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## RECOMMENDED CITATION

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Running title: Global map of Zika Virus

# Mapping the global geographic potential of Zika virus spread

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## **Abstract**

The Americas are presently experiencing the most serious outbreak of Zika virus (ZIKV) known. Here, we present a novel set of analyses using environmental characteristics, vector distributions, and socioeconomic risk factors to develop the first map to detail global ZIKV transmission risk in multiple dimensions based on ecological niche models. Our model predictions were tested against independent evaluation data sets, and all models had predictive ability significantly better than random expectations. The study addresses urgent knowledge gaps regarding the potential geographic scope of the current ZIKV epidemic, as well as the global potential for spread. It also provides a highly informative view of potential drivers of ZIKV distributions globally, pointing out areas vulnerable in terms of some drivers, but not in others. The results of these analyses can guide regional education and preparedness efforts, such that medical personnel will be prepared for diagnosis of potential ZIKV cases as they appear.

## **Keywords:**

Zika virus, Global distribution, Risk, Aedes, Brazil, climate, socioeconomic, accessibility.

Zika virus (ZIKV) is a member of the family *Flaviviridae*, transmitted to humans via bites of infected *Aedes* mosquitoes. ZIKV is spreading rapidly in the Americas; WHO anticipates 4M cases in 2016. Zika virus disease is usually a mild febrile illness with rash and conjunctivitis, but global concern about ZIKV transmission centers on suspected increased incidence of microcephaly and other birth defects in fetuses born to mothers infected with ZIKV (Mlakar et al. 2016; Oliveira Melo et al. 2016; Ventura et al. 2016). Guillain-Barré syndrome has also co-occurred with ZIKV emergence in the Americas, as it did previously in French Polynesia (Oehler et al. 2014). ZIKV's geographic potential is not well understood, emphasizing the need for models that consider the entire transmission cycle; recent models (Bogoch et al. 2016) consider only vector distribution and human travel in the Americas.

We used maximum entropy ecological modeling implemented in Maxent version 3.3 (Phillips et al. 2006) to anticipate the potential distribution of ZIKV worldwide, and to infer major drivers of the spread of the virus. For this reason, we developed four models, based on ZIKV occurrences and different combinations of climate, socioeconomic, land-cover, mosquito abundance, and accessibility variables (see Supplementary Materials for details of methods). Models were calibrated across Mexico, Central, and South America; models were then projected worldwide for interpretation. For each combination of drivers, we ran 100 bootstrap replicates; the median of those replicates was used as an estimate for the ZIKV ecological niche. These models are thresholded based on a maximum allowable omission error rate of 5% [ $E = 5\%$ ; (Peterson et al. 2008)]. For visualization, we combined thresholded versions of two of these models to illustrate differences in prediction deriving from

different combinations of possible drivers of ZIKV transmission. Model predictions were evaluated using partial receiver operating characteristic (ROC) tests applied to random subsets of 50% of available occurrence data (Peterson et al. 2008).

Our results present the first detailed predictions of ZIKV potential distribution worldwide, identifying possible drivers of risk (see Figure and Supplementary Materials). All model predictions had predictive ability regarding independent subsets of occurrence data significantly better than random expectations (all  $P < 0.001$ ). Our models corroborated ZIKV's large-scale potential for expansion in South and Central America, and identifies other regions at risk of ZIKV transmission, particularly Sub-Saharan Africa, Australia, Melanesia, and parts of New Zealand. Northern Australia is at risk as a function of vector availability and environmental suitability, but less so based on human conditions. Other at-risk regions include Angola, Zambia, the Amazon Basin, and northern South America. Risk in Europe and northern India was driven mainly by accessibility and socioeconomic factors, respectively.

Our models anticipate some potential for autochthonous ZIKV transmission in the USA, although risk areas are generally scattered and narrow. However, Florida, southern Texas, and Louisiana are clearly vulnerable to autochthonous ZIKV transmission. Areas southeast of the Appalachians and Pacific coastal areas may also be affected. Other parts of the USA will see imported cases and limited local transmission, particularly if other *Aedes* species participate in transmission. Large areas of Asia, including densely populated regions, were indicated as at risk for autochthonous ZIKV transmission, including parts of India, Bangladesh, southern China, and Thailand; the southwestern coast of the Arabian Peninsula is also at risk of ZIKV

transmission. In Western Europe, ZIKV transmission risk is enhanced by travel times and connectivity to known transmission areas; as such, isolated autochthonous cases may occur at least seasonally when competent vector species are present.

Our model adds key parameters to the present picture of risk of ZIKV arrival, establishment, and autochthonous transmission worldwide, for a more comprehensive model than has to-date been available. ZIKV transmission risk and disease can be reduced by (1) reduction of mosquito populations and eliminating breeding sites and human contact; (2) enhanced public and clinical awareness of ZIKV risk; (3) prompt reporting of new ZIKV cases to public health authorities; (4) enhanced research into the ecology, evolution, clinical manifestations, vector associations, and transmission dynamics of ZIKV; and (5) prospective screening for potential cases in areas at high risk. A crucial question in looking toward a next generation of such models is the role of vector mosquito species beyond the globally distributed *Aedes aegypti* and *Ae. albopictus*.

## **Declarations**

### **List of abbreviations**

ZIKV=Zika Virus

WHO= World Health Organization

## **Availability of data and materials:**

Digital grids of all models are openly available via Figshare online repository (DOI: *LINK TO BE PROVIDED UPON ACCEPTANCE OF MANUSCRIPT*)

## **Competing interest**

Authors declare that they have no competing interest.

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## **Authors' contribution**

AMS Conceived and designed the experiments. AMS performed the experiment and analyzed the data. AMS drafted the manuscript. AA, SMT, KPC, and ATP helped in data analysis and reviewed the manuscript. All authors revised and agreed the manuscript.

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## Figure Legend

**Figure.** Predicted global potential distribution of ZIKV, based on ecological niche models integrating occurrences with data on climate, socioeconomic status, land-cover, mosquito abundance, and accessibility. Orange areas were identified as suitable based on drivers related to physical environment and vector populations; purple areas were identified as suitable based on drivers related to human conditions and accessibility; blue areas were identified as suitable in terms of all drivers considered (individual models are presented in the Supplementary Materials). Note some potential for autochthonous transmission in the southeastern USA, but broader potential for accessibility-related cases (e.g., imported infections that may turn into autochthonous transmission via seasonal vector activity) across the USA and Europe. A raster GIS version of this map is provided at (*LINK TO BE PROVIDED UPON ACCEPTANCE OF MANUSCRIPT*).

