# Articles

# Estimating the potential risk of transmission of arboviruses in the Americas and Europe: a modelling study

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## Summary

**Background** Estimates of the spatiotemporal distribution of different mosquito vector species and the associated risk of transmission of arboviruses are key to design adequate policies for preventing local outbreaks and reducing the number of human infections in endemic areas. In this study, we quantified the abundance of *Aedes albopictus* and *Aedes aegypti* and the local transmission potential for three arboviral infections at an unprecedented spatiotemporal resolution in areas where no entomological surveillance is available.

**Methods** We developed a computational model to quantify the daily abundance of *Aedes* mosquitoes, leveraging temperature and precipitation records. The model was calibrated on mosquito surveillance data collected in 115 locations in Europe and the Americas between 2007 and 2018. Model estimates were used to quantify the reproduction number of dengue virus, Zika virus, and chikungunya in Europe and the Americas, at a high spatial resolution.

Findings In areas colonised by both *Aedes* species, *A aegypti* was estimated to be the main vector for the transmission of dengue virus, Zika virus, and chikungunya, being associated with a higher estimate of  $R_0$  when compared with *A albopictus*. Our estimates highlighted that these arboviruses were endemic in tropical and subtropical countries, with the highest risks of transmission found in central America, Venezuela, Colombia, and central-east Brazil. A non-negligible potential risk of transmission was also estimated for Florida, Texas, and Arizona (USA). The broader ecological niche of *A albopictus* could contribute to the emergence of chikungunya outbreaks and clusters of dengue autochthonous cases in temperate areas of the Americas, as well as in mediterranean Europe (in particular, in Italy, southern France, and Spain).

Interpretation Our results provide a comprehensive overview of the transmission potential of arboviral diseases in Europe and the Americas, highlighting areas where surveillance and mosquito control capacities should be prioritised.

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#### Introduction

In 2016, a public health emergency of international concern was declared for a Zika epidemic that, upon detection in Brazil in 2015, rapidly spread to almost 50 countries and territories across the Americas.<sup>1,2</sup> Additionally, more than 390 million dengue virus cases, including more than 9000 deaths, have been estimated to occur worldwide every year,<sup>3,4</sup> and local dengue virus transmission has been observed in continental Europe<sup>5,6</sup> and the USA.<sup>7</sup> Local outbreaks of Chikungunya in the Americas and in temperate areas of Europe have also occurred in the last two decades.<sup>8-11</sup>

Spatial patterns and temporal trends in vector-borne diseases have been investigated through various modelling approaches.<sup>12</sup> A widely used approach relies on the simulation of detailed population models, which mimic the biological processes driving the entire developmental cycle

of the vectors.<sup>8,9,13,14</sup> However, such mechanistic models are usually tailored to local entomological<sup>8,9,14</sup> or epidemiological data9 and might be computationally intensive when applied at a large, but high-resolution, spatial scale. Complementary to mechanistic approaches, correlative models (ranging from simple regressions to advanced machine learning methods) have been trained on large and heterogeneous datasets of mosquito or disease occurrences to provide spatial estimates of the habitat suitability and distributional patterns for different mosquito species15-18 and to identify areas at a higher risk of vector-borne diseases.34,11,19 However, most of these studies do not account for the seasonal variations characterising the mosquito density in an area, and the resulting estimates provide neither any information on the adult mosquito abundance nor on the transmission intensity over time associated with different vector-borne diseases.





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#### **Research in context**

#### Evidence before this study

We performed a literature review to identify manuscripts estimating the spatiotemporal abundance of Aedes species or the potential transmissibility of dengue virus, Zika virus, or chikungunya at a continental scale, or both. We searched PubMed for articles published in any language from database inception to Dec 6, 2022, with the abstract or title containing the terms ("map\*" OR "model") AND ("global" OR "America" OR "Europe") AND ("density" OR "abundance" OR "distribution" OR "transmission") AND ("albopictus" OR "aeqypti" OR "chikungunya" OR "dengue" OR "Zika"). We found a total of 354 studies. Of these, 27 provided detailed estimates of the habitat suitability associated with the considered Aedes species. We identified three studies quantifying the annual mean density of the mosquito species; one of these studies showed the seasonal differences in the number of mosquitoes per breeding site. The maximum spatial resolution of the provided estimates was 0.25 degrees × 0.25 degrees.

Despite several studies investigating the transmission potential of arboviral infections at a local spatial scale, very few studies covered more than one country. We identified 28 studies estimating the environmental suitability for the transmission of dengue virus, Zika virus, or chikungunya. Seven studies provided estimates of the number of infections or incidence associated with mosquito-borne diseases. Nine studies provided quantitative insight into the basic reproduction number ( $R_0$ ) at a global or continental scale. Only three studies

To overcome these limitations, we developed a modelling approach generating detailed spatiotemporal estimates of the abundance of both *Aedes albopictus* and *Aedes aegypti* and of the consequential risks of arboviral transmission, by relying solely on temperature and precipitation data. We aimed to provide a comprehensive overview of the potential risk of *Aedes*-borne infection in Europe and the Americas, identifying regions where surveillance activities, preventive measures, and targeted control efforts should be prioritised.

# Methods

# Study design

Our modelling approach is based on two main assumptions. The first assumption is that the relative density of *Aedes* species across different regions is proportional to their climate suitability, which we modelled as driven by temperature and precipitation. The second assumption considers that seasonal variations in *Aedes* mosquito abundance depend on persisting favourable temperature conditions over time. The model provided daily estimates of the absolute number of adult mosquito females of *A albopictus* and *A aegypti* in any region of interest in Europe and the Americas at a spatial resolution of  $1 \text{ km} \times 1 \text{ km}$ . These estimates were used to quantify the risk of autochthonous transmission (in terms of  $R_0$  and the

analysed seasonal transmission patterns at a high spatial resolution. These approaches were informed with data collected during epidemics that had occurred in the past.

# Added value of this study

In this study, we provided daily estimates of the number of mosquito adult females per hectare at a spatial resolution of 1 km × 1 km and of the transmission potential of dengue virus, Zika virus, and chikungunya in Europe and the Americas, at a spatial resolution of 250 m × 250 m. The developed approach could be used to infer the absolute abundance of mosquito vector species and the risk of local arbovirus transmission at an unprecedented spatiotemporal resolution in areas where no entomological surveillance is available, by relying solely on temperature and precipitation data. This analysis also highlights the relative differences of transmission intensity for different arboviral infections and of their seasonal patterns.

## Implications of all the available evidence

Our results provide high-resolution maps of the risk of *Aedes*-borne infections, which can be instrumental in allocating resources for entomological and epidemiological surveillance activities, and in planning information campaigns and preventive measures. The obtained estimates could inform future modelling efforts and epidemiological investigations focusing on areas where the risk of arboviral infection is estimated to be high, but data are scarce.

number of consecutive days in which  $R_0$  was more than the epidemic threshold of 1) of dengue virus, Zika virus, and chikungunya in Europe and in the Americas at a spatial resolution of 250 m×250 m.

#### Data

The entomological data used to calibrate our model consisted of: (1) georeferenced presence–absence records of *A albopictus* available for 4372 locations in Europe;<sup>20</sup> (2) aggregated presence–absence data of *A aegypti* and *A albopictus* available for 1892 US counties, based on records of mosquito collection at any developmental stage between 1960 and 2016;<sup>16</sup> and (3) 300 time-series of female adult mosquitoes collected between 2007 and 2018 in 115 different locations across Italy, Brazil, and the USA, providing an average of eight monthly data points per location and year in which the data were collected.<sup>8,14,21-23</sup>

Female adult mosquito captures were gathered from multiple sources by combining entomological surveillance data collected during different breeding seasons and under different trapping conditions. In Italy, records of *A albopictus* were collected in three regions. In Trentino and Veneto (northern Italy), entomological surveillance was carried out in 2014 and 2015 from April to November using Biogents Sentinel traps (Biogents, Regensburg,

Germany), baited with Biogents lures and CO, from dry ice.14 In Lazio (central Italy), female adult mosquitoes were captured from July to December, 2012, through sticky traps.8 The same type of trap was used between 2012 and 2016 in Porto Alegre, the largest city in Rio Grande do Sul, Brazil.<sup>22</sup> In the USA, adult female mosquito capture records were obtained by combining the results of entomological surveillance conducted in Miami through Biogents Sentinel traps between 2016 and 2018,21 with data for 95 counties in eight US states made available by the Centers for Disease Control and Prevention Aedes Forecasting Challenge 2019.23 The Centers for Disease Control and Prevention dataset includes captures obtained with Biogents Sentinel traps, gat traps, traps baited with CO<sub>2</sub> (Centers for Disease Control and Prevention traps, ABC light traps, and Fay-Prince traps), and traps targeting gravid female mosquitoes with open water containers. Heterogeneous trapping conditions were considered for model calibration.

Temperature and precipitation records were retrieved from the WorldClim database.<sup>24</sup> Data on human density was retrieved from the Global Human Settlement Layer project.<sup>25</sup> Details are provided in the appendix (p 3).

## **Climate suitability**

To investigate how local climatic conditions influenced the occurrence of the two Aedes vectors across different regions, we estimated a climate suitability index ranging from 0 to 1 by applying an ensemble of nested logistic regression models to presence-absence records from 996 US counties for A aegypti, and from 1761 US counties and 4372 specific locations of Europe for A albopictus.<sup>16,20</sup> The presence of the species was used as the binary response variable. The considered explanatory variables included the annual mean temperature, the annual precipitation, the maximum temperature of the warmest month, and the precipitation of the warmest quarter. The best fit was separately identified for A aegypti, for A albopictus in the USA, and for A albopictus in Europe, on the basis of the Akaike information criterion.26 To generalise estimates of the climate suitability index to other regions, we accounted for climatic conditions that are known to prevent the persistence of Aedes species, hindering the oviposition of eggs or not guaranteeing the availability of adequate breeding sites. Specifically, we classified areas where the annual rainfall is less than 200 mm,<sup>17,18</sup> or where adult female mosquitoes could not survive long enough to complete the gonotrophic cycle (ie, the period between the blood meal and oviposition), as unsuitable.<sup>15</sup> Estimates were compared with in-sample records of presence, absence, and co-occurrence of the two mosquito populations by means of Cohen's K coefficient. The estimated climate suitability of A aegypti for European countries was compared with the historical distribution of this mosquito species between 1900 and 1955.27 However, we assumed A aegypti to be absent in Europe, because no permanent populations have been reported after the 1950s.18 The effect of ongoing climate change on the potential spatial distribution of the mosquitoes was explored, considering diverse scenarios for future climate conditions. Details are provided in the appendix (pp 18-19).

# Estimating the spatiotemporal variations in mosquito abundance

The abundance of female adult mosquitoes on a given day was approximated with a logistic function of the mean temperature observed in the *w* preceding days, therefore accounting for the persistence of favourable conditions during the whole lifecycle of the mosquito's development and the vector abundance in the preceding generations. The number of mosquitoes captured on a day *d*, in location *i*, with a trap type *t* was defined as:

$$C_{i}^{t}(d) = \frac{L_{i}^{t}}{1 + e^{-k(\tilde{T}(d,i,w)-T_{0})}}$$

where  $L_{i}^{t}$ ,  $T_{0}$ , and k are the maximum, midpoint, and For the WorldClim database see steepness of the temperature modulation function C<sub>i</sub>  $(\tilde{T})$ , respectively, and  $\tilde{T}(d,i,w)$  represents the average See Online for appendix temperature recorded between d-w and d in location i.

We assumed that model parameters regulating the seasonal variations in the mosquito abundance, namely w,  $T_0$ , and k, did not depend on the type of trap, nor on the site or year of data collection. In contrast,  $L_i^t$  was allowed to vary across different locations and trap types. For each area of interest *i*,  $L_i^i$  was approximated as:

## $L_i^t = \alpha^t \sigma_i$

where  $a^{t}$  reflects the heterogeneous effectiveness associated with different trap types identified by their design and target, and  $\sigma_i$  is the climate suitability index in location *i* as estimated with the best regression model for the considered species and continent. The same  $a^t$  is used for all traps belonging to the same type t. Free model parameters (ie, w,  $T_0$ , k, and  $\alpha'$ ) were calibrated separately for A aegypti and A albopictus through a Markov chain Monte Carlo approach applied to the Negative Binomial likelihood of observing the number of female adult mosquitoes captured over time, in different years and locations. Once calibrated, the model produced estimates of the number of collected adult mosquitoes on any day, for any trap type and site of interest, given the underlying climatic conditions.

We assumed that the captured mosquitoes were those living in a radius equal to the flight range of the considered species.14,22 We thus quantified the daily absolute number of female adults per hectare as:

# $N_V(i,d)=f_VC_i^t(d)/r_t$

Where r, is the capture rate for the vector species estimated through mark and recapture field experiments,<sup>28,29</sup> and  $f_{v}$  is https://www.worldclim.org/

a scaling factor reshaping estimates obtained within the flight range to an abundance per hectare. Details are provided in the appendix (pp 5–7).

## Estimating the transmission potential of arboviruses

The estimated mosquito density was combined with human population data<sup>25</sup> to assess the spatiotemporal risk of autochthonous transmission of dengue virus, Zika virus, and chikungunya for the Americas and Europe ( $\geq$ 45 million km<sup>2</sup>), corresponding to approximately 730 million model patches (ie, cells of 250 m $\times$ 250 m). The arbovirus transmissibility potential was assessed by computing-for each day, location, virus, and vector of interest-the reproduction number  $R_0$ , representing the mean number of secondary human infections caused by a primary human infector, assuming no pre-existing immunity. Model estimates of  $R_0$  were obtained for each day of the year following a widely adopted approach to investigate the host-vector transmission dynamics, on the basis of a standard Susceptible, Exposed, Infectious, Recovered host and Susceptible, Exposed, Infectious vector model:2,8,9,14

$$R_{0}(i,d) = (\beta \phi)^{2} \frac{N_{v}(i,d)}{N_{H}(i)} \frac{\chi_{v} \chi_{H}}{\gamma \mu_{v}} \frac{\omega_{v}}{\omega_{v} + \mu_{v}}$$

where  $\beta$  is the mosquito biting rate,  $\phi$  is the proportion of mosquito blood meals taken from humans,  $N_{\rm H}(i)$  is the number of human individuals in the patch *i*,  $\chi_{\rm V}$  is the probability of transmission from an infected human to a susceptible mosquito per bite and  $\chi_{\rm H}$  is the probability of transmission from an infected mosquito to a susceptible human per bite,  $1/\gamma$  defines the human infectious period,  $1/\omega_{\rm V}$  represents the extrinsic incubation period, and  $\mu_{\rm V}$  is the mortality rate of the adult mosquito.

To highlight the potential duration of the estimated epidemic risks, we computed the number of consecutive days associated with an  $R_0$  larger than the epidemic threshold ( $R_0>1$ ). Areas with a population density lower than ten inhabitants per hectare were excluded from this analysis.<sup>14</sup> Details are provided in the appendix (pp 7–10).

# Model validation

Model estimates of the climate suitability for the different mosquito species were compared with out-of-sample occurrence records in Europe and the Americas,<sup>30</sup> and with historical records on the presence of *A aegypti* in Europe.<sup>37</sup> A cross-validation analysis was also performed to test model predictive performance against adult capture data. The original data was divided into five complementary subsets (either consisting of 20% of datapoints or 20% of trapping sites). The model was recalibrated using only four of these subsets and tested against the residual 20% of datapoints, using the root mean square error between model estimates and out-ofsample data. Cross-validation was repeated using each of the five subsets as the validation set and for 100 different random partitions of the initial data. Details are reported in the appendix (p 26). Analyses were performed using a code developed ad-hoc by our team in the programming language C, using R software version 4.1.2 and QGIS software version 3.30.2.

#### Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

# Results

Estimates obtained from the regression models were statistically accurate when compared with in-sample records of presence, absence, and co-occurrence of the two mosquito populations<sup>16,20</sup> (Cohen's  $\kappa$ >0.5; appendix pp 16–17). We compared the estimates obtained from the regression model applied to precise presence-absence records of A albopictus in Europe with those obtained from data aggregated over spatial subunits of Europe. The obtained results confirmed that using climate values averaged over a region could be considered a reasonable approximation when more precise data were not available (appendix p 17). The simulated climate suitability of A aegypti and A albopictus was also compliant with out-ofsample occurrence data,30 identifying 98% and 99% of locations where the species have been observed across Europe and the Americas, respectively (appendix p 17). Additionally, the climate suitability of A aegypti estimated for European countries was in good agreement with evidence of the historical distribution of this mosquito between 1900 and 1955 (appendix p 18).27 However, ongoing climate trends were found to markedly increase the potential dispersal of both species between 2020 and 2040, especially in Europe and the USA (appendix pp 19-24). Model estimates on the abundance of the two mosquito species capture the temporal dynamics observed in the analysed entomological surveillance data from Italy, Brazil, and the USA (appendix pp 25-26). The cross-validation analysis showed that, when 20% of datapoints or 20% of trapping sites were excluded from model calibration, the model estimates on out-of-sample data did not significantly differ from those obtained using the entire dataset, with similar parameter estimates (appendix pp 26-32).

We estimated that 40% of the Americas had a climate suitability index higher than 0.5 for both *Aedes* species (appendix p 12). In these areas, *A aegypti* was estimated to be more abundant compared with *A albopictus*, showing on average a 6.4 times (range 1.0-50.2) higher number of mosquitoes per hectare during the peak month (figure 1). Outside sympatric areas, *A albopictus* showed a wider ecological niche, extending to temperate areas of the American continents (appendix p 12). In Europe, the climate suitability index for *A albopictus* was estimated to be higher than 0.5 in 25% of patches (appendix p 15).



Figure 1: Estimated seasonal patterns for the absolute abundance per hectare of Aedes aegypti and Aedes albopictus in the Americas Estimates are provided at a spatial scale of 1 km × 1 km; displayed values represent average estimates obtained with 500 model runs. The SD associated with the estimated maximum abundance of the two species is provided in the appendix (p 34).

For both species, the highest mosquito density was identified in the tropical and subtropical areas of the Americas (figure 1). In tropical areas, the vector density was constant all year round, with an estimated daily number of adult female mosquitoes per hectare of more than 4000 for A aegypti and more than 800 for A albopictus in the rainforests of Latin America. Outside of the tropical and subtropical areas, the abundance of both species showed a strong seasonal pattern (figures 1, 2). In the USA, the highest mosquito density was estimated in Florida, Texas, and Arizona (USA), showing a peak of approximately 3000 A aegypti and 800 A albopictus per hectare at the end of the summer. In Europe, the highest abundance of A albopictus was found to occur between July and October, with an estimated maximum of more than 500 adult female mosquitoes per hectare in several areas of Italy, Spain, southern France, and in the coastal areas of Balkan countries.

Our estimates highlighted that the three arboviral diseases could be potentially endemic in many American countries in or close to the tropical areas (figure 3). Although dengue virus and Zika virus could be endemic because of the high density of *A aegypti, A albopictus* could markedly contribute to the endemicity of chikungunya (figure 3; appendix p 40). Our estimates suggested that dengue virus and Zika virus could represent the major epidemic threats for Latin America, with the highest risks

found in central America, on the northern coast of Venezuela and Colombia, and in the central-east of Brazil (figure 4). Although for all the considered infections a generally higher  $R_0$  was associated with *A aegypti* compared with *A albopictus* (figure 4; appendix p 35), *A albopictus* might contribute to the spread of dengue virus and chikungunya in large portions of the Americas and Europe.

A marked seasonality in the transmission risks was estimated in temperate areas of both the Americas and Europe (figures 4, 5; appendix pp 35–37). In these regions, the  $R_0$  for all the considered infections was lower than the epidemic threshold between December and March in the Northern hemisphere and between July and September in the Southern hemisphere. We found large proportions of Florida, Texas, and Arizona (USA) to be at a significant risk of autochthonous transmission for all three diseases. In the southern parts of the USA, Zika virus was estimated to cause the longest epidemic risk among the three analysed arboviruses (figure 3). At northern latitudes, the highest and longest risk of infection was found for chikungunya (figures 3, 4; appendix p 40). In Europe, where Aedes-borne diseases were assumed to be transmitted only by A albopictus, chikungunya was associated with the highest and longest risk of autochthonous transmission (figures 3, 5; appendix pp 36-37, 40). In most of Europe, the epidemic risk was estimated to last less than 6 months



Figure 2: Estimated seasonal patterns for the absolute abundance per hectare of Aedes albopictus in Europe Estimates are provided at a spatial scale of 1 km × 1 km; displayed values represent average estimates obtained with 500 model runs. The SD associated with the estimated maximum abundance is provided in the appendix (p 34).

for any considered arboviral infection (figure 3; appendix p 40), with a moderate risk of chikungunya outbreaks in Italy, Spain, France, and Balkan countries (figure 5). Non-negligible risks were estimated for dengue virus along the Mediterranean coast of these countries during August (appendix p 43); no significant risk of Zika transmission was estimated for Europe (appendix p 37). The analysis of model uncertainty shows the highest variability in the estimated reproduction numbers and duration of the epidemic risks for chikungunya in the Americas, when assuming *A aegypti* to be the main vector of transmission (appendix p 38–40, 41–43).

The estimated values of  $R_0$  for chikungunya and dengue were in line with estimates obtained from the analysis of local outbreaks (figure 6).<sup>8,9,22</sup> For example, our average estimates of  $R_0$  for dengue in Porto Alegre, a non-endemic metropolis in Brazil, were in line with the reproduction numbers quantified for this location between 2013 and 2016.<sup>22</sup> Similarly, our estimates of  $R_0$  for chikungunya in three Italian municipalities were consistent with results published on the outbreaks that occurred in these locations in 2007 and 2017<sup>89</sup> Comparing estimates of  $R_0$  with the distribution of observed cases can be misleading because of possible spatial heterogeneity in the under-reporting of cases, pre-existing immunity, and the importation of viraemic cases. Nonetheless, the findings of which areas were estimated to be at a high risk of infection reflected current areas with disease occurrence in Brazil and the USA (appendix pp 44–45).<sup>710,31</sup> Finally, areas of Italy, France, and Spain where clusters of autochthonous cases of dengue virus and chikungunya were reported in the last decade<sup>56,89,32</sup> were among those we identified to be at a higher risk of transmission in Europe (appendix pp 43–44).

## Discussion

Evidence-based methods providing indications of the spatiotemporal distribution of different mosquito species and of the associated risks of viral transmission could be instrumental to design adequate policies for preventing the spread of local outbreaks and for reducing the number of human infections in endemic areas.



#### Figure 3: Estimated duration of the epidemic risk

The estimated duration of the epidemic risk is provided in terms of the number of consecutive days in which  $R_o$  is more than the epidemic threshold, for dengue virus (A), Zika virus (B), and chikungunya (C) in the Americas, as obtained by assuming *Aedes aegypti* to be the main vector species. The figure also shows the estimated duration of the epidemic risk of chikungunya in the Americas (D) and Europe (E), as obtained by considering *Aedes albopictus* as the main vector species. Estimates are shown only for areas at risk of transmission for at least 1 day and provided at a spatial scale of 250 m × 250 m; displayed values represent average estimates obtained with 500 model runs. The SD associated with these estimates is provided in the appendix (pp 41–43). Patches are shown as proportional to the population size to highlight potential epidemic risks.

The simulated spatial distribution of A aegypti and A albopictus from our study is consistent with available data<sup>30</sup> and estimates regarding their habitat suitability.<sup>15,17</sup> The cross-validation analysis we performed suggests that the number of datapoints used in our analysis was sufficient for estimating the parameters of our model and that our modelling approach provides a consistent output for both species. Although a validation of our estimates of mosquito abundance was not feasible because of the absence of data on the absolute number of adult mosquitoes per hectare, the model estimates were in good agreement with estimates from markrelease-recapture experiments (appendix p 33). The estimated dominance of A aegypti in the transmission of arboviral infections confirms previous findings suggesting that this species might cause more than 90% of the risk of Zika virus outbreaks in tropical areas.1 Areas that were identified as probably endemic for dengue virus were in agreement with published epidemiological evidence.3,31 In addition, our estimates highlighted that Zika virus and chikungunya might potentially be (or become in the future) endemic in Latin America. In general, the estimated spatial distribution of the risk of autochthonous transmission for the different arboviral diseases was in agreement with estimates previously provided for dengue virus,19 Zika virus,<sup>1,2</sup> and chikungunya,<sup>11</sup> as well as with observed dengue and chikungunya cases in Brazil, the USA, and across European countries.<sup>5-9,31,32</sup> The estimated values of  $R_0$  for chikungunya and dengue virus also were in line with estimates obtained from the analysis of local outbreaks.8,9,22



Figure 4: Estimated temporal dynamics of the reproduction number in the Americas for different arboviral infections Estimated temporal dynamics of the reproduction number,  $R_{0}$ , for dengue virus (A), Zika virus (B), and chikungunya (C) in the Americas, as obtained by assuming Aedes aegypti to be the main vector species. (D) The temporal dynamics of the reproduction number R<sub>0</sub> for chikungunya in the Americas, as obtained by considering Aedes albopictus to be the main vector species. Estimates are shown only for areas with at least ten inhabitants per hectare and an estimated  $R_{\circ}$  greater than 0.1. Estimates are provided at a spatial scale of 250 m × 250 m; displayed values represent average estimates obtained with 500 model runs. The SD associated with the estimated maximum reproduction number R<sub>o</sub> is provided in the appendix (p 38). R<sub>o</sub> values are shown as proportional to the population size to highlight potential epidemic risks.



Figure 5: Estimated temporal dynamics of the chikungunya reproduction number in Europe Estimated temporal dynamics of the reproduction number,  $R_{\omega}$  for chikungunya in Europe, as obtained by assuming *Aedes albopictus* to be the main vector species. Estimates are shown only for areas with at least ten inhabitants per hectare and an estimated  $R_{o}$  greater than 0.1. Estimates are provided at a spatial scale of 250 m × 250 m; displayed values represent average estimates obtained with 500 model runs. The SD associated with the estimated maximum reproduction number  $R_{o}$  is provided in the appendix (p 39).  $R_{o}$  values are shown as proportional to the population size to highlight potential epidemic risks.

As with all modelling analyses, our work has several limitations. First, our analysis focuses on the transmissibility potential of different arboviruses rather than the risk of contracting the disease. However, estimates provided for  $R_0$  might not reflect the risk of the local spread of an epidemic, which could be strongly influenced by human mobility, the likelihood of case importation, the proportion of the population actually exposed to mosquito bites (which might relate to the socioeconomic status of individuals residing in specific areas<sup>33</sup>), the interventions adopted by national and local authorities, and the immunity level in a population. In particular, primary dengue infection is thought to confer lifelong immunity against the infecting serotype,<sup>4</sup> and immunity acquired in Latin America during the 2016 Zika epidemic might delay the re-emergence of this disease in the affected areas.<sup>34</sup> Second, because epidemic risks were separately estimated for the two species, we were not able to quantify the expected reproduction number when both species contributed to the transmission. Third, because we assessed the risk of infection only for areas with at least ten inhabitants per hectare, our estimates might not have reflected the actual risk of autochthonous transmission in areas with low population densities. Fourth, the estimated density of female adult mosquitoes per hectare crucially depended on the estimates of the capture rate for sticky traps we retrieved from mark-release-recapture field experiments conducted in diverse regions: Brazil and Italy.28,29 Unfortunately, field-based studies on the effectiveness of the different types of traps are still scarce. As such, further investigations based on different traps and conducted under different climate and entomological conditions are required to increase the robustness of the estimated absolute abundance of different mosquito species. Fifth, model estimates should also be carefully interpreted in the light of the large uncertainty surrounding disease-specific parameters (eg, the probability of transmission from an infected mosquito to



Figure 6: Average model estimates of  $R_o$  for dengue virus and chikungunya in Brazil and Italy (A) Average model estimates of the dengue virus  $R_o$  in Porto Alegre, Brazil, as obtained by considering Aedes aegypti to be the dominant competent vector for the transmission.  $R_o$  estimates reported in the literature for this area peak at 1-4–1-9 between 2013 and 2016.<sup>22</sup> Average model estimates of the chikungunya  $R_o$  as obtained by considering Aedes albopictus as the dominant vector in Rome, Italy (B), and in two villages of Emilia Romagna (Castiglione di Cervia and Castiglione di Ravenna), Italy (C). Published estimates of  $R_o$  associated with the outbreaks that occurred in these locations were 1.8–6.0 in the 2007 outbreak<sup>®</sup> and 1.5–2.6 in the 2017 outbreak<sup>®</sup>. Estimates are shown only for areas at risk of autochthonous transmission (ie,  $R_o$ =1) in the considered month.

susceptible human per bite) when translating а the estimated vector-to-human ratio into estimates of the associated risk of transmission (R<sub>a</sub>). Sixth, to estimate the climate suitability in the Americas, a logistic regression was calibrated against data aggregated at the county level, and climate records might have been more trustworthy for areas associated with a homogeneous climate. Seventh, potential biases led by the low availability of entomological data for south America and Europe compared with the number of collection records included for the USA cannot be excluded as well. Finally, our analysis did not account for the effect of competition between different mosquito species and heterogeneous mosquito competence in transmitting different viral strains (eg, a higher competence of A albopictus in transmitting specific chikungunya genotypes).35

Several factors, including land cover, vegetation, amount of urbanisation, population density, and income, were associated with mosquito presence.<sup>12,21,33,36</sup> Given the resolution of the available mosquito presence and absence data (eg, at the county-level) and the high variability of these indicators over wide geographical areas (appendix pp 4–5), these factors were not included in our analysis. The availability of mosquito presence and absence records at a finer spatial scale would allow for including these environmental factors into the model, possibly enhancing model accuracy.

Despite these limitations, our analysis represents, to the best of our knowledge, the first attempt to quantify the absolute abundance of *A albopictus* and *A aegypti*, and the consequent transmission potential of *Aedes*-borne arboviral infections at a continental scale, while maintaining a high spatiotemporal resolution. Estimating seasonal variations in the mosquito abundance and the  $R_0$  associated with one arboviral disease and one variable set over 730 million patches using daily temperature data took less than 12 min on a modern laptop (appendix p 8). We believe our modelling approach represents a major advancement when compared with current methods because it can be used to quantify, almost in real-time, the mosquito abundance and related epidemic risks in areas where entomological data are scarce or unavailable, by relying on freely available data on the local temperature and precipitation only. Additional entomological data could be used to extend the developed framework to study other continents, mosquito species, and mosquitoborne diseases. Finally, our estimates could inform future modelling efforts and epidemiological investigations as well as support public health authorities in planning the allocation of resources for entomological and epidemiological surveillance activities, information campaigns, and preventive measures.

#### Contributors

PP, MA, and SM conceived the study. PP, MA, AV, and SM supervised the study. AZ, FMe, and AG performed the analyses. AZ and PP wrote the first draft of the manuscript. PP, AZ, and FMe directly accessed and verified the underlying data reported in the manuscript. All authors had full access to the data; contributed to interpreting the results; and read, reviewed, and approved the final version and the submission of the manuscript.

#### **Declaration of interests**

MA has received research funding from Seqirus. The funding is related to influenza vaccination in Italy and thus not related to this manuscript. All other authors declare no competing interests.

#### Data sharing

The code and the processed data (including detailed model estimates) will be made available in a public repository (Zenodo) upon publication, with no restrictions.

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