RAPID RISK ASSESSMENT

Chikungunya outbreak in Caribbean region

25 June 2014

Main conclusions and options for action

- This is the first documented autochthonous transmission of chikungunya virus in the Americas. The outbreak started on the Caribbean island of Saint Martin in early December 2013 and expanded through the Caribbean during the first half of 2014. Recently, suspected autochthonous cases have been reported from Central America (Costa Rica and El Salvador), raising concern about virus spread in continental America where *Aedes aegypti* is endemic.
- Exposure to infected mosquitoes is the principal risk for infection in currently affected areas. Prevention of chikungunya among travellers and local residents is essentially based on personal protection against mosquito bites and vector control; these are the same as the preventive measures to be taken against dengue.
- With the present holiday season in Europe, high vigilance must be maintained regarding imported cases of chikungunya and dengue in the EU, including awareness among clinicians and travel clinics, notably in those EU areas where competent vectors are present.
- The risk for onward transmission in Europe is linked to importation of virus by viraemic patients in areas with competent vectors (*Aedes albopictus* on mainland Europe and *Aedes aegypti* in Madeira). Autochthonous transmission from an imported viraemic chikungunya case during the summer season in the EU is possible. Madeira is particularly vulnerable due to the presence of *Aedes aegypti* and favourable climatic conditions.
- Travellers returning from outbreak areas should seek medical care if presenting with chikungunya compatible symptoms and apply personal protection measures to avoid mosquito bites. Such measures will reduce the risk of viral introduction in the European mosquito population and furthermore limit the establishment of a local cycle of transmission during the summer season.
- Preparedness regarding chikungunya in the EU includes strengthened surveillance systems and rapid notification of cases; review of contingency plans for mosquito-borne outbreaks; education and collaboration of the general public in the control of mosquito breeding sites; strengthened vector surveillance systems and rapid implementation of vector control measures around each case.
- EU blood safety authorities need to be vigilant regarding the epidemiological situation in the Americas in line with measures taken for West Nile virus infection.

Source and date of request

ECDC Internal Decision, 16 June 2014.

Public health issue

Autochthonous transmission of chikungunya in Caribbean islands and its extension to America: what is the risk for the EU?

Consulted experts

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Disease background information

Chikungunya is a mosquito-borne viral disease caused by an alphavirus from the Togaviridae family. It is transmitted by the bite of *Aedes* mosquitoes, primarily *Aedes aegypti* and *Aedes albopictus*, which are active during the day [1]. The incubation period ranges from 2 to 10 days, with an average of 3 days [1]. The typical clinical signs of the disease are high fever, myalgia, skin rash and arthralgia, the latter may persist for weeks or months causing a significant disease burden in the community [2-5]. Non-steroidal anti-inflammatory drugs are only recommended for treating persistent arthralgia after proved chikungunya virus (CHIKV) infection [6]. General complications include myocarditis, hepatitis, ocular and neurological disorders [7]. Some infected individuals are asymptomatic or only mildly symptomatic, challenging the case detection. It is difficult to distinguish chikungunya and dengue based on clinical findings alone in tropical settings where dengue outbreaks may be occurring simultaneously. The majority of infection are symptomatic (>75%) [6]. In humans, the viral load in the blood can be very high at the beginning of the infection and lasts 5–6 days after onset of fever [8]. A person who has recovered from chikungunya infection is likely to be lifelong immune against repeated infections [9]. Mother-to-child transmission has also been reported in women who developed the disease within the week prior to delivery and children are also at risk for severe manifestations of the disease [10,11]. Neither specific treatment nor a licensed vaccine is currently available. The medical management and productivity costs for large CHIKV outbreaks are associated with a considerable economic burden [12].

Transmission of CHIKV infection through transfusion and transplantation has not been reported in humans although animal models showed the ability of such transmission using intravenous inoculation. It was found that about 25% of infected people remain asymptomatic and are potential disseminators of donor-derived chikungunya. The viraemic levels in asymptomatic CHIKV-infected individuals are in the range that is known to be capable of transmitting the disease as shown in experimental animal models [13]. Thus the possibility of donor-derived CHIKV transmission requires that preventive safety measures are applied to donors residing in or returning from an affected area. The appropriate deferral period for clinical chikungunya is unknown but would likely be in the order of several weeks after the resolution of symptoms.

Chikungunya is endemic in parts of Africa, South-east Asia and on the Indian subcontinent. No autochthonous transmission of the virus has been detected in the Americas before. Globally, the most recent large outbreaks were reported in 2005–2006 from Réunion Island, Mauritius, Mayotte and various Indian states. Autochthonous cases within continental Europe were reported from Emilia Romagna, Italy (217 cases in 2007) [14] and in Var, France (two cases in 2010) [15].

Every year, imported cases among tourists are identified in several European countries. During the period 2008–2012, 473 imported chikungunya cases were reported to ECDC by EU/EEA countries (41 cases in 2008, 149 cases in 2009, 177 cases in 2010, 55 cases in 2011 and 51 cases in 2012):

- Among 321 cases for which the probable country of infection was mentioned, 87% (280 cases) originated from Asia: India (117 cases), Maldives (34 cases), Thailand (30 cases), Sri Lanka (29 cases), Indonesia (26 cases), Malaysia (13 cases), Philippines (13 cases), and other Asian countries (18 cases). Forty-one cases originated from Africa including islands in the Indian Ocean.
- In 2012, 51 cases of chikungunya fever were reported by 22 reporting EU/EEA countries. The probable country of infection was reported for 43 cases, including 12 cases from India, eight cases from the Philippines and five cases from Indonesia.
- In 2013, chikungunya fever outbreaks have been occurring in a variety of geographic locations within the Philippines archipelago, including Manila city, as well as Singapore, India (Gujarat, Tamil Nadu, Kerala, Odisha states), Micronesia (Yap), Indonesia (East Java, East Jakarta) Papua New Guinea and New Caledonia (sporadic cases in late April 2013).

In comparison, during the outbreak in La Réunion with more than 250 000 suspected cases from April 2005 to June 2006, 766 cases were imported to France, pointing to the association between large chikungunya outbreaks in endemic regions and imported CHIKV cases in the EU [16].

Chikungunya virus is a single-strand, positive-sense RNA virus belonging to *Alphavirus* genus. The virus belongs to the Semliki forest complex, and is closely related to O'nyong'nyong virus found in Africa, to Ross-River virus in Australia, and to a lesser extent to Mayaro virus circulating in America. The latter is circulating in forests in the Caribbean (e.g. Trinidad) and South America in sylvatic mosquito vectors.

Three different genotypes of chikungunya virus, Asian, West African, and East/Central/South African (ECSA), have been identified. The acquisition of an A226V mutation in the envelope protein E1 of the ECSA genotype, as observed in La Réunion in 2005, has increased the transmissibility of the virus through the widely distributed *Aedes albopictus* mosquitoes [17]. This mutated virus spread from the Indian Ocean to East Africa and Asia (e.g. India, Sri Lanka, Singapore, Malaysia and China) and caused the chikungunya outbreak in Italy. In 2010, the chikungunya virus strain responsible for the two autochthonous cases in France belonged to the ECSA genotype but without the mutation at position 226 [15].

The virus involved in the chikungunya outbreak in the Caribbean belongs to the Asian genotype. It is related to strains recently identified in Indonesia, China and the Philippines [18]. According to current knowledge, *Aedes albopictus* has not been incriminated as a vector of large outbreaks of chikungunya caused by the Asian genotype. This seems to be linked to presence of an amino acid in the E1-98 region which blocks the ability of the Asian genotype virus to adapt to *Aedes albopictus* by means of the E1-A226V mutation [19-21]. Yet, laboratory studies showed that populations of *Aedes albopictus* from the Americas are able to transmit the strain from New Caledonia (NC/2011-568) belonging to the Asian genotype [20].

In the EU, *Aedes albopictus* is established primarily around the Mediterranean ([22] and in annex) and has been confirmed as a competent vector of strains belonging to the ECSA genotype [23]. *Aedes aegypti*, an efficient vector of strains belonging to the Asian genotype, is present around the Black Sea and in Madeira.

Aedes albopictus is an opportunistic feeder: blood hosts include humans, domestic and wild animals, reptiles, birds and amphibians. This mosquito species bites during the daytime as well as at dusk. It has the ability to breed in natural and artificial habitats, such as tyres, barrels, rainwater gulley, catch basins, and drinking troughs [24]. *Aedes aegypti* prefers mammalian hosts and will preferentially feed on humans, even in the presence of alternative hosts. Its activity is both diurnal and crepuscular. The species prefers human habitations which provide resting and host-seeking possibilities [25].

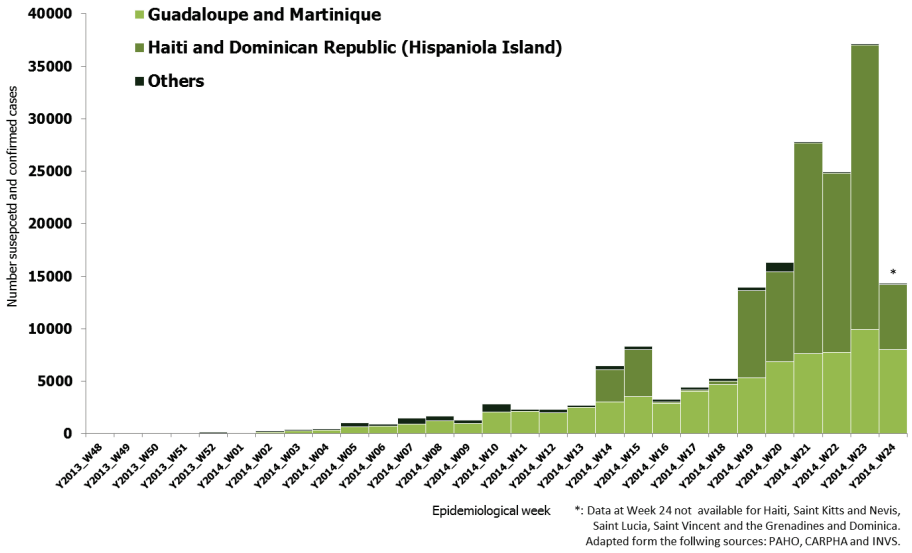
Chikungunya virus can be identified using RT-PCR or viral isolation during the first week of illness. Serological diagnosis can be performed by detection of specific IgM antibodies in serum specimens from day 4–5 after the onset of symptoms, or a four-fold rise of specific chikungunya IgG antibody titre in a paired serum sample (acute and convalescent specimens). Specific IgM can persist for many months, in particular in patients with long-lasting arthralgia [26]. Differential diagnosis with dengue should be considered as both viruses are circulating and co-infections are reported: e.g. in Saint Martin 2.8% of clinical suspected chikungunya cases were reported as dengue/chikungunya co-infections in December 2013–January 2014 [27].

Event background information

As of 20 June 2014, 5 294 confirmed cases and more than 180 000 suspected cases of chikungunya have been reported from the start of the outbreak in Saint Martin in December 2013 [28]. A phylogenetic study of the virus causing the outbreak on Saint Martin island demonstrated that the current strain belongs to the Asian genotype, and is closely linked to strains recently identified in Asia (Indonesia in 2007, China in 2012, and Philippines in 2013) [18].

During the 29 weeks that the outbreak has been ongoing in the Caribbean, 21 deaths were related directly or indirectly to CHIKV infection. The number of suspected and confirmed cases in the Caribbean showed a significant increase from week 21 onwards (Figure 1). This increase is mainly linked to a recent outbreak on the island of Hispaniola (Haiti and Dominican Republic) and the continuation in French overseas departments (Martinique and Guadeloupe). In continental America, several confirmed outbreaks are evolving: French Guiana reported an outbreak of chikungunya with a total of 390 suspected and confirmed cases since week 7/2014; Guyana reported 16 confirmed cases in the last three weeks; and El Salvador declared a National Emergency with 1 200 suspected cases (molecular confirmation pending), an outbreak likely evolving since late May 2014 [29,30]. In Guatemala, suspected cases are under investigation and one traveller returning from Costa Rica was diagnosed with chikungunya infection [31]. Overall, the viral circulation is now expanding to Central America where *Aedes aegypti* and *Aedes albopictus* are widely distributed (See: E3 Viewer - Habitat Suitability Model - Aedes aegypti) [32].

Figure 1: Number of reported cases of chikungunya by week in the Caribbean region (as of 20 June 2014)

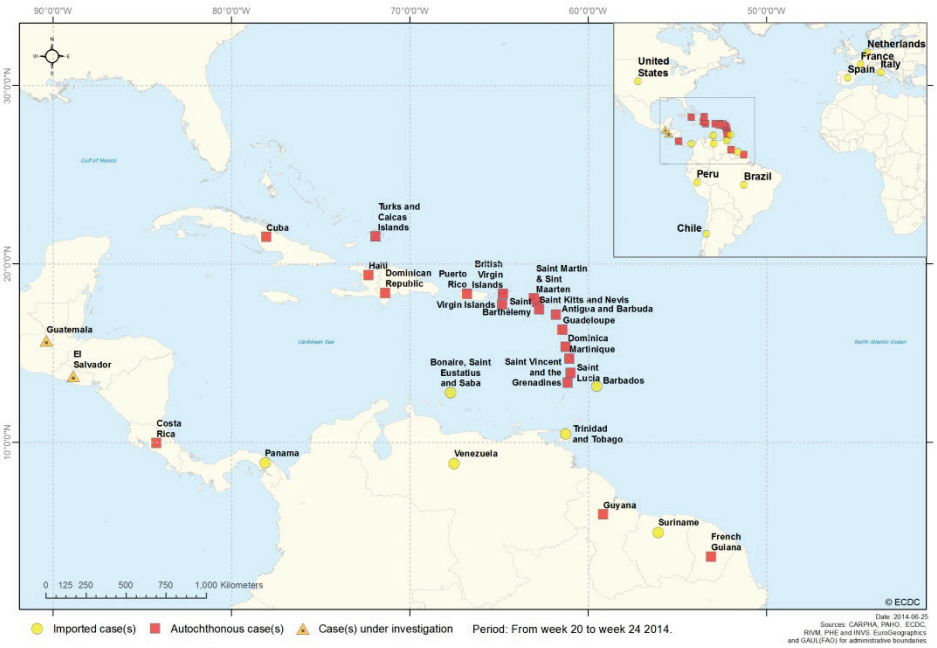


Note: The WHO Regional Office for the Americas defines a suspected case as a patient with an acute onset of fever >38°C and severe arthralgia or arthritis not explained by other medical conditions, and who resides or has visited epidemic or endemic areas within two weeks prior to the onset of the symptoms. Confirmed case corresponds to a suspected case with any specific chikungunya test (viral isolation, RT-PCR, IgM, or four-fold increase of chikungunya-specific antibody titres) [33].

During the past four weeks (week 21 to 24/2014), numerous imported cases have been reported from the Americas and Europe among travellers returning from the Caribbean region, in particular from Haiti or Dominican Republic [34]:

- North America: USA (cumulative number of 57 imported cases with 34 cases in Florida, week 24) [35];
- Central America and Caribbean: Panama (two cases, week 21), Suriname (one case), Cuba (six cases between week 21 and 24), Barbados (one case, week 23), and Bonaire island (according to media reports) [36-39];
- South America: Venezuela (two cases, week 23), Brazil (seven cases, week 24), Peru (one case, according to media reports), Chile (one case, week 22) [39,40];
- Europe: France (as of 20 June, 74 cases returning mainly from French Antilles), Italy 10 cases of which eight are returning travellers from the Caribbean, Spain (three cases in Catalonia) and the Netherlands [41-44].

Figure 2: Countries and territories with recent chikungunya notifications related to the Caribbean outbreak



During the past four weeks, Haiti, El Salvador, and Dominican Republic have been affected by an outbreak and in parallel there has been a significant increase in the number of notified imported cases in the Americas. It is likely that the expansion of chikungunya will occur as the vector is present, the climatic conditions are favourable (current start of the seasonal increase of dengue transmission in Puerto Rico, for instance) and the human population is naïve with regards to the infection. The importation of cases to Europe has already occurred and will continue and is most likely to increase. The extension of the epidemic to Portuguese- and Spanish-speaking countries in the Americas and Caribbean will modify the pattern of imported cases returning to Europe.

ECDC threat assessment

Risk for continental EU

The chikungunya outbreak which started in December 2013 on the island of Saint Martin has spread to almost all Caribbean islands over the last 29 weeks. Further, local transmission has been reported in several countries of the Americas and will likely spread to other countries in the region. The current occurrence of chikungunya and its possible establishment in the Caribbean region, and possibly in the Americas, adds an additional source of introduction of the CHIKV in the northern hemisphere overlapping with the *Aedes albopictus* and *Aedes aegypti* seasons in Europe [28].

There is a relatively intensive traffic between the overseas territories and the EU. Imported cases of chikungunya are already reported in Member States where *Aedes albopictus* is present (France, Spain and Italy). In 2012 and 2011 about 50 cases of imported chikungunya were reported in Europe. France, where an enhanced surveillance system is implemented starting on 1 May in areas where *Aedes albopictus* is present, has already reported 74 imported cases up to 20 June 2014 [44]. Further, the Caribbean and Central America are popular travel destinations for EU residents and increased travel can be expected during the coming weeks with summer holidays in Europe. Therefore, more travel-related cases of chikungunya, as well as of dengue, can be expected in travellers returning from affected areas. It should be noted that both autochthonous dengue cases in France in 2010 and 2013 followed the introduction of a patient from the French Caribbean overseas territories [28].

The invasive mosquito species *Aedes albopictus* is well established in many countries of the EU, primarily around the Mediterranean. This mosquito species is an efficient vector of ECSA strains bearing the E1-A226V mutation, but it can also transmit ECSA strains without this mutation. Vector competence of the European *Aedes albopictus* populations of the Asian genotype needs further investigation. Though, *Aedes albopictus* mosquitoes from the Americas are competent to transmit the strain from New Caledonia belonging to the Asian genotype.

For onward transmission to occur, the introduction of this virus into Europe would need to coincide with high vector abundance and activity, and permissive temperature for outbreaks. The monthly mean temperatures of outbreak locations were: 20°C in Italy and Réunion Island, 22°C in India, 24°C in Africa, and 26°C in Asia [45,46]. Vector activity is high in summer months mainly from July to October [47]. Onward autochthonous transmission from an imported viraemic chikungunya case during the mosquito season might be possible given the fact that the competent vector is present and the environmental requirements are met during the summer and early autumn in Europe [45].

Aedes aegypti, an efficient chikungunya vector, is known to occur around the Black Sea (Georgia and south-western Russia) and in Madeira [48]. In Madeira a large dengue outbreak occurred in 2012 upon the introduction of a viraemic dengue case from Venezuela [49,50]. Given the connectivity between Madeira and the Americas—mainly South America, its climate profile, and the presence of a competent vector—*Aedes aepypti*, the island is at high risk for a chikungunya outbreak.

The EU has the laboratory capacity to detect chikungunya, and imported cases would be detected through surveillance systems. However, the early detection of imported cases is critical to prevent onward transmission in areas where the vector is present. Therefore:

- awareness among clinicians is essential for early detection of cases. Further, the clinical picture of chikungunya and dengue, which currently circulates in the Caribbean, can be similar and might be a challenge for clinicians that are not familiar with the clinical presentation of these infections;
- travellers returning from outbreak areas should seek medical care if presenting with chikungunya compatible symptoms and continue personal protective measures after onset of symptoms to avoid mosquito bites and further transmission. These protective measures should be maintained for at least one week after the onset of symptoms.

Viraemic asymptomatic returning travellers could contribute to transmission of the disease if giving blood. The specific chikungunya transfusion safety measures are not defined at EU/EEA level. In an affected area temporary deferral of potential blood donors based on CHIKV nucleic acid amplification testing (NAT) screening of donated blood is an effective way to prevent transmission. If NAT screening is not available temporary deferrals based on the answers to specific questions about recent travel history in an area endemic or epidemic for CHIKV and screening for symptoms can be applied. Additionally, donors should be asked for information of disease

development after blood donation while quarantining blood up to five days after donation prior to releasing it. Pathogen inactivation of platelet and plasma can also be applied. If feasible, blood collection can be ceased in an affected area and blood components supplied from unaffected areas.

Risk for EU overseas countries and outermost regions

Since the start of the chikungunya outbreak, almost all EU overseas territories and countries in the Caribbean region have been affected. The presence of a human population naïve to the CHIKV, competent vectors in the region, permissive climate, and the intense movement of people in and between countries are factors that most likely contributed to the extension of the virus circulation and the risk of establishment of chikungunya is therefore high. The establishment of autochthonous transmission in countries of the Americas will likely have a significant public health impact in the region.

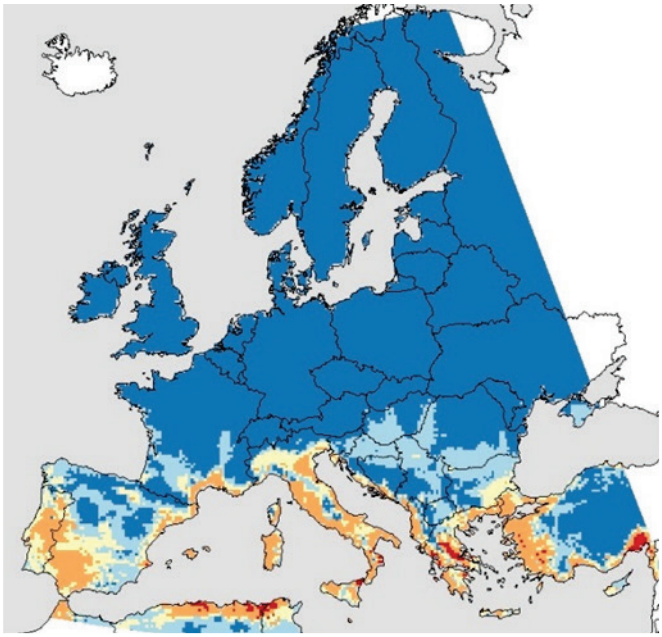
With the increased transmission of chikungunya in Asia and Africa in the last decade, the Caribbean region has been considered highly vulnerable and therefore preparedness plans for the introduction of chikungunya virus into the Americas has been developed [33].

Conclusions and options for action

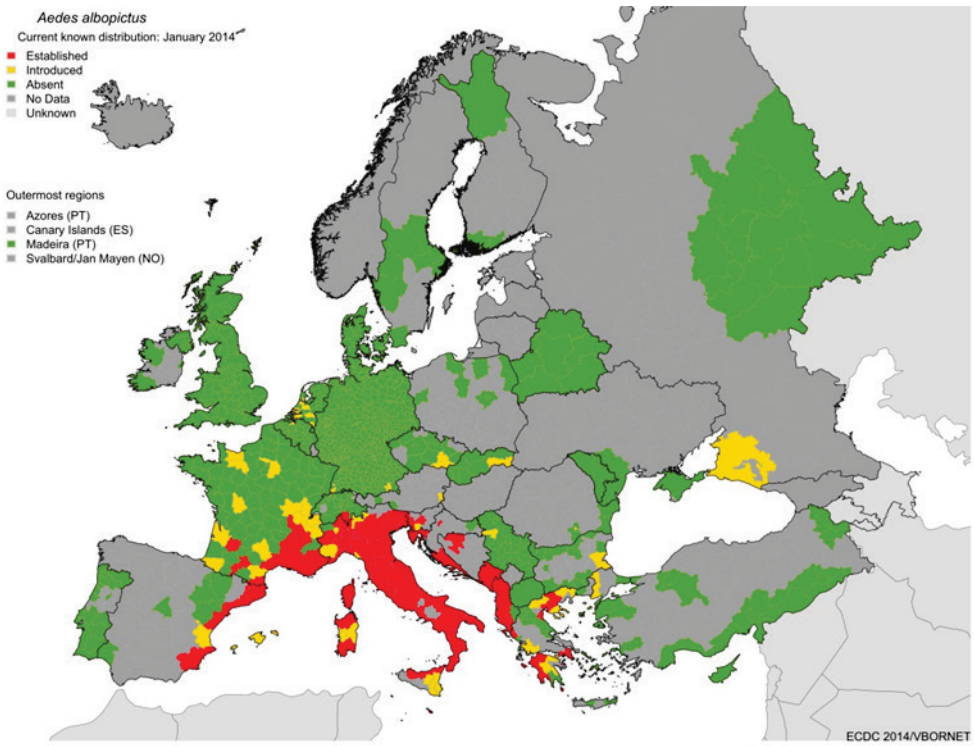
- This is the first documented autochthonous transmission of chikungunya virus in the Americas. The outbreak started on the Caribbean island of Saint Martin in early December 2013 and expanded through the Caribbean during the first half of 2014. Recently, suspected autochthonous cases have been reported from Central America (Costa Rica and El Salvador), raising concern about virus spread in continental America where *Aedes aegypti* is endemic.
- Exposure to infected mosquitoes is the principal risk for infection in currently affected areas. Prevention of chikungunya among travellers and local residents is essentially based on personal protection against mosquito bites and vector control; these are the same as the preventive measures to be taken against dengue.
- With the present holiday season in Europe, high vigilance must be maintained regarding imported cases of chikungunya and dengue in the EU, including awareness among clinicians and travel clinics, notably in those EU areas where competent vectors are present.
- The risk for onward transmission in Europe is linked to importation of virus by viraemic patients in areas with competent vectors (*Aedes albopictus* on mainland Europe and *Aedes aegypti* in Madeira). Autochthonous transmission from an imported viraemic chikungunya case during the summer season in the EU is possible. Madeira is particularly vulnerable due to the presence of *Aedes aegypti* and favourable climatic conditions.
- Travellers returning from outbreak areas should seek medical care if presenting with chikungunya compatible symptoms and apply personal protection measures to avoid mosquito bites. Such measures will reduce the risk of viral introduction in the European mosquito population and furthermore limit the establishment of a local cycle of transmission during the summer season.
- Preparedness regarding chikungunya in the EU includes strengthened surveillance systems and rapid notification of cases; review of contingency plans for mosquito-borne outbreaks; education and collaboration of the general public in the control of mosquito breeding sites; strengthened vector surveillance systems and rapid implementation of vector control measures around each case.
- EU blood safety authorities need to be vigilant regarding the epidemiological situation in the Americas in line with measures taken for West Nile virus infection.

Annex: Modelled risk map for chikungunya transmission and the currently known *Aedes albopictus* distribution in continental Europe

Risk map for chikungunya transmission in Europe generated by combining temperature requirements of the chikungunya virus with the climatic suitability of the vector *Aedes albopictus*



Adapted from Fischer D, Thomas SM, Suk JE, Sudre B, Hess A, Tjaden NB, et al. Climate change effects on Chikungunya transmission in Europe: geospatial analysis of vector's climatic suitability and virus' temperature requirements. Int J Health Geogr. 2013 Nov 12;12(1):51.



Source: Climate change effects on chikungunya transmission in Europe: geospatial analysis of vector's climatic suitability and virus' temperature requirements (see: E3 Viewer - Disease model - Chikungunya suitability model) and Aedes albopictus *distribution (Link to Vbornet Moquito maps), [32,45].*

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