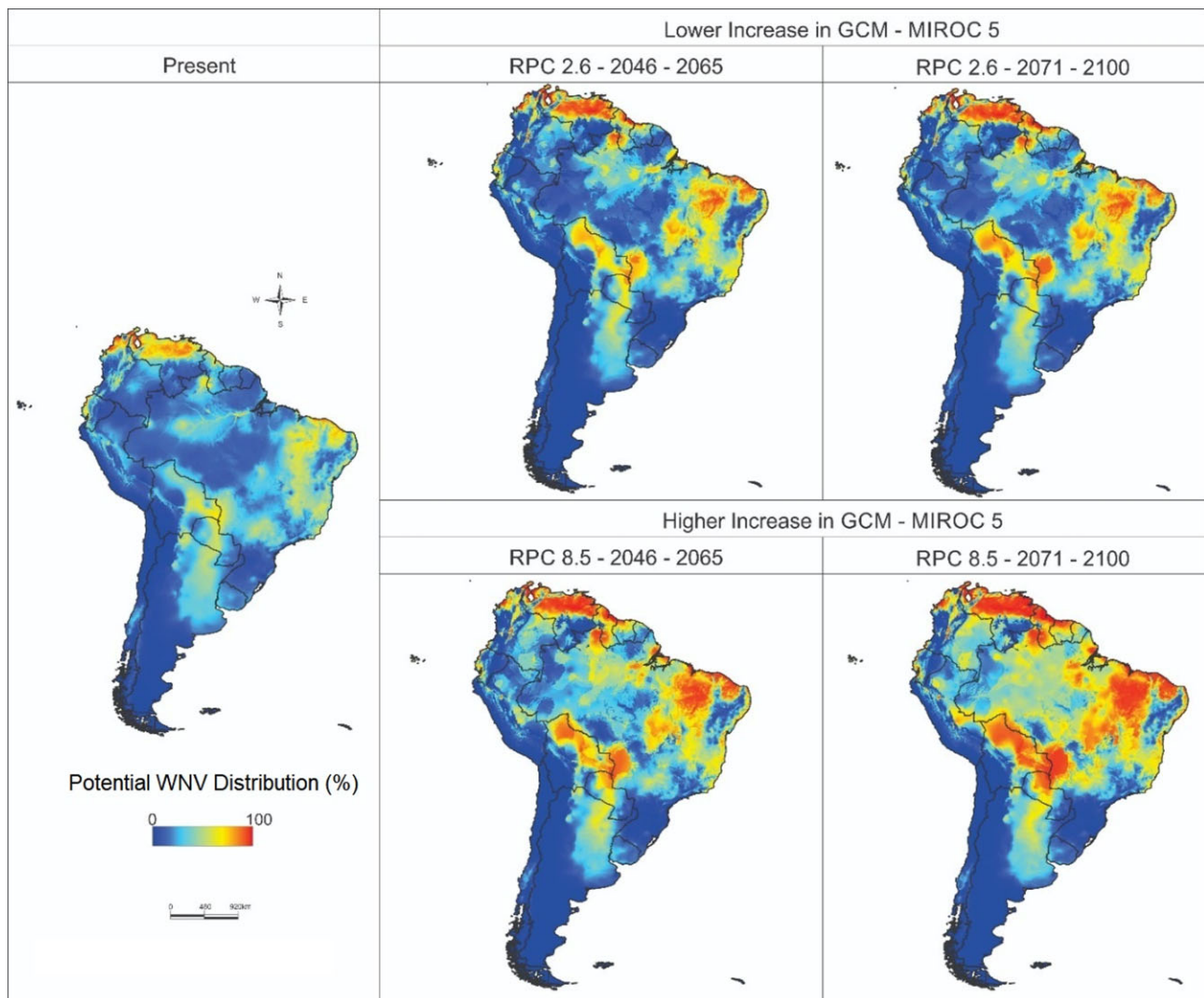


Figure 4. Predicted WNV range expansion in South America based on MIROC-5. The maps show the distribution under two climate change scenarios: RCP 2.6 (lower increase in GGEs) and RCP 8.5 (higher increase in GGEs). The maps were built using QGIS version 2.10.1.

occurrence of sharp peaks in the frequency of mosquitoes, with explosive development between generations, after the summer rains means that there is an association between the seasonality of precipitation (summer rains) and the occurrence of the vector mosquito.

According to the predictive MIROC-5 model, high-risk areas for WNV may change over the next few decades. This scenario can be more or less dramatic and depends on GGE levels. Countries such as Bolivia and Paraguay would be greatly affected, drastically changing their current WNV distribution. Several Brazilian areas also would increase the likelihood of presenting WNV, mainly in the northeast and midwest regions, including the Brazilian Pantanal biome. This is possibly associated with the singular environmental and ecological aspects of Pantanal, such as the prevalence of avian migration from North America.²⁹ This area is also characterized by strong anthropogenic disturbances, which includes the recent enlargement of farming and human

activities related to deforestation. These issues can alter the natural cycle of WNV, increasing the risk of virus infection in humans.²⁰ In contrast, looking at the current and future distribution maps, the Andes Mountains may act as a physical barrier against the dispersion of WNV in South America, which can be related to the absence of bird migration paths in this area.

With the expansion of the geographical range of WNV, it is almost certain that more epidemics of meningoencephalitis will be reported in the coming years. Cities with precarious economic and infrastructure conditions and those that lack efficient arbovirus surveillance measures and mosquito vector control programs are especially susceptible.³⁰ WNV may have become endemic in some regions, taking into account the abundant population of avian reservoirs and the huge diversity of mosquito species in South America. Among the several species of *Culex* reported in South America, *C. quinquefasciatus* is the most abundant anthropophilic species.³¹ Some studies indicate that the

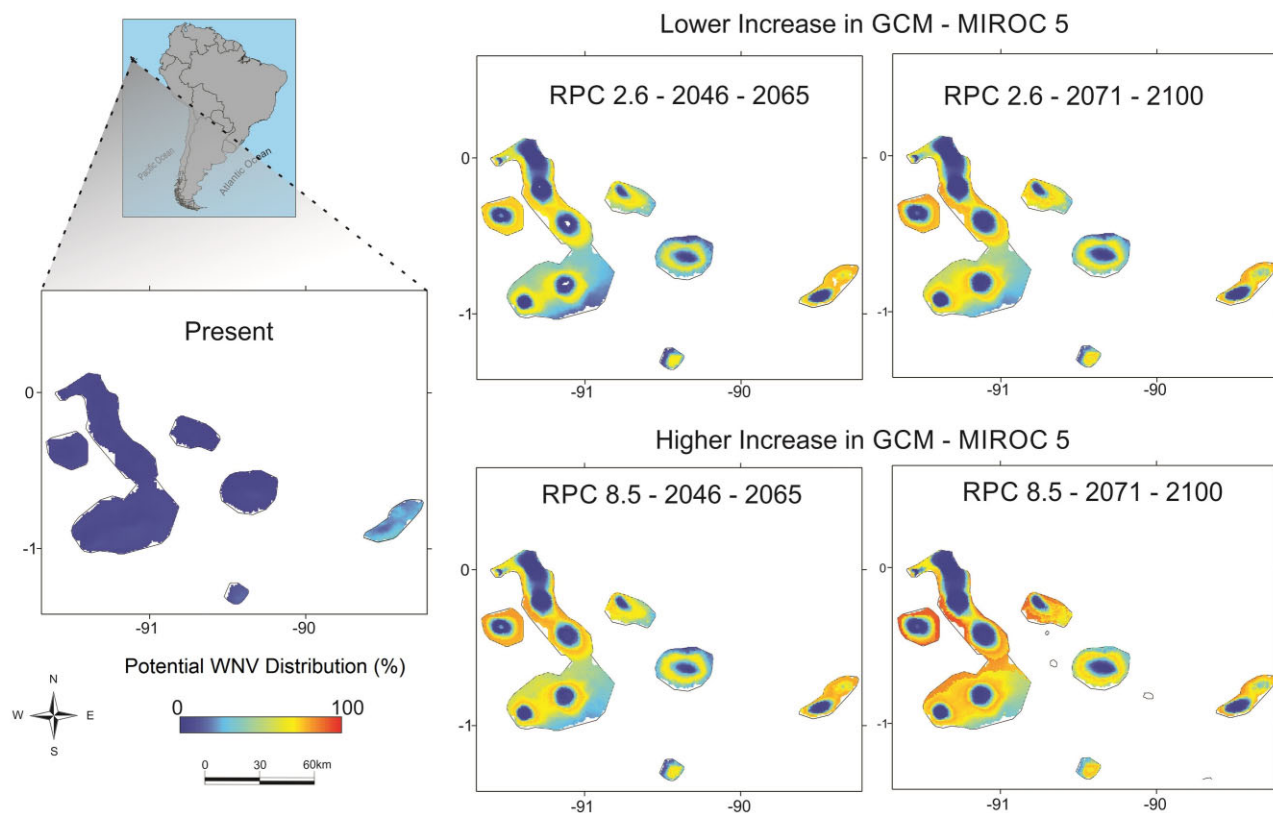


Figure 5. Current and predictive distribution of WNV on the Galapagos Islands through Maxent modelling. The maps were built using QGIS version 2.10.1.

emergence and dissemination of *Culex*-transmitted diseases will possibly intensify in the coming years due to the strong adaptation of these mosquitoes to climate change and ineffective urban sanitary infrastructure.³⁰ The continuous evolution of WNV in North America and the potential effects of WNV dissemination in South America on the economy and public health highlight the urgency of establishing WNV active surveillance and research programs. It is necessary to minimize eventual risks to society from the introduction of another dangerous arbovirus beyond those already established, such as dengue, Zika, chikungunya and yellow fever.²⁵ It is also important to point out that contrary to the Zika, chikungunya and yellow fever viruses, humans are not reservoirs of WNV.

This study has some limitations. It is worth mentioning that WNV epidemiology is not as straightforward as other arboviruses, such as dengue transmitted by *Aedes aegypti*. WNV is vectored by many different mosquito species and human infections are due to spillover events from bird populations. Humans and horses are considered accidental and terminal hosts, since viremia occurs for a short period of time and at levels that are insufficient to infect mosquitoes, ending the transmission cycle. Another important factor that limits a more precise analysis of WNV distribution is that it is not known which are the true *Culex* species involved in the transmission cycle. Climate conditions alone are not the main driver of WNV, but they may serve as a proxy to estimate the most suitable areas for the virus to circulate in the future. Regarding specific limitations of this study, the projections presented here

were processed based on the assumption that all variables except temperature remained stable over time. For example, our models considered the human population size as stable. Second, the deforestation rate, which is an important factor in determining WNV outbreaks, was not included. However, other factors that were not part of our model, such as the quality of vector surveillance, clinical case detection and the development of some vaccines, could change over time. In this study we did not consider the distribution areas of the mosquito vectors, which are essential for transmission but are significantly difficult to estimate. Finally, WNV may circulate in asymptomatic or misdiagnosed patients, and the difficulty in determining their exact distribution directly affects the predictive power of our model. Despite its limitations, our study serves as an important initial step in predicting the emergence of WNV in South America, as current studies have focused on only a few specific small regions. It also warns the surveillance healthcare systems that WNV may remain underestimated before the outbreak occurs.

Conclusions

This is the first spatiotemporal study in South America to predict WNV distribution. Our findings show that the probable high-risk areas could be significantly larger than those in which WNV was detected. Environmental factors can precisely alter the distribution of WNV, with higher temperatures and lower precipitation

associated with increased virus incidence. High-risk areas may be modified in the coming years, being more pronounced with high GGE levels. Countries such as Bolivia and Paraguay could be greatly affected, drastically changing their current WNV distribution. Several Brazilian areas also could increase the likelihood of presenting WNV, mainly in the northeast and midwest regions and the Pantanal biome. The Galapagos Islands also may increase their geographic range suitable for WNV occurrence.

Although our approach is limited, we propose that future studies should be multidisciplinary and include other variables such as mosquito distribution and components of the natural cycle of WNV. Analysing the role of climate in the emergence of WNV will require interdisciplinary cooperation among researchers and society. Overall, this study provides useful indications regarding the dynamics of WNV in the South American region. Considering the avian reservoirs and *Culex* mosquitoes found in South America and the potential availability of new animal reservoirs due to the vast size of this region, the WNV can spread across countries once it establishes its replication cycle in the environment, as observed in the USA.

Authors' contributions: CL was responsible for conceptualization, data acquisition, investigation and draft preparation. TSA was responsible for conceptualization, methodology, investigation, software and reviewing and editing the manuscript. FC-N was responsible for conceptualization, visualization, supervision and reviewing and editing the manuscript.

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Competing interests: None declared.

Ethical approval: Not required.

Data availability: The data that support the findings of this study are openly available in the Google Scholar (<https://scholar.google.com/>) and PubMed (<https://pubmed.ncbi.nlm.nih.gov/>) databases.

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