



RAPID RISK ASSESSMENT

Zika virus disease epidemic: potential association with microcephaly and Guillain–Barré syndrome

Second update, 8 February 2016

Main conclusions and options for response

Considering the continued rapid spread of Zika virus in the Americas and Caribbean, the growing evidence of an association between Zika virus infection during pregnancy and adverse pregnancy outcomes, the association between Zika virus infection and post-infectious Guillain–Barré syndrome (GBS), and the risk of establishment of local vector-borne transmission in Europe during the 2016 summer season, EU/EEA Member States are recommended to consider the following mitigation measures.

- Travellers visiting countries where Zika virus is currently being transmitted should be made aware of the ongoing outbreak of Zika virus infection. A list of countries and territories with documented autochthonous transmission during the past two months is maintained on the [ECDC website](#) (see also Table 1).
- Travellers visiting these countries should use personal preventive measures based on protection against mosquito bites indoors and outdoors, especially from sunrise to sunset when mosquitoes are most active in biting. Such measures include:
 - using mosquito repellent in accordance with the instructions indicated on the product label. DEET-based repellent is not recommended for children under three months of age but pregnant women can use it.
 - wearing long-sleeved shirts and long trousers, especially during the hours when the type of mosquito that carries the Zika virus (*Aedes*) is most active.
 - sleeping or resting in screened or air-conditioned rooms, otherwise use mosquito nets, even during the day.
- Pregnant women and women who are planning to become pregnant, and who are intending travel to affected areas, should discuss their travel plans and evaluate the risk with their healthcare providers and consider postponing their travel.
- Travellers with immune disorders or severe chronic illnesses should consult their doctor or seek advice from a travel clinic before travelling, and be given advice on effective prevention measures.
- There is evidence that Zika virus can be transmitted sexually through semen, and there are indications that Zika virus can be present in semen for several weeks after a man has recovered from a Zika virus infection. Travellers to Zika-affected areas should be advised that the risk of sexual transmission from an infected man to another person can be reduced by using condoms.
- Travellers showing symptoms compatible with Zika virus disease within three weeks of return from an affected area are advised to contact their healthcare provider and mention their recent travel.
- Pregnant women that have travelled in areas with Zika virus transmission should mention their travel

Erratum

On 12 February, the words 'mosquito vectors of Zika virus' replaced the word 'mosquito' in the third bullet point under 'Preparedness in the EU' on page 10.

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during antenatal visits in order to be assessed and monitored appropriately.

- Male travellers returning from areas with local transmission of Zika virus should consider using a condom with a female partner at risk of getting pregnant or already pregnant:
 - for 28 days after their return from an active Zika transmission area if they have not had any symptoms compatible with Zika virus infection;
 - for 6 months following recovery from a laboratory-confirmed Zika virus infection.

This precautionary advice is based on limited evidence and will be revised as more information becomes available.

Information to healthcare providers

- Ensure that Zika virus-infected patients in areas with *Aedes* mosquitoes take measures to avoid getting bitten during the first week of illness (insecticide-treated bed nets, screened doors and windows as recommended by PAHO/WHO).
- Increase awareness among health professionals who provide prenatal care of the possible association between Zika virus and microcephaly and adapt prenatal monitoring in accordance with the exposure to the vector.

In addition, due to the unprecedented size of the Zika virus epidemic, health services and practitioners should be alert to the possible occurrence of neurological syndromes (GBS and other neurological syndromes such as meningitis, meningoencephalitis and myelitis according to WHO/PAHO) and potential disease complications not yet described in the scientific literature and atypical clinical presentation among specific populations (i.e. children, the elderly, immunocompromised individuals and those with sickle cell disease).

This document also includes more specific options for substances of human origin, surveillance and preparedness.

Source and date of request

Request from the European Commission, 2 February 2016.

Public health issue

This document assesses the risks associated with the Zika virus epidemic currently affecting countries in the Americas. It assesses the association between Zika virus infection and congenital central nervous system (CNS) malformations, including microcephaly, as well as the association between Zika virus infection and the Guillain-Barré syndrome (GBS).

In the past, ECDC has published four risk assessments related to the Zika virus epidemic:

- 'Zika virus infection outbreak, French Polynesia', 14 February 2014 [1];
- 'Zika virus infection outbreak, Brazil and the Pacific region', 25 May 2015 [2];
- 'Microcephaly in Brazil potentially linked to the Zika virus epidemic', 24 November 2015 [3];
- 'Zika virus epidemic in the Americas: potential association with microcephaly and Guillain-Barré syndrome', 10 December 2015 [4];
- 'Zika virus disease epidemic: potential association with microcephaly and Guillain-Barré syndrome (first update)', 21 January 2016 [5].

Consulted experts

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Disease background information

Zika virus disease is caused by an RNA virus transmitted to humans by *Aedes* mosquitoes, especially by the *Aedes aegypti* species. Up to 80 per cent of infections are asymptomatic [6]. Symptomatic infections are characterised by a self-limiting febrile illness of 4 to 7 days' duration accompanied by maculopapular rash, arthralgia, conjunctivitis, myalgia and headache. In the past, Zika virus has not been noted to cause death, nor has it been linked to intra-uterine infections and congenital CNS anomalies. Zika virus infection was linked to GBS for the first time in 2014 when a possible association between Zika virus infection and GBS was reported during an outbreak in French Polynesia [7]. There is no vaccine to prevent Zika virus infections nor is any specific anti-viral treatment available.

Zika virus infection can be confirmed by direct detection of Zika virus RNA or specific viral antigens in clinical specimens. Virus-specific antibodies can be detected usually from day 5 or 6 of illness but serological results should be interpreted with caution due to cross reactivity with other flaviviruses such as dengue.

More information on Zika virus disease can be found in the previous risk assessments [1-4] and in the ECDC factsheet for health professionals [8].

Event background information

Key events in past 12 months

- In May 2015, autochthonous transmission of Zika virus was confirmed in the states of Bahia and Rio Grande do Norte in Brazil [9]. However, it is likely that Zika virus had been circulating in Salvador de Bahia City earlier than that, as an outbreak of exanthematous illness was reported there between 15 February and 25 June 2015 and 10 cases of Zika infection were confirmed in March 2015 in Camaçari, Salvador Metropolitan Region, state of Bahia [10,11].
- In October 2015, following reports of an unusual increase of cases of microcephaly among newborns in the state of Pernambuco in Brazil, a retrospective analysis of records in the Brazilian live birth information system (SINASC) identified substantial increases in the number of reported cases of microcephaly compared with previous years in several Brazilian states [12]. On 11 November 2015, the Brazilian Ministry of Health declared a public health emergency in response to this public health event, activated the emergency operations centre for public health (COES, Centro de Operações de Emergências em Saúde Pública) and deployed teams to the affected states to support surveillance and response activities [13].
- On 24 November 2015, the health authorities of French Polynesia reported an increase from an average of one reported case annually to 17 cases of congenital CNS malformations in fetuses and infants during 2014 and 2015. Different CNS malformations were observed in 12 of these cases [4,5]. The health authorities postulated that Zika virus infection during the first two trimesters of pregnancy may be associated with these malformations on the basis of the temporal association between the two events [3].
- On 17 January 2016, the Pan American Health Organization/World Health Organization (PAHO/WHO) issued an epidemiological update on neurological syndromes, congenital anomalies and Zika virus infection [14]. PAHO/WHO acknowledged the spread of Zika virus in several countries of South/Central America and in the Caribbean. PAHO/WHO recommended that its Member States 'establish and maintain the capacity to detect and confirm Zika virus cases, prepare healthcare facilities to respond to a possible increased demand of specialized care for neurological syndromes, as well as to strengthen antenatal care'.
- On 1 February 2016, the Emergency Committee convened by the Director-General of WHO to assess the public health significance of clusters of microcephaly cases and other neurological disorders in some areas affected by Zika virus advised that the current event constitutes a Public Health Emergency of International Concern [15]. The Committee highlights the importance of measures to reduce infection with Zika virus, particularly among pregnant women and women of childbearing age, and the need to enhance standardised surveillance of microcephaly and GBS. In addition, the Emergency Committee highlights the need for further research on the aetiology of new clusters of microcephaly and other neurological disorders with an assessment of the causal relationship between Zika virus and possible other factors or co-factors. In her summary of the Emergency Committee's conclusions, the WHO Director-General said that a causal relationship between Zika infection during pregnancy and microcephaly is strongly suspected, though not yet scientifically proven.

Epidemiological update

Evolution of Zika virus epidemic

Since the last Rapid Risk Assessment, dated 21 January, eight new countries have reported autochthonous transmission: American Samoa, Costa Rica, Curaçao, Dominican Republic, Jamaica, Nicaragua, Tonga and US Virgin Islands [16-22]. As of 4 February, 31 countries or territories in the world have reported autochthonous Zika virus infections within the past two months (Table 1 and Figure 1). The epidemic continues to evolve rapidly in the Americas and has recently expanded to new countries and territories in the Caribbean and Central America. Thirty-five countries or territories have reported autochthonous cases of Zika virus infection within the past nine months (see Figure 1*).

A recent case report from Colombia about a fatal Zika virus infection in a 15-year-old girl with sickle cell disease (SCD) has raised the question whether SCD is a risk factor for severe Zika virus disease, as it is known to be for severe dengue and chikungunya [23]. This publication is the first report about Zika infection in a patient with sickle

* For the latest information, see http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/zika-outbreak/Pages/Zika-countries-with-transmission.aspx

cell disease. Due to the current spread in areas where sickle cell disorders are present (e.g. the Caribbean), Zika infection evaluation should be monitored among those patients.

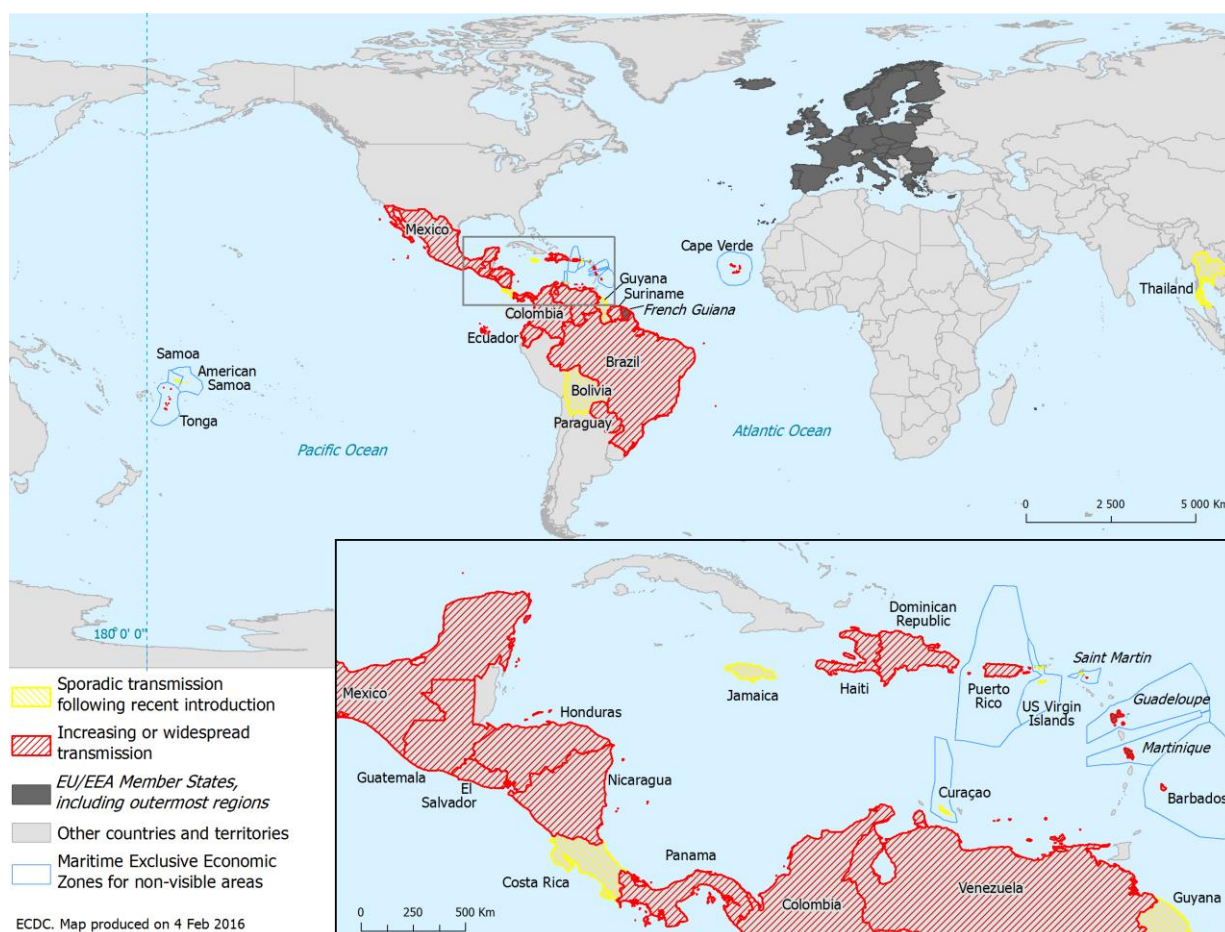
On 2 February 2016, the local health authorities in Texas, US, notified a confirmed case of sexually transmitted Zika virus infection [24]. This is the second documented case of sexual transmission to date [25].

Table 1. Countries and territories with reported confirmed autochthonous cases of Zika virus infection in the past two and nine months, as of 4 February 2016

Countries and territories	Affected in the past 2 months	Affected in the past 9 months
American Samoa	Sporadic transmission following recent introduction	Yes
Bolivia	Sporadic transmission following recent introduction	Yes
Costa Rica	Sporadic transmission following recent introduction	Yes
Curaçao	Sporadic transmission following recent introduction	Yes
Guyana	Sporadic transmission following recent introduction	Yes
Jamaica	Sporadic transmission following recent introduction	Yes
Saint Martin	Sporadic transmission following recent introduction	Yes
Samoa	Sporadic transmission following recent introduction	Yes
Thailand	Sporadic transmission following recent introduction	Yes
US Virgin Islands	Sporadic transmission following recent introduction	Yes
Barbados	Increasing or widespread transmission	Yes
Brazil	Increasing or widespread transmission	Yes
Cape Verde	Increasing or widespread transmission	Yes
Colombia	Increasing or widespread transmission	Yes
Dominican Republic	Increasing or widespread transmission	Yes
Ecuador	Increasing or widespread transmission	Yes
El Salvador	Increasing or widespread transmission	Yes
French Guiana (France)	Increasing or widespread transmission	Yes
Guadeloupe (France)	Increasing or widespread transmission	Yes
Guatemala	Increasing or widespread transmission	Yes
Haiti	Increasing or widespread transmission	Yes
Honduras	Increasing or widespread transmission	Yes
Martinique (France)	Increasing or widespread transmission	Yes
Mexico	Increasing or widespread transmission	Yes
Nicaragua	Increasing or widespread transmission	Yes
Panama	Increasing or widespread transmission	Yes
Paraguay	Increasing or widespread transmission	Yes
Puerto Rico	Increasing or widespread transmission	Yes
Suriname	Increasing or widespread transmission	Yes
Venezuela	Increasing or widespread transmission	Yes
Tonga	Increasing or widespread transmission	Yes
Fiji	No	Yes
Maldives	No	Yes
New Caledonia (France)	No	Yes
Solomon Islands	No	Yes
Vanuatu	No	Yes

Note: An up-to-date version of this table is maintained at http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/zika-outbreak/Pages/Zika-countries-with-transmission.aspx

Figure 1. Map of countries and territories with reported confirmed autochthonous cases of Zika virus infection in the past two months, as of 4 February 2016



Note: An up-to-date version of this map is maintained at http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/zika-outbreak/Pages/Zika-countries-with-transmission.aspx

Europe, EU Overseas Countries and Territories (OCT) and EU Outermost Regions (OMR)

As of 4 February, no autochthonous Zika virus transmission has been reported from continental Europe.

Several EU OCT and OMR continue to report autochthonous Zika virus circulation as follow [22,26-28]:

- Martinique: 3 940 suspected cases reported from December 2015 to 31 January 2016
- French Guiana: 430 suspected cases reported from December 2015 to 31 January 2016
- Guadeloupe: 17 confirmed autochthonous cases reported as of 31 January
- Saint Martin: one confirmed autochthonous case reported on 15 January
- Curaçao: one confirmed autochthonous case reported on 28 January 2016.

In the EU in 2015 and 2016, Denmark, Finland, France, Germany, Italy, Portugal, the Netherlands, Spain, Sweden and the UK reported imported cases.

Microcephaly and congenital central nervous system malformations

Between 22 October 2015 and 30 January 2016, Brazilian authorities received 4 783 notifications of microcephaly or central nervous system (CNS) anomalies [29]. Investigation and classification of these cases are in progress [30]. So far, 404 cases from 156 municipalities in nine Brazilian States have been confirmed to have microcephaly and/or CNS anomalies suggestive of congenital infections. Pernambuco, the first state to identify an increase of microcephaly, has reported the highest number of confirmed cases (153, 37.9%), followed by Bahia (99, 24.5%), Rio Grande do Norte (63, 15.6%), Paraíba (37, 9.2%), Piauí (27, 6.7%), Alagoas (15, 3.7%), Ceará (7, 1.7%), Rio de Janeiro (2, 0.5%) and Rio Grande do Sul (1, 0.2%) [29]. For seventeen (4.2%) of the 404 cases, an infection with Zika virus was confirmed by serology or PCR. Studies to examine a possible causal association between Zika virus infection during pregnancy and congenital CNS malformations are ongoing.

On 29 January, the US Centers for Disease Control and Prevention (US CDC) and the Ministry of Health Brazil published an assessment of 35 infants with microcephaly born from August to October 2015 [31]. All mothers had lived in or visited Zika virus affected areas during their pregnancies and 26 (74%) reported a rash during the first (n=21) or the second (n=5) trimester of pregnancy. All 27 infants for whom neuro-imaging studies were

performed (computed tomography scans and transfontanelar ultrasounds) presented with cerebral anomalies. Laboratory results of the investigation of cerebrospinal fluid from all babies for Zika virus infection are pending. Tests for other congenital infections were negative.

The Colombian Ministry of Health is monitoring 2 116 pregnant women among whom 205 are suspect cases, 1 735 are clinical cases and 176 are laboratory-confirmed cases by RT-PCR according to the Colombian case definition [32].

Since the last risk assessment, the US reported one case of microcephaly in a baby born with Zika virus infection in Hawaii. The mother lived in Brazil in May 2015 [33].

On 4 January, French authorities reported 23 pregnant women with Zika virus infection in Martinique (13), French Guiana (8) and Guadeloupe (2) [28]. These women are the subject of enhanced monitoring and no congenital abnormalities have been detected.

Guillain–Barré syndrome

Several countries in South and Central America have reported unusual increases in Guillain–Barré syndrome (GBS):

Brazil

North-eastern states have reported 121 cases of neurological manifestations and GBS with a history of illness with a rash between January and July 2015 [34]. According to a PAHO/WHO alert on 1 December 2015, 76 patients with neurological syndrome had been identified as of 13 July 2015, the majority in the state of Bahia where 42 cases were classified as GBS and five as other neurological conditions. Among the patients with GBS, 62% (26/42) reported symptoms consistent with Zika virus infection preceding the onset of the neurological symptoms [35].

For 2015, Brazil reported that 1 708 cases of GBS were registered nationwide, representing an overall 19% average increase compared with 2014 (1 439 cases of GBS) [36].

Venezuela

On 13 January, authorities reported 23 cases of GBS [37]. On 29 January, media reports quoting the Ministry of Health reported 255 GBS cases [38]. Among these, 55 were reported as having required admission to intensive care units.

El Salvador

On 30 January, media reports quoting the Ministry of Health reported 104 GBS cases between 1 December 2015 and 30 January 2016, compared with a yearly average of 169 cases in the past [39,40].

Martinique

On 29 January, authorities reported two cases of GBS in confirmed Zika virus cases [28].

Guadeloupe

On 4 February, authorities reported one case of myelitis in a confirmed Zika virus case.

France

On 4 February, authorities reported one imported case of Zika infection with neurological symptoms out of nine imported cases in 2016 [28].

New Zealand

On 29 January, the Ministry of Health reported one GBS case in an imported confirmed Zika virus case who had recent travel history in the South Pacific region [20].

Travel-related measures

Although a causal association between Zika virus infection during pregnancy and adverse pregnancy outcomes has not been conclusively established, the evidence is compelling enough for public health authorities around the world to issue travel advice concerning the affected areas. The focus is on reducing the risk of infection for pregnant women. WHO issued a statement on 1 February recommending that there should be no restrictions on travel or trade with countries, areas and/or territories with Zika virus transmission [15].

Non-EU countries

The US CDC, 'out of an abundance of caution,' issued an interim [Travel Guidance for pregnant women](#) travelling or planning to travel to countries and territories with local transmission in the Americas and the Caribbean [41]. On 3 February 2016, the Public Health Agency of Canada updated its [Travel Health Notice](#) [42]. Seven countries in Latin America advised people to delay pregnancy: Brazil, Colombia, Dominican Republic, Ecuador, El Salvador, Jamaica and Paraguay [43-48].

EU countries

The European Commission published an [Information for travellers](#) to areas with local transmission of Zika virus on 16 December 2015 [49]. As of 4 February 2016, 28 EU/EEA countries had published advice for travellers to Zika-affected countries. The following EU/EEA countries recommend that pregnant women consider postponing travel to affected countries and territories: Austria, Belgium, the Czech Republic, Denmark, Estonia, Finland, France, Germany, Iceland, Ireland, Italy, Malta, the Netherlands, Norway, Portugal, Slovakia, Slovenia and the United Kingdom.

France, Ireland and the United Kingdom have recommended that men who return from affected areas should use condoms with a partner that is pregnant or at risk of becoming pregnant [26,50,51].

In this context, the United Kingdom recommends that returning male travellers should use condoms:

- for 28 days after their return from an active Zika transmission area if they have not had any symptoms compatible with Zika virus infection;
- for 6 months following recovery if a clinical illness compatible with Zika virus infection or laboratory-confirmed Zika virus infection was reported.

ECDC threat assessment for the EU

The Zika epidemic is still evolving and expanding given that eight new countries and territories have reported autochthonous transmission since the 21 January 2016 Rapid Risk Assessment. Uncertainties about the clinical spectrum of Zika infection persist.

Severe outcomes

Microcephaly and congenital central nervous system malformations

There is a significant increase in the number of babies born with microcephaly in the north-eastern states of Brazil. However, the magnitude and geographical spread of the increase has not yet been well characterised. To date, Brazilian health authorities have reported adverse pregnancy outcomes and/or congenital CNS malformations with laboratory confirmation of Zika virus in amniotic fluid, placenta or foetal tissues [5,30]. The evidence regarding a causal link between Zika virus infections during pregnancy and congenital CNS malformations is substantial. Although the available information is not yet sufficient to scientifically confirm it, there is sufficient evidence to warrant public health actions as supported by the declaration of a Public Health Emergency of International Concern on 1 February 2016 [52].

Guillain–Barré syndrome and other post-infectious neurological syndromes

Cases of GBS are continuing to be reported from the affected countries but no new scientific evidence regarding the association between Zika virus and GBS has been published since the 21 January 2016 Rapid Risk Assessment.

Following French Polynesia, Venezuela and El Salvador have reported an unusual increase in GBS above the baseline, concomitant with the development of Zika outbreaks in those countries. Two GBS cases among patients with confirmed Zika virus infection were reported in Martinique within two months after the start of the Zika outbreak. These observations support the role of Zika virus infection as a presumptive infection event preceding GBS. The consistency of the concomitant occurrence of Zika infections and GBS over place and time indicate the strong likelihood of an association between Zika virus infection and GBS. However, GBS is known to be associated with other infectious diseases that are prevalent in the Americas and the Caribbean. Therefore well designed prospective studies are required to firmly establish the strength of this association.

Risk of Zika virus transmission via substances of human origin

People with asymptomatic infections and those who are in the incubation period of Zika disease could potentially donate contaminated substances of human origin (SoHO) without their infections being recognised at the time of donation [8]. Zika virus has been detected in blood, urine and saliva during the acute phase of the disease, and seminal fluid after the acute illness [53-56]. Musso et al. reported the presence of Zika virus RNA by PCR and replicative Zika virus particles in semen of a 44-year-old man in Tahiti three weeks after onset of symptoms [56]. Hearn et al. detected Zika virus RNA by PCR in a semen sample 28 days after onset of clinical symptoms of Zika virus infection [57]. The virus has also been isolated from the neural tissues of experimentally infected animals [58,59]. Data on the survival of Zika virus in processed and stored substances of human origin are lacking.

Assessing the risk of Zika virus transmission through contaminated SoHO is currently difficult because of the paucity of data on the prevalence of Zika virus in the donor population and the limited number of case reports of transmission. There are only two reported probable cases of transfusion-related transmission of Zika virus [60,61]. According to Musso et al., during the last Zika virus outbreak in French Polynesia, 42 of 1 505 (3%) blood donors, although asymptomatic at the time of donation, were found to be positive for the Zika virus genome by PCR, supporting a potential risk of transfusion-derived transmission [53,62]. The Brazilian media reported probable cases of transfusion-transmitted Zika virus in March 2015 and February 2016 [60,63].

The limited set of data indicates that a risk of donor-derived transmission of Zika virus through SoHO is small. However, the strongly suspected association between Zika virus infection and congenital malformations and GBS justifies preventive measures to reduce the risk of transmission via SoHO supply [52].

Risk of sexual transmission

Two studies have demonstrated Zika virus RNA in semen and one study found replicable Zika virus particles in semen more than three weeks after onset of Zika symptoms [56]. There is no data on viral concentration in semen and only two case reports of sexual transmission of Zika virus [24,25]. The limited data suggest that sexual transmission of Zika virus through semen is possible but that these events are rare. The risk of sexual transmission will be re-assessed as more information becomes available.

The Zika virus genome has also been detected in saliva during the acute phase of the disease but there is no information about the presence of viable virus, viral load and duration. The risk of transmission via saliva cannot be further assessed at this time.

Travel-related risk for EU citizens

The spread of Zika virus infections in the Americas and in the Caribbean constitutes a significant development in the epidemiology of this emerging vector-borne disease. Travellers to countries where competent vectors are present and Zika virus circulation is documented are at risk of becoming infected through mosquito bites. Due to the growing evidence of a link between Zika infection and severe congenital anomalies, pregnant women and women who are trying to become pregnant constitute a high-risk group with regards to Zika virus infection.

Residents in EU Overseas Countries and Territories, and Outermost Regions are at increased risk of exposure to Zika virus.

Risk related to mass gatherings

The Rio 2016 Olympics (5–21 August 2016) and the Paralympics Games (7–18 September 2016) are the two most prominent mass gathering events that will take place in the Americas in the coming months. A large number of visitors are expected for these events. The Olympic Games will take place during Brazil's winter when the cooler, drier weather will reduce mosquito populations and significantly lower the risk of infection for visitors. An analysis carried out for the 2014 World Cup in Brazil indicated that the density of dengue cases in Brazil is very low in the southern hemisphere, from mid-June to mid-September. Therefore, a low risk of vector-borne transmission of Zika virus infection during the Olympic Games is expected by analogy with dengue transmission involving the same vectors [64]. During the Football World Cup 2014, only three exported cases of dengue were reported and modelling data estimated the risk for a visitor to be bitten by a mosquito during the tournament to be less than 5% (unpublished data). Furthermore, the Brazilian authorities plan to implement mosquito control measures, which should further reduce the risk.

ECDC is preparing a comprehensive risk assessment ahead of the Games to assess the health risks related to communicable diseases. This document will re-evaluate the risk from Zika virus, together with other health threats for European citizens during their stay in Brazil for the Games.

Although the probability of being bitten by an infected mosquito is expected to be very low during the events, it cannot be excluded that Zika-infected travellers will return to Europe. If they return to regions of the EU where competent vectors are active, this may create an opportunity for local vector-borne transmission.

Risk of importation and further transmission in EU OCT and OMR

The epidemic is currently spreading in the Americas and Caribbean. Because *Aedes aegypti* mosquitoes are present in the EU Overseas Countries and Territories (OCT) and Outermost Regions (OMR) in the Americas and the Caribbean, it is expected that local transmission will occur there once the virus is introduced. The risk of spread is significant because of the highly susceptible (naïve) populations, presence of competent vectors, permissive climate and the intense movement of people in and between countries and territories.

Other EU OMRs and OCTs outside of the Caribbean where mosquito vectors are present such as La Réunion and Madeira are at risk of establishment of local transmission should the virus be introduced. Madeira is of particular concern because of the close relationship with Brazil and Venezuela where Zika virus is currently circulating. The 2012 dengue epidemic demonstrated the favourable conditions for vector-borne outbreaks in Madeira.

Risk of importation and transmission in the continental EU

Cases of Zika virus infection coming from countries with autochthonous transmission continue to be reported in the EU. This pattern is expected because of the large number of air passengers travelling between Europe and the Americas and Caribbean. The 2014 chikungunya outbreak in the Americas and the Caribbean resulted in a 20-fold increase in the number of imported cases into the EU in 2014 compared with 2013 (ECDC data, not shown). An association between the number of reported dengue cases imported into Europe in 2010 and the volume of airline travellers arriving from dengue-affected areas internationally was found significant [65].

There is no evidence to date that 'airport transmission' of mosquito-borne viral disease occurs, similar to airport malaria [66]. The risk of importation of Zika-infected vectors in aircraft cabins is low and there is no evidence that it plays a role in the transmission of arbovirus infections. WHO has issued specific guidance and recommendations for aircraft disinsection [15,67].

The *Aedes albopictus* mosquito species is established in several places around the Mediterranean [68]. Onward transmission from imported cases within the continental EU is possible because *Aedes albopictus* is considered a competent vector for the transmission of Zika virus, even though this has not yet been confirmed for European mosquito populations [69,70].

The risk of transmission of Zika virus infection is extremely low in the EU during winter season as the climatic conditions are not suitable for the activity of the *Aedes albopictus* mosquito. During the summer season, autochthonous transmission in the EU following the introduction of the virus by a viraemic traveller is possible in areas where *Aedes albopictus* is established. For the months February to April the International Research Institute for Climate and Society predicts above-normal temperatures in Europe coinciding with a normal precipitation pattern, which might result in an early start of the mosquito activity season in Europe [71].

Conclusions and options for response

Considering the continued rapid spread of Zika virus in the Americas and Caribbean, the growing evidence of an association between Zika virus infection during pregnancy and adverse pregnancy outcomes, the association between Zika virus infection and post-infectious Guillan–Barré syndrome, and the risk of establishment of local vector-borne transmission in Europe during the 2016 summer season, EU/EEA Member States are recommended to consider the following mitigation measures.

Information to travellers and EU residents in affected areas

ECDC classifies countries affected by the Zika virus epidemic (Figure 1. For the latest information, [see map on ECDC website](#)) into areas with:

- Sporadic transmission following recent introduction: American Samoa, Bolivia, Costa Rica, Curaçao, Guyana, Jamaica, Saint Martin, Samoa, Thailand and the US Virgin Islands;
- Increasing or widespread transmission: Barbados, Brazil, Cape Verde, Colombia, Dominican Republic, Ecuador, El Salvador, French Guiana, Guadeloupe, Guatemala, Haiti, Honduras, Martinique, Mexico, Nicaragua, Panama, Paraguay, Puerto Rico, Suriname, Venezuela and Tonga.

Information for travellers to areas with local transmission of Zika virus

- Travellers visiting countries where Zika virus is currently transmitted should be made aware of the ongoing outbreak of Zika virus infection. A list of countries and territories with documented autochthonous transmission during the past two months is maintained on the [ECDC website](#).
- Travellers visiting these countries should use personal preventive measures based on protection against mosquito bites indoors and outdoors, especially from sunrise to sunset when mosquitoes are most active in biting. These measures include:
 - using mosquito repellent in accordance with the instructions indicated on the product label. DEET-based repellent is not recommended for children under three months of age but pregnant women can use it.
 - wearing long-sleeved shirts and long trousers, especially during the hours when the type of mosquito that carries the Zika virus (*Aedes*) is most active.
 - sleeping or resting in screened or air-conditioned rooms, otherwise use mosquito nets, even during the day.
- Pregnant women and women who are planning to become pregnant, and who are intending to travel to affected areas, should discuss their travel plans and evaluate the risk with their healthcare providers and consider postponing their travel.

- Travellers with immune disorders or severe chronic illnesses should consult their doctor or seek advice from a travel clinic before travelling, and be given advice on effective prevention measures.
- There is evidence that Zika virus can be transmitted sexually through semen, and there are indications that Zika virus can be present in semen for several weeks after a man has recovered from a Zika virus infection. Travellers to Zika-affected areas should be advised that the risk of sexual transmission from an infected man to another person can be reduced by using condoms.

Information for travellers returning from areas with local transmission of Zika virus

- Travellers showing symptoms compatible with Zika virus disease within three weeks of return from an affected area are advised to contact their healthcare provider and mention their recent travel.
- Pregnant women that have travelled in areas with Zika virus transmission should mention their travel during antenatal visits in order to be assessed and monitored appropriately.
- Male travellers returning from areas with local transmission of Zika virus should consider using a condom with a female partner at risk of getting pregnant or already pregnant:
 - for 28 days after their return from an active Zika transmission area if they have not had any symptoms compatible with Zika virus infection;
 - for 6 months following recovery from a laboratory-confirmed Zika virus infection.

This precautionary advice is based on limited evidence and will be revised as more information becomes available.

Surveillance of imported cases and monitoring of transmission in the continental EU

- Increase awareness among clinicians and travel health clinics about the evolution of the Zika virus outbreak and the affected areas so that they can include Zika virus infection in their differential diagnosis for travellers from those areas.
- Enhance vigilance towards the early detection of imported cases of Zika virus infection in EU Member States, EU Overseas Countries and Territories, and EU Outermost Regions, in particular where vectors are present, in order to reduce the risk of autochthonous transmission.
- Strengthen laboratory capacity to confirm suspected Zika virus infections in the European region in order to differentiate Zika virus infections from other arboviral infections (e.g. dengue, chikungunya).
- Increase awareness among obstetricians, paediatricians and neurologists in the EU/EEA that Zika virus infections should be investigated in patients presenting with congenital CNS malformations, microcephaly and GBS.

Preparedness in the EU

Preparedness regarding Zika in the EU includes:

- strengthening surveillance systems to ensure early detection and rapid notification of cases;
- reviewing contingency plans for mosquito-borne outbreaks to ensure rapid vector control measures around imported cases in areas with competent vectors;
- strengthening intersectoral collaboration and promoting community involvement for the control of the *Aedes* mosquito vectors of Zika virus;
- strengthening integrated mosquito surveillance, including invasive species.

Safety of blood supply

Persons with diagnosis of Zika fever may be accepted for blood donation 28 days after cessation of symptoms. Competent authorities, establishments and clinicians dealing with blood supply need to be vigilant and aware of the risk of donor-derived Zika virus transmission through transfusion. The identification of cases may improve disease surveillance and contribute to the timely implementation of preventive interventions in response to an outbreak.

Non-affected areas

- Health authorities may consider a precautionary deferral of asymptomatic blood donors for 28 days after return from an affected area. This deferral period covers a double incubation period of the disease [8]. The blood donors need to be encouraged to inform the blood establishment if they develop symptoms compatible with Zika virus infection within 14 days after donation.
- The list and map of areas/countries affected with Zika virus are maintained on the [ECDC website](#). In unaffected areas with competent vectors for Zika virus, a preparedness plan for prevention and control of outbreaks of Zika virus infection should cover the safety and continuity of the blood supply.

Affected areas

- As 80% of humans infected with Zika virus are asymptomatic, donor deferral measures based on fever will be of limited value in detecting viraemic donors.
- Experience from previous flavivirus outbreaks shows that blood establishments may consider the following:
 - Temporarily interrupting donations in affected areas and importing blood components from unaffected parts of the country.
 - Quarantining collected blood components for five days and releasing if the donor reports the absence of acute illness.
 - Using pathogen inactivation for plasma, platelets and some tissues in affected areas. Such methods are effective for other flaviviruses (West Nile virus and dengue virus) [72-75]. The amotosalen UV method has been demonstrated to inactivate Zika virus in plasma [76].
- As Zika virus infection may have serious consequences for the health of the recipient, the screening of all donated blood for the presence of Zika virus RNA by NAT may be considered necessary in affected areas. Due to the potential association between Zika virus infection and congenital CNS malformations, health authorities in affected areas may particularly anticipate taking the precautionary measures of using Zika virus-negative blood for the transfusion of pregnant women.

Information to healthcare providers

- Ensure that Zika virus-infected patients in areas with *Aedes* mosquitoes avoid getting bitten during the first week of illness (insecticide-treated bed nets, screened doors and windows as recommended by PAHO/WHO).
- Increase awareness among health professionals who provide prenatal care of the possible association between Zika virus and microcephaly and adapt prenatal monitoring in accordance with the exposure to the vector.

In addition, due to the unprecedented size of the Zika virus epidemic, health services and practitioners should be alert to the possible occurrence of neurological syndromes (GBS and other neurological syndromes such as meningitis, meningoencephalitis and myelitis according to WHO/PAHO [14]) and potential disease complications not yet described in the scientific literature and atypical clinical presentation among specific populations (i.e. children, the elderly, immunocompromised individuals and those with sickle cell disease).

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