Articles

Impact of climate and Aedes albopictus establishment on dengue and chikungunya outbreaks in Europe: a time-to-event analysis

Zia Farooq*, Leo Segelmark*, Joacim Rocklöv, Kate Lillepold, Maguines Odhiambo Sewe, Olivier J T Briet, Jan C Semenza

Summary

Background The rapid spread of the Asian tiger mosquito (*Aedes albopictus*) poses a notable public health threat in Europe due to its ability to transmit tropical diseases such as dengue and chikungunya. We aimed to quantify the underlying drivers facilitating and accelerating Europe's transition from sporadic arbovirus outbreaks to *Aedes*-borne disease endemicity, focusing on dengue and chikungunya outbreaks.

Methods We conducted a time-to-event analysis to investigate the period between establishment of *Ae albopictus* and autochthonous dengue and chikungunya outbreaks across Nomenclature of Territorial Units for Statistics (NUTS) 3 regions in the EU. We incorporated data from the European Centre for Disease Prevention and Control, WHO, technical and surveillance reports, and other entomological data sources on regional *Ae albopictus* establishment and subsequent dengue and chikungunya outbreaks from 1990 (when *Ae albopictus* was first introduced to an EU country) to 2024. The main outcome was survival time (ie, the time from *Ae albopictus* establishment to an outbreak of dengue or chikungunya), accounting for land-use types, demographic and socioeconomic factors, imported cases, and climatic variables via univariable and multivariable regression. To address recurrent outbreaks, we applied the Andersen–Gill extension of the Cox proportional hazards model to analyse all events. We further stratified regions into warm and cool groups on the basis of mean summer temperatures above or below 20°C and conducted a stratified analysis with Kaplan–Meier curves and the log-rank test to evaluate differences between these groups. We also estimated projected outbreak hazards from the 2030s to the 2060s at a decadal scale under three distinct shared socioeconomic pathways (SSPs; SSP1–2·6, SSP3–7·0, and SSP5–8·5) to assess the future impact of climate change on outbreak hazard estimates.

Findings Between 1990 and 2024, the interval from the first NUTS 3 regional establishment of *Ae albopictus* to the first outbreak of dengue or chikungunya decreased from 25 years to less than 5 years. Similarly, the interval from the first outbreak to the second outbreak decreased from 12 years in 1990 to less than 1 year in 2024. Our regression analyses indicate that increasingly favourable climatic conditions play a significant role in this trend. A 1°C rise in mean summer temperature was associated with a hazard ratio of 1.55 (95% CI 1.30-1.85; p<0.0001) after controlling for health-care expenditure and imported cases and land-use type. First outbreak events might have occurred more frequently and earlier in warmer regions than cooler ones (log-rank p=0.088), reflecting a lower probability of remaining outbreak-free over time. This trend is expected to intensify under extreme climate change scenarios, with projections under the SSP5–8.5 scenario suggesting an almost five-fold increase in dengue or chikungunya outbreaks by the 2060s, relative to the 1990–2024 baseline period.

Interpretation The findings in this study underscore the pressing need for robust control measures, enhanced surveillance, and early warning systems in the EU to mitigate the impending risk of *Aedes*-borne disease endemicity in the region.

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Introduction

An estimated 4 billion individuals in more than 129 countries are now at risk of dengue and chikungunya virus infection.¹ The principal vectors of dengue virus (DENV) and chikungunya virus (CHIKV) are *Aedes aegypti*, the yellow fever mosquito, and *Aedes albopictus*, the Asian tiger mosquito.² *Ae albopictus*, which is native to southeast Asia, has, during the past half century, spread throughout the world, including in Europe, due to increased globalisation, urbanisation, trade, travel, and climate change.³ *Ae albopictus* is ranked as the world's fourth-worst invasive alien species in the top 100 list and is the most invasive vector species worldwide.⁴ In Europe, *Ae albopictus* first appeared in 1979 in Albania and was later introduced to Italy in 1990. It has since been established in 21 European countries and introduced to six more.⁵





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*Contributed equally Department of Epidemiology and Global Health, Umeå University, Umeå, Sweden (Z Farooq PhD, L Segelmark MD, Prof J Rocklöv PhD, M O Sewe PhD, Prof J C Semenza PhD); Heidelberg Institute of Global Health, University of Heidelberg, Heidelberg, Germany (Prof J Rocklöv, Prof J C Semenza);

Interdisciplinary Center for Scientific Computing, University of Heidelberg, Heidelberg, Germany (Prof J Rocklöv); ECDC Traineeship Programme, European Centre for Disease Prevention and Control, Solna, Sweden (K Lillepold MPH); European Centre for Disease Prevention and Control (ECDC), Solna, Sweden (O J T Briet PhD)

Correspondence to:

Prof Jan C Semenza, Department of Epidemiology and Global Health, Umeå University, Umeå 907 37, Sweden jan.semenza@lateralPHC.com

Research in context

Evidence before this study

Dengue and chikungunya are Aedes-borne diseases that are endemic in tropical and subtropical regions, but not in Europe, where most cases are imported from outside the European mainland. However, sporadic outbreaks of these infections can occur locally when returning viraemic travellers generate transmission cycles in areas of Europe where the vector (Aedes albopictus) is established. Since 2010, there have been recurrent dengue and chikungunya outbreaks that have increased in frequency and magnitude, exemplified by the largest dengue outbreak to date, with over 200 notifications in October, 2024, in Italy. We performed a comprehensive review of the available literature to identify factors contributing to the establishment of Ae albopictus and subsequent dengue and chikungunya outbreaks in the EU. We searched PubMed, Scopus, and Web of Science, from Jan 1, 1990, to Oct 31, 2024. We included peer-reviewed articles, systematic reviews, reports from organisations such as the European Centre for Disease Prevention and Control and WHO, and grey literature from technical and surveillance reports. The search terms comprised combinations of "Aedes albopictus", "dengue outbreaks", "chikungunya outbreaks", "vector-borne diseases", "climate change", "Europe", "longitudinal analysis", "time-to-event analysis", and "survival analysis". The resulting studies examined the relationships between climatic, environmental, socioeconomic, entomological, or demographic factors and the proliferation of Ae albopictus or the risk of local outbreaks in Europe. Studies without specific geographical or temporal contexts were excluded. Although numerous studies have examined the establishment of Ae albopictus and the transmission of vector-borne diseases in Europe, we did not find any longitudinal studies that have analysed the impact of climate and other factors on the spread of Ae albopictus and resulting local outbreaks over the past three decades. Additionally, previous research has not used survival analysis to investigate the time gaps between vector establishment and subsequent local outbreaks, nor between recurring outbreaks in the same area.

Added value of this study

This study was prompted by a paucity of long-term, spatiotemporal analyses quantifying the accelerating trend of autochthonous dengue and chikungunya transmission.

In Europe, where dengue and chikungunya are not endemic, autochthonous vector-borne transmission occurs when an *Ae albopictus* mosquito becomes infected with DENV or CHIKV by biting a viraemic traveller and then transmits the virus to another individual during a subsequent bite.⁶ The first autochthonous outbreak of chikungunya in Europe was documented in Ravenna, Italy, in 2007, resulting in 330 cases.⁷ Similarly, the first autochthonous dengue outbreak in Europe occurred in Croatia in 2010 and was detected when a German traveller returned home from Croatia and displayed signs of dengue fever.⁸ Since then, Italy, France, and Spain We compiled 35 years of entomological data (1990-2024) from both grey and peer-reviewed literature on Ae albopictus establishment in the EU (excluding overseas territories), quantifying the time lag until the onset of autochthonous outbreaks. We assessed the influence of climatic factors, land use, imported cases, and socioeconomic determinants on the progression from mosquito establishment to dengue or chikungunya outbreaks. With a survival analysis framework, we revealed a stark chronological shift: in the 1990s, European regions experienced a grace period of more than 25 years between mosquito establishment and the first outbreak, whereas now this period has decreased to under 5 years. Moreover, our stratified time-to-event analysis suggests a steeper decline in survival probability in warmer regions than cooler regions, indicating a higher outbreak risk in warmer regions. Climatic variables emerged as the strongest predictors of outbreak risk, even after accounting for health-care expenditure and imported case numbers. Warmer summer temperatures were found to substantially elevate outbreak risk, particularly in urban and semi-urban settings, whereas human travel and mobility were found to facilitate the spread of these two Aedes-borne diseases.

Implications of all the available evidence

Our findings highlight that the EU is transitioning from sporadic outbreaks of *Aedes*-borne diseases towards an endemic state. The interval between vector establishment and local outbreaks has substantially shortened over the past three decades and is expected to decrease further. These trends underscore the urgent need for robust public health measures, including stringent vector control, enhanced entomological and disease surveillance, citizen science, and early warning systems. Our analysis delineates areas currently at risk and those likely to face future risks, guiding targeted control and surveillance efforts. Moreover, our multivariable model highlights actionable parameters for early warning systems to pre-empt outbreaks. In the context of a warming climate, mitigating the transition to endemicity will require proactive, vigilant, and well targeted public health interventions.

have experienced recurrent autochthonous dengue and chikungunya outbreaks.

Vector-borne transmission of dengue and chikungunya requires the introduction of the virus and the presence of a competent vector and susceptible humans.⁶ A conducive climate and suitable natural and human environments promote the mosquito's ability to transmit the virus and increase the vector population size.^{9,10} Climatic factors, such as temperature and rainfall, influence vector abundance and mosquito activity. Mean temperature during winter months affects the survival of mosquito eggs during diapause, whereas mean

temperature during warmer months affects adult mosquito survival and activity.11 Temperature is also an important factor determining the speed of virus replication in the mosquito,11 making dengue and chikungunya climate-sensitive diseases.¹² Climate change affects the risk of infection by altering the geographical range and length of the transmission season.¹³ In Europe, arbovirus outbreaks, which were rare in the past, have increased in frequency and size.9 Without accounting for asymptomatic cases, the largest outbreaks have caused 330 chikungunya cases and 213 dengue cases. Moreover, as the climate continues to warm, susceptibility to sustained outbreaks is likely to increase.13 Therefore, understanding the nature and trajectory of Aedes-borne outbreaks in Europe under different climate change scenarios is crucial.

In this study, we aimed to use vector surveillance data to catalogue the spread of *Ae albopictus*, collate imported cases of dengue and chikungunya from endemic areas, and map autochthonous outbreaks in relationship to the regional establishment of *Ae albopictus*. We also aimed to identify key factors driving local dengue and chikungunya outbreak risk in the EU and project the risk of future outbreaks under climate change scenarios in regions already inhabited by *Ae albopictus*.

Methods

Data sources

We catalogued the introduction and establishment of *Ae albopictus* at the Nomenclature of Territorial Units for Statistics (NUTS) 3 regional level (the most detailed level) in the EU with an integrative review of peerreviewed literature, reports from organisations such as the European Centre for Disease Prevention and Control and WHO, grey literature from technical and surveillance reports, and other entomological data sources from Jan 1, 1990 (the year *Ae albopictus* was first introduced to an EU country), to July 31, 2024. Epidemiological, land use, socioeconomic, and climatic data were collected for the study period. An overview of the variables, including their sources and descriptions, is provided in the appendix (pp 5–6).

Model design and statistical analysis

Descriptive and inferential statistics

We analysed regional traits across NUTS 3 regions in the EU. We distinguished NUTS 3 areas with documented autochthonous outbreaks from those without. Differences were compared with the Mann–Whitney *U* test for continuous variables and the χ^2 test for categorical variables. Because continuous variables don't follow a normal distribution, their data are reported as median (IQR; appendix pp 7–8).

Survival time and survival probability

In the context of our study, the main outcome of survival time refers to the duration between the establishment of *Ae albopictus* and the occurrence of an autochthonous dengue or chikungunya outbreak in a given region. Longer survival times indicate a delayed outbreak occurrence, whereas shorter survival times suggest a higher likelihood of early outbreaks. Survival probability represents the proportion of regions that have not yet experienced an outbreak at a given timepoint after vector establishment. A declining survival probability over time means that an increasing number of regions have experienced outbreaks, highlighting cumulative risk.

Cox proportional hazard model (Andersen–Gill extension)

We applied the Andersen-Gill extension of the Cox proportional hazard model to analyse all events, including both initial and later outbreaks.14 This model serves as a generalised version of the standard Cox model, designed to incorporate repeated and timevarying covariates. Specifically, it allows a NUTS 3 region to experience multiple outbreak events over time, indicating that the region remains at risk throughout the study and that past events do not alter the baseline risk.14 Furthermore, the model treats the occurrence of events as a counting process to monitor the number of events experienced. As with the standard Cox model, the Andersen-Gill extension allows for time-varying covariates (ie, those that fluctuate over time) while maintaining the proportional hazard assumption. It also handles gaps in at-risk periods and effectively addresses censoring issues.

Modelling details

The univariable hazard rate with the standard Cox model for a NUTS 3 region *i* at time *t*, $h_i(t)$, is modelled with the following expression:

 $h_i(t)=h_0(t) \exp(\beta^T X_i(t)),$

where $h_0(t)$ denotes the baseline hazard and is assumed to remain constant at 1, $X_i(t)$ is the vector of covariates for region *i* at time *t*, and β is the vector of regression coefficients (which quantify the effect of each covariate on the hazard of an outbreak occurring in a given region at a given time). In the context of this study, the regression coefficients correspond to the log hazard ratios (HRs) associated with each predictor (such as temperature, precipitation, land-use type, imported cases, and health-care expenditure). A positive β value indicates that an increase in the corresponding covariate $X_i(t)$ is associated with a higher hazard of an outbreak, whereas a negative β value suggests a protective effect.

The Andersen–Gill model extends the Cox proportional hazards model by incorporating recurrent event data, meaning that each NUTS 3 region remains at risk of additional outbreaks even after experiencing one. The model uses the intensity process to describe the likelihood of experiencing an event at any given time. See Online for appendix

The intensity process (or hazard function) for the counting process is described by

$h_i(t|F_t) = Y_i(t)h_0(t) \exp(\beta^T X_i(t)),$

where $Y_i(t)$ is the risk indicator, which equals 1 if region *i* is at risk at time *t*, and equals 0 otherwise. In our study, a region enters the risk set once *Ae albopictus* is established and remains at risk until the end of the study period, allowing for multiple outbreaks. F_i - accounts for the history of the process just before time *t*, ensuring that the hazard function reflects past outbreak occurrences within a region. This term accounts for the accumulation of outbreak events and allows the model to properly estimate the risk of subsequent outbreaks without assuming previous events alter the baseline hazard function.

In the multivariable implementation of the Andersen– Gill model, the covariate vector $X_i(t)$ includes multiple time-dependent and time-independent predictors. The hazard function for region *i* at time *t* is given by

$h_{i}(t|F_{t}) = Y_{i}(t)h_{0}(t) \exp(\beta_{1}^{T}X_{i1}(t) + \beta_{2}^{T}X_{i2}(t) + \dots + \beta_{p}^{T}X_{ip}(t)),$

where $X_{ij}(t)$ represents the *j*th covariate for region *i* at time *t* (eg, temperature, precipitation, land-use type, imported cases, or health-care expenditure), and β_j is the corresponding regression coefficient, which quantifies the effect of covariate X_{ij} on the outbreak hazard. The covariate matrix *X* has dimensions $N \times p$, where *N* is the number of observations and *p* is the number of covariates. The function $exp(\beta_{ij}X_{ij}(t))$ ensures that the effects of each covariate on the hazard function are multiplicative.

The covariates for multivariable analysis were chosen with a stepwise backward elimination, retaining only those variables with a p value <0.05 (table). HRs were used to interpret the strength of association between covariates and outbreaks. A p value of <0.05 was considered statistically significant.

Stratified time-to-event analysis

We further stratified regions into warm and cool groups on the basis of mean summer temperatures above or below 20°C. We conducted a stratified analysis with Kaplan–Meier curves and the log-rank test to evaluate differences between these stratified groups.

Projected climate-driven outbreak hazard estimates

With the projected estimations of covariates selected through the backward elimination method in the multivariable analysis, we assessed the future impact of climate change on outbreak hazard estimates for dengue and chikungunya for NUTS 3 regions in the EU inhabited by *Ae albopictus*. We projected these estimates from the 2030s to the 2060s at a decadal scale. In Europe, the optimal temperature envelope for transmission is 20–28°C. Beyond this temperature range, transmission

might decline.¹⁰ Although the same relationship does not apply to the decadal climatic variables we modelled, we nevertheless capped our projections at the 2060s. We considered three distinct shared socioeconomic pathways (SSPs) that consider national population, urbanisation, gross domestic product (per capita), and representative concentration pathways (RCPs): SSP1–2.6, SSP3–7.0, and SSP5–8.5. These scenarios correspond to radiative forcing levels of 2.6, 6.0, and 8.5 W/m² by 2100 (relative to pre-industrial values), indicating low, medium–high, and high greenhouse gas emissions, respectively.¹⁵

To describe uncertainties in the multimodel estimates within each RCP, we considered five general circulation models (GCMs): IPSL-CM6A-LR, MPI-ESM1–2-HR, MRI-ESM2–0, UKESM1–0-LL, and GFDL-ESM4. These GCMs (which are numerical representations of physical processes illustrating the Earth's climate system with a three-dimensional grid encompassing the ocean, cryosphere, and land surface across the globe) are bias-corrected for the third simulation round of the Inter-Sectoral Impact Model Intercomparison Project. In total, we therefore used 15 SSP–GCMs for the HR projections.^{16,17}

At any future timepoint, say decade *d*, to estimate the climate-driven projected change in the outbreak hazard for each GCM in an SSP–RCP, we modelled an outbreak hazard estimate, $(h_p)^d$ (ie, the climate-driven effect of the covariate), with the following expression:

$$h_{p}^{d} = h_{0}(t) h_{T_{3}}^{(T_{3}^{d} - T_{3}^{b})}$$

where $h_0(t)$ denotes the baseline hazard and h_{T_3} is the hazard ratio for the mean summer temperature (T_3) . The expression in the exponents denotes the absolute change in the expected values of the covariate. For example, $(T_3^{d} - T_3^{b})$ denotes the change in the mean summer temperature for the decade, where T_3^{b} is the average summer temperature of baseline period *b* from 1990 to 2024 and T_3^{d} is the projected mean summer temperature for decade *d*. The baseline and projected decadal values of the mean summer temperature per scenario are reported in the appendix (p 6).

All statistical analyses were conducted with R (version 4.2.0) in RStudio (version 2022.2.3.492). The Andersen–Gill model was fitted with the coxph() function with a clustered frailty term to account for repeated events within the same region.

Role of the funding source

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

Results

Ae albopictus was first introduced in 1990 in Genova, Italy, and rapidly spread to 37 regions throughout Italy in the subsequent decade. It appeared in France only in 1999, and by 2010 was established (with evidence of local reproduction and overwintering) in 129 regions across seven countries. This establishment increased to 289 regions in 12 countries by 2022. In less than 2 years, the number of affected regions in the EU had increased to 358 regions in 14 countries. The invasion and establishment of *Ae albopictus* in EU regions over the past 35 years are shown in figure 1.

To date, there have been 66 autochthonous dengue and chikungunya outbreaks in the EU across 32 NUTS 3 regions. In 2024, there were a total of 304 dengue cases—a historic peak compared with the combined total of 275 cases in the previous 15 years (figure 2A). Autochthonous outbreaks have been reported in four countries—Croatia, Italy, France, and Spain—and the trend suggests a progression from sporadic cases towards endemicity in these countries, coupled with a geographical expansion into naive areas (figure 2B).

According to European Centre for Disease Prevention and Control data, most outbreaks (63 [95%] of 66) took place between July and September, with 64 occurring in the third quarter of the year. Outbreak locations stratified by land-use characteristics (ie, rural *vs* urban or semiurban) are mapped in figure 2C, revealing that 24 (75%) of 32 affected areas are urban or semi-urban areas and eight (25%) of 32 affected areas are rural areas. Regions affected by autochthonous outbreaks reported on average $4 \cdot 0$ imported cases annually, whereas unaffected regions reported fewer than one, highlighting the role of imported cases in outbreak risk.

Survival time (ie, the interval from the establishment of Ae albopictus to the emergence of dengue and chikungunya outbreaks) in the EU has decreased considerably (figure 3). In the 1990s, regions experienced a hiatus of over 25 years between Ae albopictus establishment and the first outbreak; however, this period has now been reduced to less than 5 years (figure 3A). Moreover, the timespan between the first and second outbreak in a region has also shortened, with an initial outbreak in an area currently potentially being followed by a second outbreak in the same area within 1 year (figure 3B). This escalating frequency highlights a trend of increasing outbreak frequency in established areas, probably driven by shifting climatic conditions and enhanced by human mobility. Together, these trends signal a shift toward endemicity and sustained outbreak activity across the EU.

Our univariable analysis revealed significant links between outbreak hazard and various epidemiological, socioeconomic, land-use, and climatic factors (table). The risk of an outbreak in urban and semi-urban areas was 3.71-times greater than the risk in rural areas (95% CI 1.56-8.81; p<0.010). Furthermore, each 1°C rise in summer temperature resulted in an HR of 1.16 (95% CI 1.04-1.29; p<0.010). Although higher precipitation levels in spring and summer correlated with a reduced HR, these findings were not statistically significant (table). Regarding epidemiological factors, each additional imported case raised the HR to 1.12 (1.10-1.15;

	Hazard ratio (95% CI)	p value
Variables in univariable regression		
Type of land use		
Urban or semi-urban	3.71 (1.56–8.81)	0.010
Epidemiological		
Imported cases	1.12 (1.10–1.15)	<0.0011
Socioeconomic and demographic		
GDP per capita†	1.03 (1.02–1.04)	<0.010
Health-care expenditure‡	1.14 (1.10–1.18)	<0.0011
Population density	1.00 (1.00–1.00)	0.010
Climatic		
Mean summer temperature§	1.16 (1.04–1.29)	<0.010
Total precipitation in Q2¶	0.86 (0.66–1.12)	0.270
Total precipitation in Q3¶	0.94 (0.69–1.02)	0.070
Variables in multivariable regression		
Type of land use		
Urban or semi-urban	2.47 (1.16-5.25)	0.020
Epidemiological		
Imported cases	1.08 (1.05–1.11)	<0.0001
Socioeconomic		
Health expenditure‡	1.20 (1.14–1.26)	<0.0011
Climatic		
Mean summer temperature§	1.55 (1.30–1.85)	<0.0001

GDP=gross domestic product. NUTS=Nomenclature of Territorial Units for Statistics. Q2=second quarter. Q3=third quarter. *Up to July, 2024. †At the NUTS 3 regional level, measured per €1000 increase. ‡At the national level, per capita, measured per €100 increase. §Measured per 1°C increase. ¶Measured per 100 mm increase.

Table: Univariable and multivariable Andersen-Gill regression of autochthonous dengue and chikungunya outbreaks in the EU, 2007–24*

p<0.0011). Socioeconomic and demographic factors, especially health-care expenditure, were similarly associated with greater outbreak risk, with an HR of 1.14 (1.10–1.18) for each €100 increase in per-capita spending (p<0.0011). Although the effect of population density is statistically significant (p<0.010), the HR remains virtually unchanged, suggesting no meaningful impact on model outcomes.

In the multivariable analysis, climatic variables emerged as the most influential predictors of outbreak risk, even after adjusting for health-care expenditure and the number of imported cases (table). Mean summer temperature showed a strikingly high HR of 1.55(95% CI 1.30-1.85) per 1°C increase (p<0.0001), indicating that warmer summer temperatures significantly amplify outbreak risk. As in the univariable analysis, precipitation-related variables were not significant. Beyond climatic factors, socioeconomic and epidemiological variables also contributed to outbreak risk. Higher health-care expenditure per capita was significantly associated with increased hazard (table), potentially reflecting the detection of cases through enhanced surveillance. Likewise, the presence of



Figure 1: Spatial and temporal expansion of Aedes albopictus establishment in EU regions, 1990–2024*

The establishment of *Ae albopictus* is defined as evidence of reproduction and overwintering that has been observed in at least one municipality within an administrative unit. Each map in the figure represents 5-year cumulative entomological data. The heatmap illustrates the percentage of regions in which *Ae albopictus* has been established in each country. *July, 2024.

France 250 dengue or chikungunya cases Number of autochthonous 🔲 Spain 225 autochthonous outbreaks Number of regions with 200 9 175 150 125 6 100 75 50 25 0. 2006 2009 2012 2015 2018 2021 2024 2006 2009 2012 2015 2018 Outbreak year Outbreak year С Aedes albopictus established areas 🔲 Rural Urban or semiurban Outside the scope of this study Not established or no data 1 • 3 • 5 • 7 . 9

> Figure 2: Number of autochthonous dengue and chikungunya cases by year (A), number of EU regions with autochthonous outbreaks by country and year (B), and map of autochthonous dengue and chikungunya outbreaks in 2007-24 in areas with Aedes albopictus establishment, stratified by land use (C)

We mapped the spatiotemporal introduction and establishment of Ae albopictus throughout the EU and found that the mosquito has expanded its range from a single region in one country to 358 regions in 14 countries over the past three decades. Since a competent vector is necessary but not sufficient for transmission, we examined the underlying determinants of autochthonous chikungunya and dengue outbreaks. We found that higher mean temperatures during the summer months in urban or semi-urban regions were associated with increased risk, potentially due to the heat island effect, in which urban areas are hotter than their rural surroundings.¹⁸ Additionally, we found that higher imported cases and higher health-care expenditure per capita were associated with an increased risk of autochthonous outbreaks.

The rise in the average annual number of events can. in part, be attributed to the expansion of Ae albopictus in Europe. However, our study also revealed that the time from Ae albopictus establishment to the first autochthonous outbreak decreased over time, indicating additional drivers of the increase in events. Moreover, we found a substantial decline in survival time from the

imported cases remained a strong risk factor, with an HR of 1.08 (1.05-1.11; p<0.0010). This increase highlights the continued impact of human travel and mobility on dengue and chikungunya transmission risk. Urban and semi-urban areas had an increased outbreak risk compared with rural areas (table), indicating that Ae albopictus can drive arbovirus transmission in densely populated regions in Europe.

Α

300 -

Furthermore, when conducting a stratified time-toevent analysis restricted to the time of the first event only, our results showed that survival probability in warm regions compared with cool regions might have been lower at all timepoints (p=0.088; figure 4). Higher cumulative outbreak probability in warmer regions over time supports the notion that temperature suitability aids vector survival and virus transmission, accounting for climatic, socioeconomic, and epidemiological factors.

Increasing dengue and chikungunya outbreak hazard estimates in response to increasing temperature, particularly under high-emission scenarios (ie, SSP3-7.0 and SSP5-8.5), are shown in figure 5. Although precipitation shows mixed results, a sharp temperature increase drives escalated outbreak risk, as warmer conditions are crucial for mosquito development and DENV or CHIKV transmission (figure 5A). This trend suggests that temperature remains an important driver of future outbreak hazards, especially under extreme climate scenarios.

The projected relative changes in outbreak hazard estimates shown in figure 5B show a substantial increase in dengue and chikungunya outbreak hazard estimates in future decades under different climate change scenarios. Under the low-emission scenario (ie, SSP1-2.6), the outbreak hazard estimate increases gradually and remains lower than the outbreak hazard estimates projected under the other scenarios by the 2060s. In the two high-emission scenarios (ie, SSP3-7.0 and SSP5– $8 \cdot 5$), there is a sharp rise in the projected outbreak hazard estimate after the 2040s, with SSP5-8.5 projecting the steepest increase. By the 2060s, the outbreak hazard estimate under the SSP5-8.5 scenario is, on average, almost five-times the baseline (in 1990-2024), highlighting the impact of more extreme climates. In later decades, particularly for the high-emission scenarios, increased uncertainty indicates greater variability in potential outbreak risks.

Discussion

Local dengue and chikungunya outbreaks are emerging public health concerns in Europe.12 To implement effective prevention and control strategies, identifying the underlying drivers of these outbreaks is crucial. We related the timings of Ae albopictus establishment in EU NUTS 3 regions to the dates of subsequent disease outbreaks in those regions. We further projected the future pathways of outbreak risk in these regions under different climate change scenarios.



R

15

Croatia



Figure 3: Relationship between survival time from the establishment of Aedes albopictus to the first autochthonous dengue or chikungunya outbreak in a region, according to year of establishment (A), and relationship between survival time from the first autochthonous dengue or chikungunya outbreak in a region to the second outbreak, according to the year of the first outbreak (B)

Each point represents a region with an outbreak. The blue regression lines indicate the negative correlation between the variables, with Spearman's correlation coefficients (r) shown in each panel.



Figure 4: Kaplan-Meier survival curves for dengue or chikungunya outbreak risk by region, stratified by mean summer temperature

The figure illustrates the survival probability of regions remaining outbreak-free over time, comparing cool regions (ie, with a mean summer temperature <20°C) and warm regions (ie, with a mean summer temperature \geq 20°C). The solid lines represent the estimated survival probabilities; the shaded areas indicate 95% Cls. The log-rank test was used to compare survival distributions between the cool and warm regions, yielding a p value of 0.088.

first to the second outbreak, compared with the survival probability from mosquito establishment to the first outbreak. Several events occurred in the same (and nearby) regions in southern France and Barcelona, suggesting that the conditions for transmission identified in our multivariable analysis, such as temperature and land use, are especially favourable in these areas.

Our recurrent event analysis ensured that all events were included in the regression model without censuring regions with multiple events. The Andersen–Gill model considers individual autochthonous events to be independent in that the occurrence of one event does not increase the risk of a subsequent event. In our study, when including all the events in a multivariable recurrent event analysis, mean temperature during the summer months was associated with increased risk of an outbreak event for every 1°C, with an HR of 1.55 (95% CI 1.30-1.85). This finding is consistent with previous research observing that temperature contributes to dengue and chikungunya transmission in Europe.^{9,10,19}

In several studies, precipitation has been shown to affect dengue and chikungunya transmission in tropical and subtropical regions.²⁰⁻²² However, Jourdain and colleagues found no statistically significant association between precipitation and autochthonous transmission events in France, consistent with our results.²³ In contrast to tropical climates, the Mediterranean climate is characterised by dry, hot summers and cool, wet winters. Moreover, *Ae albopictus* is an artificial container breeder, which makes it less dependent on rain in urban and semi-urban settings in Europe, where stormwater is also managed differently compared with tropical and subtropical regions.²⁴

Health-care expenditure per capita was included as a covariate to mitigate potential differences in surveillance among countries and areas. The number of countries not reporting a single event raises the question of whether dengue and chikungunya cases might be under-reported in some countries. Looking at the countries that have reported cases further supports the idea of potential under-reporting. Notably, the only autochthonous dengue outbreak in Croatia was detected in Germany when a German tourist returned home after a trip to Croatia. Similarly, one of the four autochthonous outbreaks in Spain was identified in Germany.8 Health expenditure per capita had an HR of 1.20 (95% CI 1.14-1.26), suggesting that higher health expenditure increases the chance of detecting and reporting cases and suggesting possible under-reporting of cases in countries with lower health expenditure.

Imported cases were also included as a covariate, as they are necessary to trigger local transmission events in the EU, where dengue and chikungunya are not endemic. In the multivariable analysis, the HR for imported cases was 1.08 (95% CI 1.05-1.11), indicating an increase in the hazard of an event with each additional imported case.

Urbanisation, which provides new habitats for *Aedes* vectors, also significantly affected outbreak risk, with urban and semi-urban areas having a higher HR for outbreak events than rural areas.²⁵ *Ae albopictus* is generally

considered less adapted to urban environments then *Ae aegypti*, but our results show that in the EU, *Ae albopictus* can thrive in urban areas and drive arbovirus transmission.^{26,27} Based on population size, the distribution of imported case data to NUTS 3 regions could have affected the magnitude of the urbanisation effect, however, potentially underestimating its independent influence. Our findings are consistent with previous research, which has established an association between urbanisation and mosquito density. A systematic review by Kolimenakis and colleagues²⁷ showed a consistent relationship between urbanisation, vector abundance, and arbovirus transmission.

Our study has several limitations. Our epidemiological data mainly relied on passive case detection within healthcare systems. Passive case-finding can result in under-reporting as it depends on affected individuals seeking medical care and being diagnosed on the basis of clinical presentation and laboratory testing. Underreporting is an issue in non-endemic areas where cases tend to be asymptomatic. Consequently, detection bias might underestimate the true burden of autochthonous transmission events and the number of imported cases. Missing data were also a potential shortcoming. Several assumptions were made about the number of imported cases that might have led to an overestimation of the number of imported cases in some regions. Another limitation of surveillance data is the risk of differences in surveillance across regions and time periods. We included health-care expenditure per capita as a proxy for surveillance capability to control for potential differences in surveillance between regions. Although this variable has been included in previous studies,28 how well it reflects surveillance capabilities is unknown. Additionally, regions that have experienced outbreak events might increase surveillance efforts. For example, dengue is a notifiable disease in France and surveillance is enhanced from May to November, with awareness campaigns targeting health professionals regarding diagnosing and reporting cases of DENV, CHIKV, and Zika virus infection.29 This response might result in overestimated HRs for regions with multiple events in our regression analysis. Therefore, these HR values should be interpreted with caution.

Travel and mobility are key to understanding outbreak risks in Europe.¹⁹ As noted, areas with high travel flow and favourable conditions for vectors and DENV or CHIKV are at greater risk.⁶ Unfortunately, we didn't have travel data for the required spatial scale during our study period. Future research should include travel-related variables as risk factors for European dengue and chikungunya outbreaks. For the projected change in outbreak hazards, we considered only the regions where *Ae albopictus* is already established. Future work can expand this analysis to extended European regions to further examine the likelihood of vector introduction and establishment driven by anthropogenic changes, including climate change and socioeconomic factors.



Figure 5: Projected change in mean summer temperature (°C) compared with the baseline period (1990–2024) under three climate change scenarios (SSP1–2-6, SSP3–7-0, and SSP5–8-5) from the 2030s to the 2060s at a decadal scale (A), and the projected relative change in outbreak hazard estimates for NUTS 3 regions with established *Aedes albopictus* populations driven by changes in the chosen variables (B) Points indicate the estimated means of the multiple climate models and bars indicate 95% CIs. NUTS=Nomenclature of Territorial Units for Statistics. SSP=shared socioeconomic pathway.

This study documents a transition towards endemicity of Aedes-borne diseases in the EU, quantifying the decrease in the time-to-event between the establishment of Ae albopictus and autochthonous dengue and chikungunya outbreaks during the study period and showing how elevated mean temperature is associated with an increased risk of dengue and chikungunya outbreaks. Climate change and other factors have contributed to the acceleration of the number of outbreaks over time. Forecasting the outbreak risk in NUTS 3 regions with established Ae albopictus populations under three climate change and socioeconomic scenarios indicates a substantial rise in outbreak risk in upcoming decades. These findings call for targeted vector control measures, entomological monitoring, citizen science for case detection and mosquito reporting, and mosquito avoidance through repellants and window screens in areas identified to be at risk.³⁰ If the EU is indeed sliding towards endemicity, donor blood deferral and blood bank screening might have to be considered in the future alongside possible vaccine deployment (eg, Dengvaxia [CYD-TDV, Sanofi Pasteur] and Qdenga [Takeda] for dengue and Ixchiq [VLA1553, Valneva] for chikungunya). This analysis documents the rapid spread of Ae albopictus and accelerating dengue and chikungunya outbreaks in the EU, highlighting the need for sensitive disease surveillance and early warning systems and responses.

Contributors

JCS and JR conceptualised this study. ZF, LS, and KL were responsible for data curation. ZF, LS, and KL conducted the formal analysis. ZF, JR, LS, KL, and JCS were responsible for the methodology. JCS administered the project. JCS and JR supervised the study. ZF, LS, and KL accessed and verified the data. ZF and LS were responsible for data visualisation. JCS, LS, and ZF wrote the original draft manuscript. All authors reviewed and edited the manuscript. All authors had full access to all the For the GitHub repository see

https://github.com/Ziaf021/

Time2Event

data in the study and had final responsibility for the decision to submit for publication.

Declaration of interests

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Data sharing

The data in this study are available on GitHub.

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