Transmission of autochthonous Aedes-borne arboviruses and related public health challenges in Europe 2007–2023: a systematic review and secondary analysis

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Summary

Background Local transmission of dengue, chikungunya, and Zika infection is an emerging public health threat in Europe. Monitoring the epidemiological trends can help define the intervention strategy. The aim of this work was to analyse epidemiological characteristics of autochthonous transmission of *Aedes*-borne arboviruses in Europe.

Methods A systematic review of the literature published from January 1, 2007, to January 31, 2024, reporting autochthonous cases of dengue, chikungunya, and Zika detected in Europe was performed. We searched MEDLINE, EMBASE, and the ECDC reports. Descriptive statistics and a secondary analysis were used to summarize the epidemiological characteristics of local transmission events (LTEs), explore potential temporal trends and identify relevant associations between epidemiological variables. Time intervals between key events were analysed to identify potential delays in LTE identification and intervention.

Findings A total of 59 studies were included, describing 56 LTEs. The frequency of LTEs increased over time, with an average of 1.25 (95% CI: 1.17–1.35) times increment every year. While the highest number of dengue LTEs was reported in France (N = 37), Italy faced the largest number of cases detected in an LTE (N = 41). Considering all the arboviral LTEs, the median time between the symptom onset of the primary case and the diagnosis of the index case ("outbreak detection") was 35.5 days (range 23.0–76.0). Only for chikungunya, higher delays correlated with higher cumulative number of cases detected per LTE, though this may be biased due to the low sample size.

Interpretation We have observed a gradual increase of *Aedes*-borne arboviral LTEs in Europe over time, and a considerable delay in outbreak detection. Improving the timeliness of LTE identification is essential.

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Keywords: Arbovirus; Dengue; Chikungunya; Zika; Local transmission event; Europe

Introduction

Arboviral infections are caused by viruses transmitted by arthropod vectors such as mosquitoes, ticks, sand flies, and *culicoides* biting midges. Travel, trade, and ecosystem changes influencing the environment (such as urbanization and agriculture practices favouring the

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Research in context

Evidence before this study

Outbreaks of dengue and chikungunya fever in Europe have been documented by public health authorities and in peer reviewed literature at increasing frequencies. During the past 25 years, autochthonous transmission of *Aedes*-borne infections was reported in Italy, France, Croatia, Spain, and Portugal (Madeira). From the literature search carried out for this work, we found three narrative and one systematic review that investigated autochthonous arboviruses in Europe. The first study reviewed arboviral outbreaks in Europe between 2007 and 2012, focusing on autochthonous cases of dengue and chikungunya fever reported in Italy, France, Croatia, and Madeira. The second study examined nine episodes of autochthonous dengue fever transmission and three of chikungunya reported in mainland France between 2010 and 2018. The third study reviewed autochthonous and imported arboviral infections in Italy over the past decade, highlighting chikungunya outbreaks in 2007 and 2017, and local dengue transmission in 2020. The systematic review was recently published as pre-print; it examined both imported and autochthonous cases of *Aedes*-borne infections in Europe from 2000 to 2023. In addition to the reviews, it is worth to mention that autochthonous transmission events for dengue and chikungunya are provided by the European Centre for Disease Control, though they recollect only the number of cases detected and the probable period of virus circulation. A comprehensive, integrated year-by-year analysis of the epidemiological characteristics of autochthonous dengue, chikungunya, and Zika virus transmission in continental Europe and Madeira has not been conducted.

Added value of this study

We systematically reviewed all cases of dengue, chikungunya, and Zika viruses acquired in continental Europe and Madeira reported in peer-reviewed literature and ECDC reports, covering studies published from January 1, 2007, to January 31, 2024. We identified a trend that shows steadily increasing frequencies of locally acquired *Aedes*-borne arbovirus infections. Though most dengue local transmission events (LTEs) occurred in France, the largest numbers of cases per LTE occurred in Italy, both for dengue (average number of cases detected 3.9 times higher than in any other country) and chikungunya. We observed that it is difficult to identify the primary case, that is the person coming back to Europe with the infection, thus starting the infection chain. We report the timeframes needed for outbreak detection and for the set-up of active public health intervention, focusing on possible delays that might favour disease spread.

Implications of all the available evidence

The increasing trend of autochthonous cases underscore the need for enhancing surveillance of human *Aedes*-borne arbovirus transmission in Europe. Following the identification of index cases, rapid public health action is required to avoid onward transmission of *Aedes*-borne arboviruses that, according to our analysis, may lead to a higher number of cases detected per LTE.

development of breeding sites) combined with favourable climatic conditions, have facilitated the dissemination of vectors, in particular mosquitoes, and have resulted in increased exposure of vertebrate hosts to arboviruses.[1] Moreover, climate change and globalization may facilitate further vector spread and higher mosquito density in Europe. Therefore, public health interest in quantifying the risk of arbovirus transmission has gradually increased in Europe after years when such risk was considered negligible. West Nile virus (WNV) is already considered endemic in several European countries.[2] Viruses like Sindbis[3] and Usutu[4] have emerged, and others, like Rift Valley fever virus,[5] are expanding their range near Europe's borders, with several potential vectors being present on the continent.[6] Although the transmission of these viruses mostly involves wild or domestic animal species, some viruses, such as the *Aedes*-borne dengue (DENV), chikungunya (CHIKV), and Zika (ZIKV) amplify in human hosts, creating potential for urban transmission cycles.

In Europe, sporadic local transmission events of DENV, CHIKV, and ZIKV have been identified since 2007.[7–9] This change in epidemiology is driven by the progressive colonization of the continent by the invasive mosquito vector species *Aedes albopictus* and by the increasing numbers of imported cases from endemic countries in the context of permissive climatic conditions for transmission.[10] One main issue characterizing arboviral infections is that symptoms are non-specific, so a high index of suspicion is needed for a rapid diagnosis and subsequent outbreak detection.

The increased risk of DENV and CHIKV autochthonous transmission prompted the development of guidelines at European and national levels to address the epidemiological risk and develop an adequate response strategy. It is however important to monitor the epidemiological trends, to evaluate the possible need for changing/enhancing the management of *Aedes*-transmitted arboviral infections in order to limit the local spread.

The aim of this work was to describe the epidemiological characteristics (i.e., location and year) of autochthonous DENV, CHIKV, and ZIKV outbreaks reported in Europe from January 1, 2007, to January 31, 2024. Specific aims were to estimate: 1) the average number of cases detected per outbreak; 2) average outbreak duration; 3) the time elapsed from symptom onset in the primary case to the diagnosis in the index

case ("time for outbreak detection"); 4) the conditions that elicited testing; 5) the average time needed to set up proper interventions from diagnosis/outbreak onset.

Methods

We conducted a systematic review of the literature and meta-analysis of arbovirus local transmission events of DENV, CHIKV, and ZIKV that occurred in Europe from January 1, 2007 to January 31, 2024. The protocol was registered with PROSPERO (registration ID: CRD42024562956). This manuscript adheres to the PRISMA 2020 reporting guidelines, with the PRISMA checklist available in Supplementary File 1.

Search strategy and selection criteria

We included studies published from January 1, 2007, to January 31, 2024, that reported epidemiological information (i.e., variables reported in the "Data items" paragraph) on autochthonous vector-borne transmission of DENV, CHIKV, or ZIKV in Europe. Autochthonous events were defined when DENV, CHIKV, ZIKV infections were reported in individuals with neither history of travel to endemic areas, nor history of sexual contact or blood exchange with infected individuals in the two weeks preceding symptom onset. Cases occurring in different locations within a country were considered as a single event only if an epidemiological or molecular link was confirmed. An epidemiological link between autochthonous cases was defined in case of occurrence of cases in the same Nomenclature of territorial units for statistics (NUTS-3) region in the same year, or in case of a direct contact between two or more cases.

We included all study designs, except systematic reviews and meta-analyses. There was no language restriction.

We excluded: systematic reviews; studies reporting molecular or phylogenetic data without epidemiological information; studies reporting autochthonous arboviral cases occurred before the year 2007; studies reporting cases retrospectively identified only through serological analysis (which could not permit to assess autochthonous transmission).

We searched MEDLINE and EMBASE for all publications indexed from January 1, 2007 to January 31, 2024. We also reviewed the reference lists of all included papers for additional studies meeting our inclusion criteria. The European Centre for Disease Prevention and Control (ECDC) reports were also screened for inclusion.[8,9] The complete search strategy is detailed in Supplementary File 2.

Two authors (P. Cattaneo and E. Salvador) independently reviewed all records by title and abstract for eligibility. Disagreements were resolved by a third reviewer/author intervention (D. Buonfrate). Relevant records were then screened by full text using the same process. The reviewers were blinded to each other's decisions throughout the process. Rayyan Systems Inc. software was used to organize search results, record screening decisions, and perform automatic deduplication, with further manual deduplication conducted by comparing similar citations.

The same two reviewers independently extracted the required data from all included papers. Discrepancies were solved by the involvement of the third reviewer. Data were recorded in a pre-defined Excel spreadsheet.

A local transmission event (LTE) was defined as all epidemiologically-linked autochthonous cases of vector-borne transmission. LTEs were analysed also separately for each pathogen (DENV, CHIKV, ZIKV).

We defined "primary case" the individual who imported the infection to Europe from an endemic area, while the "index case" was the first autochthonous case diagnosed in an LTE. The "first case" with symptoms within an LTE was defined as the first symptomatic case, which may or may not coincide with the index case.

The following data were extracted: DENV, CHIKV, ZIKV infection; viral serotype (if applicable); country and specific location where the LTE occurred; month and year of occurrence; type of setting[11]: urban (including urban centres, dense urban clusters, and semi-dense urban clusters), suburban (suburban grid cell), or rural (rural cluster, low-density rural grid cell, and very low-density grid cell); extension of the focus, expressed into the following categories[12]: focal (all events identified within an area of less than 1.5 km), local (confined to one village or neighbouring villages within an area less than 13 km), exported (remaining cases); total number of confirmed autochthonous cases identified; symptoms observed in the index case; conditions prompting arboviral testing; country where the primary case (when identified) acquired the infection; date of symptom onset and date of diagnosis of the primary case; date of symptom onset, of sample collection for arboviral testing, and of confirmed diagnosis of the index case; date of symptom onset of the first symptomatic case; date of symptom onset and of diagnosis of the last identified case; date of set up of public health interventions.

Cases that were reported as "possible" or "suspected" were excluded from the analyses, unless subsequently confirmed.

After extracting data from all included papers, data from different studies reporting about the same LTE were merged in a second Excel spreadsheet, in order to have a comprehensive description of each LTE. In case of inconsistencies between studies reporting data about the same LTE, but with different follow-up periods, the data from the most recent publication was considered valid. Persistent inconsistencies were resolved by contacting the study authors.

The primary aim was to perform a systematic review of the epidemiological characteristics of autochthonous

DENV, CHIKV, and ZIKV transmission events in Europe from 2007 to 2023.

Specific outcomes included: the number and frequency of LTEs in continental Europe over the study period and across regions; number of detected cases per LTE; number of days elapsed from the symptom onset of the index case or the first autochthonous case to the diagnosis of the last case associated with each LTE; number of days elapsed from symptom onset in the primary case to diagnosis in the index case; number of days elapsed between symptom onset in the index case and the implementation of active response protocols.

Risk of bias was assessed using the Joanna Briggs Institute (JBI) critical appraisal tool for case series studies.[13] The assessment was performed at the study level. Question 8 and Question 10 were deemed "not applicable" to the purpose of our review. Possible answers to the remaining questions were "yes," "no," or "unclear," as recommended by the tool creators. We assigned 1 point to "yes", 0.5 points to "unclear", and 0 points to "no". Each included study had a final score calculated by summing the scores of each response. Studies were then categorized based on their scores as high (scores of 6.5 or more), moderate (scores of 5–6) and low quality (scores of 4.5 or less).

The quality assessment was performed independently by two authors (P. Cattaneo and E. Salvador). In cases of discrepancy between reviewers' scores, disagreements were resolved through discussion. If no agreement could be reached, a third reviewer (D. Buonfrate) was involved to make the final decision.

Data analysis

Descriptive statistics, including measures of central tendency (mean, median) and dispersion (standard deviation, range), were employed to summarize the specific outcomes of the systematic review where appropriate. Information gathered from studies documenting individual LTEs was used to identify potential gaps in LTE identification and quantified the time required for initiating response interventions. To do this, we provided descriptive statistics on delays between the symptom onset in the primary case and diagnosis in the index case, as well as between the symptom onset of the index case and the initiation of active response protocols. In cases of incongruent dates (e.g., primary case symptom onset) between studies/reports the earliest one was chosen. We analysed the number of LTEs over the years by applying a generalized linear regression model (GLM) assuming a Negative Binomial distribution (NB). Moreover, we analysed by means of NB GLM the different number of confirmed cases across countries. NB GLM was also used to assess the relationship between the number of confirmed DENV cases and the DENV serotype. Finally, we applied NB GLMs to analyse the relationships between: *i)* the number of cases detected and the time interval between the symptom onset of the primary case and the diagnosis of the index case, *ii)* the number of cases detected and the time interval between the date of the first symptom onset and the start of interventions, and *iii)* the LTE duration, defined as the number of days between the earliest reported date of symptom onset and either the latest date of symptom onset (or latest date of diagnosis when the former was not reported) across identified autochthonous cases, and the time interval between the date of the first symptom onset and the start of interventions. The geographical extent, type of setting, and population density characteristics of the areas affected by LTEs were summarized using descriptive statistics. The statistical analysis was performed using R statistical software version 4.2.2 2022 (R Project for Statistical Computing).

Role of the funding source

The funding sources had no role in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the paper for publication.

Results

Study selection and characteristics

The search strategy identified 4130 records; 889 documents were retrieved through additional sources (review of references of included papers, ECDC reports, and national reports).[8,9] The study flow is described in Fig. 1.

Eventually, 59 studies/reports (listed in Supplementary File 3) were included in this study, describing 56 LTEs occurred in the last 17 years (from 2007 to 2023) in five European countries: Croatia (n = 1 LTE), France (n = 41), Italy (n = 8), Spain (n = 5), and one outermost region (Madeira, Portugal, n = 1). DENV caused the largest proportion of LTEs, as shown in Table 1, followed by CHIKV. ZIKV caused a single LTE in France.

Twelve studies[14–25] were published while the described LTE was still ongoing, therefore presenting preliminary data. Quality was deemed low for 17 studies, moderate for 19, and high for 23 (Supplementary File 4). For the quantitative analysis we considered only continental Europe for homogeneity reason (i.e., LTEs in Madeira were excluded).

Spatiotemporal distribution of LTEs

Fig. 2 shows the geographical distribution of the LTEs. Most LTEs occurred in France and Italy: 74.5% (41/55) and 14.5% (8/55) of all LTEs reported in continental Europe, respectively. Transmission occurred predominantly in urban and/or suburban (67.3%, 37/55) areas. The extent of the area involved was reported or could be inferred in about 82% of studies (45/55). However, there was very limited information on accurate location (i.e., geocoordinates) and population density.

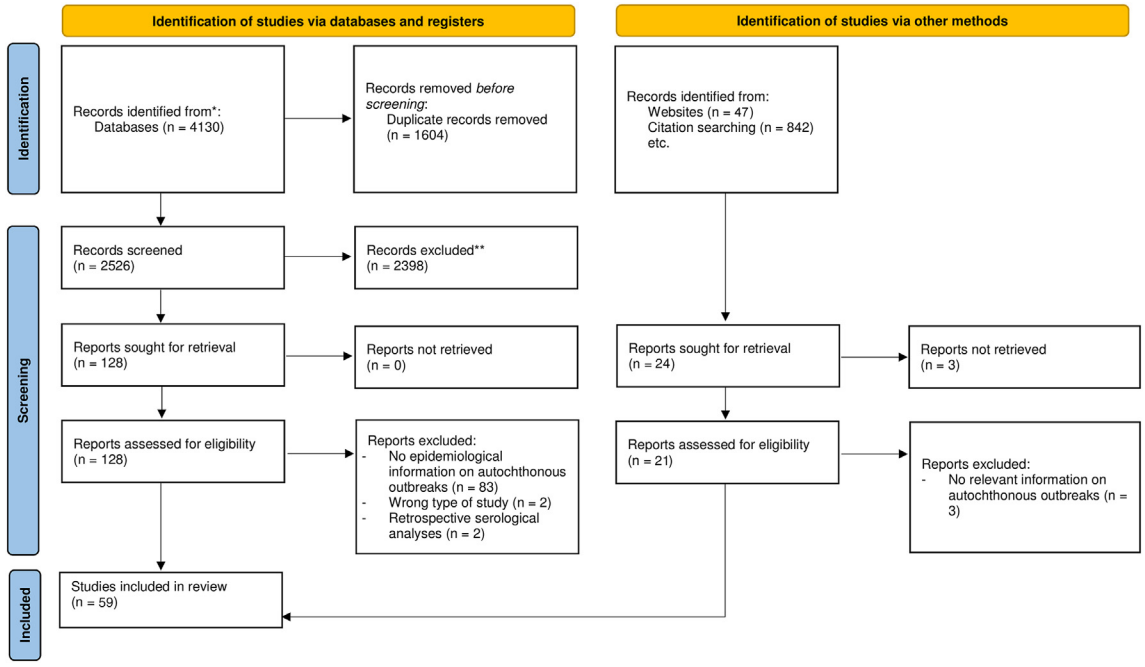

Fig. 1: PRISMA flow diagram.

The frequency of LTEs reported increased over time, with an average of 1.24 (95%CI: 1.15–1.35) times increment every year, resulting in 43 LTEs in the last six years *vs* 13 LTEs from 2007 to 2017 (Fig. 3).

LTE size and duration

The distribution of the overall number of confirmed cases in each LTE was highly skewed.

The median number of DENV cases per LTE was two (range 1–41); in 86% (42/49) of DENV LTEs less than ten cases were confirmed. The largest number of DENV cases was observed in Lodi province, Italy, in 2023. The average number of DENV cases per LTE was 3.9 times higher (95%CI 1.8–9.3) in Italy than in any other country, despite France having an overall higher number of cases detected (153 *vs* 93). Interestingly, according to the reported LTEs, the transmission of the DENV-1 serotype was associated with a significantly higher number of cases (mean: 8.9, 95% CI: 5.9–13.7) compared to DENV-2 (mean: 3.3, 95% CI: 1.7–6.5), but not when compared to DENV-3 (mean: 6.7, 95% CI: 3.3–13.4).

The median number of CHIKV cases per LTE was 15 (range 2–270). The largest numbers of CHIKV cases were observed again in Italy: 270 and 217 cases in 2017 and 2007, respectively.

For 28 LTEs, we were able to retrieve the LTE duration, defined as the number of days between the earliest

	Number of reports	Total cases	Number of LTEs	Number of LTEs by country	Years of occurrence of LTEs
DENV	39[a]	1346[b]	50	Croatia 1	2010
				France 37	2010, 2013, 2014, 2015, 2018, 2019, 2020, 2021, 2022, 2023
				Italy 6	2020, 2023
				Portugal (Madeira) 1	2012
				Spain 5	2018, 2019, 2022, 2023
CHKV	21[a]	515	5	France 3	2010, 2014, 2017
				Italy 2	2007, 2017
ZIKV	1	3	1	France 1	2019
Total	59[a]	1864	56		

[a]A total of 59 reports are included in the meta-analysis; 2 reports deal with both DENV and CHIKV autochthonous outbreaks. [b]266 cases from outbreaks in continental Europe; 1080 cases from the DENV outbreak in Madeira.

Table 1: **Number of reports and related cases/LTEs (local transmission events) per viral infection.**

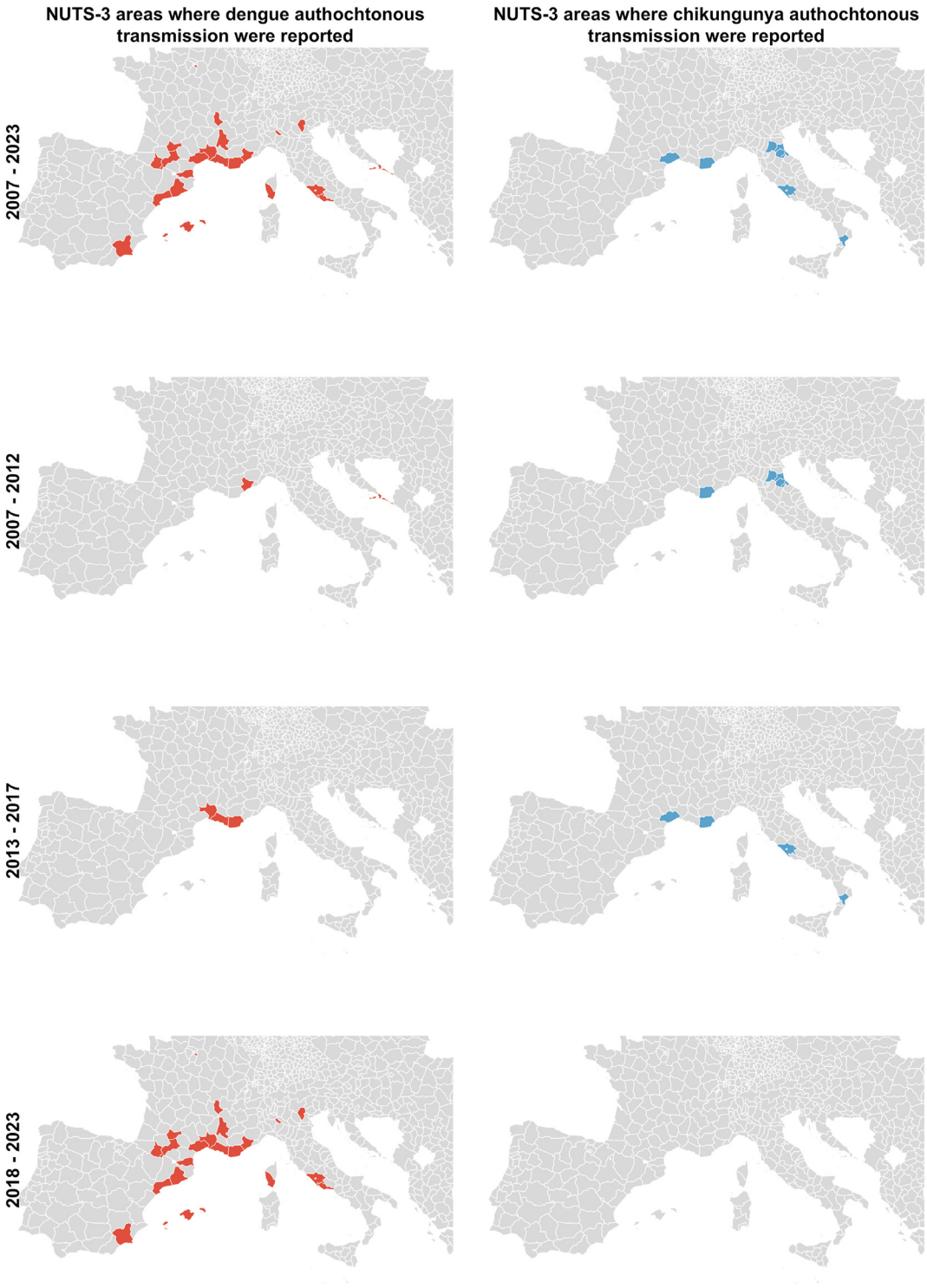

Fig. 2: NUTS-3 areas in mainland Europe where local autochthonous transmission events occurred between January 1, 2007 and January 31, 2024. Left panel: dengue virus. Right panel: chikungunya virus.

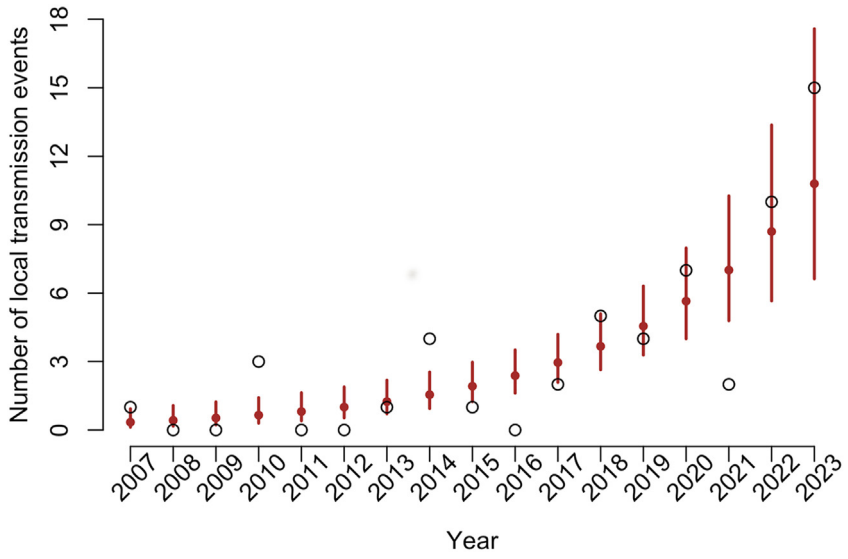

Fig. 3: Number of local transmission events in Europe over time. Circles represent the number of transmission events (LTEs) over the years identified in the literature. Points represent the mean estimate of the generalized linear model; the vertical lines represent the corresponding 95% confidence interval.

reported date of symptom onset and either the latest date of symptom onset (or latest date of diagnosis when the former was not reported) across identified autochthonous cases. The median duration of LTE was 32 days (range: 0–132) overall, 31 days (range: 0–69, 22 LTEs) for DENV, 44 days (range: 0–132, 5 LTEs) for CHIKV. The single ZIKV LTE lasted eight days. For DENV, the autochthonous transmission started as early as the second week of June, and ended at the end of October, whereas for CHIKV, it was documented from the end of June to the first week of November (Fig. 4). Seventy percent of LTE started before mid-August (9/13); 94% (52/55) of LTE were over by the end of October.

Primary and index cases

Information about the country where primary cases got infected, the date of symptom onset, and the date of diagnosis was available for a few LTEs. No information on the primary case was reported for ZIKV. The importation routes of DENV and CHIKV were identified for 35% (17/49) and 80% (4/5) of LTEs, respectively. Among the 21 LTEs where the primary case was identified, 8 involved travellers from French overseas territories. During the study period, triggers for local DENV transmission included travel from Eastern (1 case) and Central Africa (2 cases), Africa (1 case), the Caribbean (6 cases), the Pacific Ocean (2 cases), Central America (1 case), and Southeast Asia (4 cases). Local CHIKV transmission was associated with travel from Central Africa (2 cases) and Southeast Asia (2 cases) (Supplementary File 4).

The dates of symptom onset for the primary case were mostly in July (6 cases) and August (4 cases), followed by June (2 cases) and September (1 case). The date of diagnosis for the primary case was reported only for five cases, ranging from September to November, with a median delay from symptom onset of 21 days (range: 6–56 days).

With respect to the index cases, date of symptom onset was reported for 33 LTEs, and date of diagnosis was reported for 26 LTEs. Both dates were reported for 23 LTEs. Diagnosis of the index case occurred mainly in August (ten LTEs), followed by September and October (seven LTEs each); two LTEs were reported in November.

The median delay between the symptom onset of the primary case and the diagnosis of the index case (i.e., outbreak detection) was 35.5 days (range 23.0–76.0, data reported for ten LTEs). There was no statistical evidence suggesting that longer delays were associated with a specific disease. While for DENV, higher delays did not correlate with higher cumulative number of cases detected per LTE, a positive correlation was found for CHIKV, although this is confounded by the collinearity between outbreak size, delays, and date of primary case importation.

The date of symptom onset in the index cases and the date of symptom onset of the first symptomatic case were both reported in 16 LTEs. In seven of these LTEs, the date of symptom onset of the index case and of the first symptomatic case coincided (6/11 for DENV, 1/4 for CHIKV and 0/1 for ZIKV). In the remaining LTEs, the date of symptom onset of the first symptomatic case preceded the date of symptom onset of the index case by approximately 14 days on average (range: 2–40). The

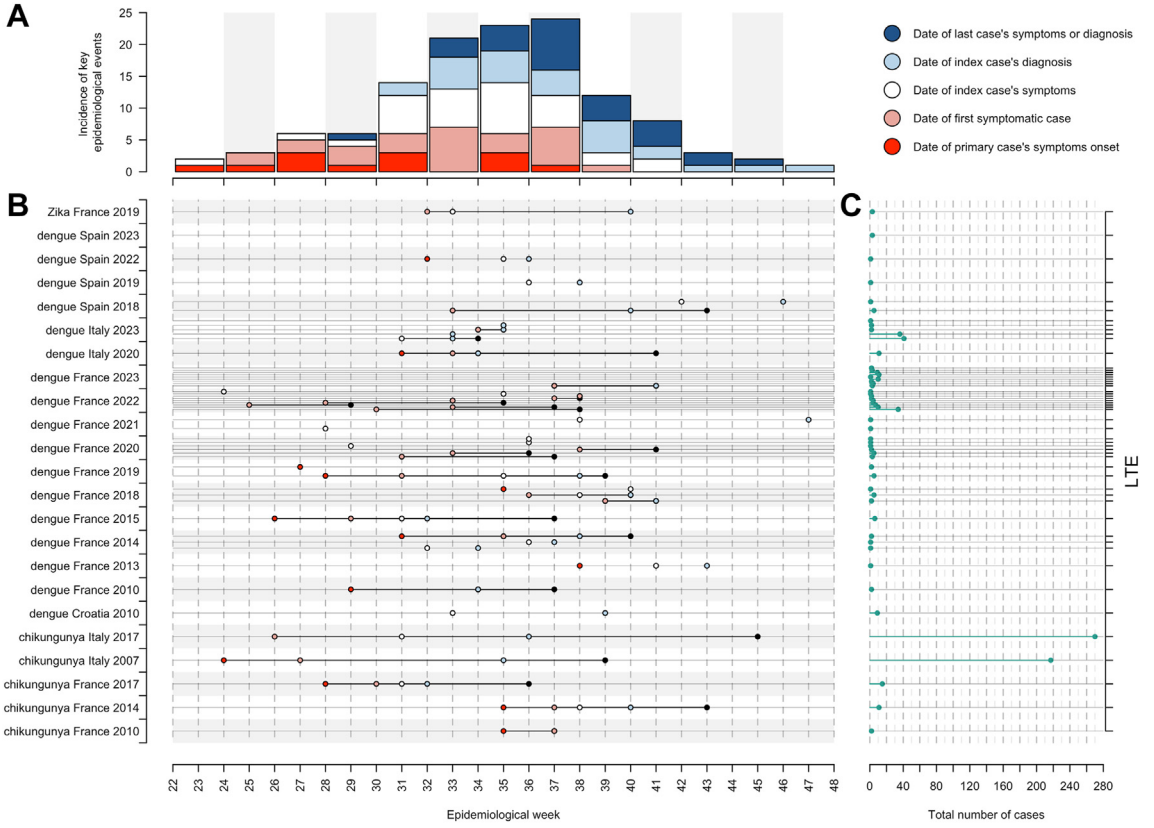

Fig. 4: Panel A) shows the incidence and timing of key epidemiological events (date of symptom onset of the primary case, of the first symptomatic case, the date of diagnosis of the index case and the date of diagnosis or symptoms onset of the last case) aggregated over two epidemiological weeks period. Panel B) shows the dates associated to key epidemiological events within different LTEs (date of symptom onset of the primary case, of the first symptomatic case, of diagnosis of the index case and the date of diagnosis or symptoms onset of the last case. Panel C) shows the total number of cases associated with each LTE.

median delay from the date of symptom onset and the diagnosis of the index case was 13 days (range: 4–64, data reported for 23 LTEs). The median delay from the date of symptoms onset in the first symptomatic case and the date of diagnosis of the index case was 24 days (range: 0–72, data reported for 16 LTEs).

Triggers leading to outbreak identification

For DENV, the reasons that prompted arboviral testing were: suspected arboviral cases identified by general practitioners (Croatia 2010, Spain 2018) or by the surveillance system (France 2010); reports of a relative with similar symptoms and a recent travel history to endemic regions (Italy 2020); suspected cases identified after following pan-flavivirus PCR testing for WNV suspicion (Italy 2023); awareness of an ongoing DENV outbreak in the country (Italy 2023). For CHIKV, the reasons that prompted arboviral testing were explicitly reported only for the first two outbreaks, highlighting two different surveillance scenarios: a high number of cases of fever of unknown origin but suspected to be viral (Italy 2007), and the known presence of a travel-related case residing in the neighbourhood (France 2010).

Public health intervention

Information on public health active response enacted during different outbreaks is limited, with the start date for implementing these interventions available for less than 30% of LTEs (16/55). The timeframe elapsed for the implementation of interventions following LTE detection was highly heterogeneous. During the Italian 2007 CHIKV outbreak, interventions were already in place due to the suspected role of biting vectors in transmitting the still unrecognized disease. In France, in three out of 37 DENV LTEs, interventions began the day before the official diagnosis of the index case. In five LTEs, interventions were implemented either on the same day or the day after the index case diagnosis. In the remaining six LTEs with data on the date of reactive interventions and index case diagnoses, interventions were delayed for more than four and up to 18 days after the index case diagnosis. The median delay between the

date of the first symptom onset and the start of interventions was 29.5 days (range: 15.0–51.0, 6 LTEs) for DENV, 43 days (range: 13–73, data reported for four LTEs) for CHIKV, and 63 days for ZIKV (one LTE). These delays did not correlate with the overall number of cases detected, nor the duration of the LTE.

Discussion

We provide a comprehensive overview of the epidemiological characteristics of autochthonous outbreaks of *Aedes*-transmitted arboviruses that occurred in Europe between 2007 and 2023. This review shows that the number of detected local outbreaks has been progressively increasing in the recent years.

On one hand, the rising number of local outbreaks detected in continental Europe may stem from several factors, including: the expanding geographical distribution of *Aedes albopictus,* higher mosquito densities during breeding seasons, an increased number of international travels, a larger inflow of viraemic travellers from endemic regions, especially when outbreaks occur in travel destinations and when climatic conditions are suitable for transmission in Europe, and the increased number of areas with climatic conditions favourable for viral transmission over consecutive weeks. In consideration of the observed trend, outbreaks of *Aedes*-transmitted arboviruses might occur in the future as well. This risk could markedly increase if the efforts to eradicate *Aedes aegypti* from Cyprus and Madeira fail[26] and/or if *Ae. aegypti* mosquitoes are introduced and the species established in continental Europe,[27] being *Aedes aegypti* the species most suitable for the transmission of DENV, CHIKV and ZIKV.

On the other hand, the increased number of LTEs could also result from improved detection capabilities of the public health systems, which have made over the years significant efforts to raise awareness about arboviral infections. In a couple of countries, France[28] and Spain,[29] a national surveillance plan was in place before detecting the first local LTE, while specific guidelines were lacking in the others.[30–33] However, over the years, national plans and international guidelines have been set up and constantly updated across Europe,[34] shifting their focus from single vector control interventions to an integrated vector management approach. This broader strategy emphasizes implementing a broader spectrum of actions encompassing both preventive or reactive measures to reduce vector densities, improve detection capabilities in terms of notification of human cases and ensuring the safety of blood, cells, tissues, and organ donations. Nonetheless, timely detection of arboviral LTEs remains a key challenge to address in order to limit onward transmission.

We found that the identification of the primary case remains highly challenging. If primary cases develop an asymptomatic infection or very mild disease, they might not refer to a clinician, and would remain unaware of their infection. Moreover, even when seeking medical care, cases often have a non-specific clinical presentation, which might not lead to the clinical suspicion needed to lead to specific laboratory testing for arbovirus infections. At least when these individuals present themselves to health care, it is important not to miss the diagnosis. However, from the economic point of view, recommending to test all individuals presenting a single symptom possibly caused by a vector-borne disease might not be possible, due to the wide range of symptoms that might be considered. In this view, some authors tried to elaborate a score with specific clinical and laboratory parameters which might help guide the screening of suspected autochthonous cases in a cost-effective way.[35] Of note, a different approach to screening is probably the reason leading to the different size of the DENV LTEs observed in France (highest number of LTEs, but limited number of cases detected per LTE) compared to Italy (less LTEs but with average number of cases detected around four times that observed in other countries).

For DENV, a larger LTE size was associated with neither the time needed to detect an LTE, nor with the time needed to set up active intervention. This was quite unexpected, as in principle longer time to set up control activities from the importation of the virus might leave more time for infection spread. Some heterogeneity in reporting, missing data and the definition of outbreak detection used for study purpose might explain these findings.

For CHIKV, the LTE size was instead associated with longer timeframe for outbreak detection, though this result should be interpreted with caution due to the limited sample size.

The time required for a full human-vector-human transmission cycle is known as generation time, and comprises incubation periods in humans (intrinsic incubation) and in the mosquito vector (extrinsic incubation). Previous estimate of the DENV and CHIKV generation time in Europe are 18 and 12 days, respectively.[12] Therefore, the estimated median delay (35.5 days) from symptom onset of the primary case to the diagnosis of the index case (i.e., detection of local outbreaks) found in this study, could be sufficient to allow, in case of onward transmission, more than one generation of secondary cases, leading to a potential expansion of local transmission. However, we did not find a direct relation between these delays and the overall number of cases identified during the outbreaks. Possible reasons may include the variability of the temperature-dependent extrinsic incubation period, among others, and its relationship with the mosquito lifespan, the relatively low vector competence of *Ae. albopictus* for the transmission of DENV in Europe, as well as the potential underreporting of cases during the period of undetected transmission.

Certainly, in any case it is worth to straighten the surveillance system in order to reduce the time to detection and the set-up of the response measures. In this view, national protocols should include the recommendation to provide at least rapid tests to as many peripheral health care centres as possible, while leaving the molecular confirmation to the referral laboratories. This might permit to speed up the alert to public health, while waiting for the second step of diagnosis. Currently, rapid tests are available for DENV only, so the development of rapid tests for CHIKV and ZIKV is badly needed. At the referral laboratory, multiplex molecular tests would be preferred, ideally with the inclusion of other viruses of local relevance (e.g., West Nile, Toscana, etc). Also, the integration of genomic epidemiology might be useful to explore the possibility of having multiple independent (and unidentified) primary cases at the origin of a large LTE, and to define connections between apparently distinct LTEs. Finally, cross-border collaboration, at least within Europe, should be enhanced for an intensified surveillance.

Our study contains some limitations. First, some studies provided limited details; hence, sample size was quite small for some sub-analyses. Furthermore, it is possible that smaller outbreaks went undetected or were not published in the scientific literature. Some studies were published while the outbreak was still ongoing, thus they included only partial and outdated information. For these reasons, we merged additional information obtained in all publications referring to a same LTE. Unfortunately, detailed epidemiological information was often lacking, thus limiting deeper investigation on local conditions that may have been key drivers for the observed transmission pattern. For instance, due to the limited information on meteorological conditions, the impact on the occurrence of autochthonous cases could not be fully analysed. In addition, we could not explore the impact of vector density on viral transmission, but this was out of the scope of this work. However, as shown in Fig. 4, 80% (32/40) of primary and first autochthonous symptomatic case occurred between early July and mid-September, which is in line with previous estimates on peaking time of both vector abundance and transmission risks.[10] Although most studies/reports provided an accurate description of the clinical history of the first cases, qualitative information about the extent or the location of an outbreak were too vague to be included in complex risk-modelling analyses (i.e., "All events occurred in suburban residential areas",[36] "among people living in a residential area, made of single-family detached houses"[37]). This may be due to privacy and ethics issues, as well as a specific focus of the included paper. Finally, reactive measures might include diverse strategies, such as epidemiological investigation, testing of exposed individuals, vector control measures, etc, but these were not extensively described in all the considered literature, so comparison of effective strategies is lacking; for the same reason, caution should be paid in comparing LTE characteristics over time and between different countries, as a diverse set of reactive measures might entail a different capacity of detecting cases. Hence, a larger LTE size might be due either to a truly large number of cases or to a greater capacity of case detection.

In conclusion, there is evidence that the number of detected *Aedes*-borne viral infection LTEs in continental Europe is increasing. Most events were reported in France and Italy; in the latter, LTEs had larger size in terms of number of cases detected compared to other countries. Proper screening protocols are of paramount importance to increment and fasten case detection, considering that larger areas of Europe, where *Ae. albopictus* is now established, are at risk.[10] Continuous and active monitoring of viral circulation in both humans and vectors is needed, through a prevention and response plan which would ideally include integrated surveillance and cross-border collaboration within European countries.

Contributors

PC and ES contributed to data collection, and to the first draft of the manuscript. MM accessed and verified the data, contributed to data analysis, methodology, first draft of the manuscript. LB, CC, FDG, RH, SM, PP, FR, AS, FS, LZ contributed to manuscript review and editing. DB accessed and verified the data, contributed to methodology, data curation, supervision, manuscript review and editing. FG conceived the work, accessed and verified the data, contributed to supervision, data validation, manuscript review and editing; he was responsible for the decision to submit the manuscript.

Data sharing statement

The raw data are available in the Supplementary File 4.

Editor note

The Lancet Group takes a neutral position with respect to territorial claims in published maps and institutional affiliations.

Declaration of interests

None.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.lanepe.2025.101231.

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