



RAPID RISK ASSESSMENT

Zika virus disease epidemic

Tenth update, 4 April 2017

Conclusions and options for response

Despite the fact that the Zika virus epidemic is showing signs of a significant slow-down in the Americas and the Caribbean since the last rapid risk assessment in October 2016 [1], the European Union/European Economic Area (EU/EEA) Member States should continue to consider a range of options for risk reduction. The predominant mode of transmission for Zika virus is through the bites of infected mosquitoes but the virus can also be transmitted by sexual contact, blood/blood components and possibly other substances of human origin (SoHO). Zika virus infection during pregnancy is associated with intrauterine central nervous system (CNS) infection, congenital malformations and foetal death. Hence, pregnant women are the main risk group and the primary target for preventive measures. ECDC continues to monitor new scientific evidence and is updating the assessment of the risk and options for response accordingly.

Options for risk reduction

Preventing mosquito transmission

The risk of mosquito-borne transmission can be reduced by applying individual personal protective measures against being bitten and by lowering the mosquito population density. Indoor and outdoor personal protective measures that reduce the risk of mosquito bites include the use of mosquito repellent in accordance with the instructions indicated on the product label, wearing long-sleeved shirts and long trousers, especially during the daytime when *Aedes aegypti* and *Aedes albopictus* mosquitoes are most active, and sleeping and resting in screened or air-conditioned rooms or using mosquito bed nets at night and during the day.

Preventing sexual transmission

Zika virus sexual transmission can be prevented by abstaining from sexual contact with a potentially infectious person or consistently using barrier methods during sexual contact with a potentially infectious person.

Safety of substances of human origin

ECDC's document 'Zika virus and safety of substances of human origin – Guide for preparedness activities in Europe' [2] is currently being updated. The update will cover the risk of Zika virus infection in SoHO donors exposed through sexual contact and changes in the ECDC's country classification.

Information to travellers and EU residents in affected areas

WHO has published information for travellers visiting Zika-affected countries [3] and developed travel advice for health authorities and healthcare practitioners [4] to provide Member States with options for travel recommendations.

Information to healthcare providers in the EU/EEA

EU/EEA Member States should consider the following:

- Ensure that clinicians and medical practitioners in travel clinics maintain awareness of current Zika virus epidemiology in order to:
 - Conduct accurate pre-travel individual risk assessments and detect Zika virus infections among travellers returning from affected areas. To support this, ECDC is regularly updating a <u>set of maps</u> and lists of affected areas on its website.
 - Consider Zika virus infection in their differential diagnosis for travellers coming from those areas or for symptomatic individuals who have not travelled but have had sexual contact with a person residing in or returning from affected areas, in particular if presenting with Guillain Barré syndrome (GBS) and other neurological presentations such as meningo-encephalitis, myelitis and acute disseminated encephalomyelitis.
- Ensure that health professionals providing antenatal care, obstetricians and paediatricians maintain awareness of current Zika virus epidemiology in order to:
 - Identify and investigate pregnant women exposed to Zika virus during their pregnancy (see
 Algorithm for public health management of cases under investigation for Zika virus infection) [2,3].
 - Monitor the neurological development of children born to women exposed to or infected by Zika virus during their pregnancy.
- Ensure timely detection and reporting to the European Surveillance System (TESSy) of cases imported to EU/EEA Member States in order to provide information about areas with ongoing transmission.

Source and date of request

ECDC internal decision, 16 January 2017.

ECDC is producing this rapid risk assessment (RRA) document in accordance with Article 7(1) of Regulation (EC) No 851/2004 establishing a European Centre for Disease Prevention and Control. In the framework of ECDC's mandate, the specific purpose of an ECDC risk assessment is to present options on matters of importance to public health. The responsibility for the choice of which option(s) to pursue and which action(s) to take lies exclusively with EU/EEA Member States.

Public health issue

This document presents an updated assessment of the risks associated with the Zika virus epidemic in affected countries, in EU Overseas Countries and Territories (OCTs) and Outermost Regions (OMRs) and in EU Member States within continental Europe. This update is triggered by the evolution of the Zika virus epidemic, revised country classification and recent scientific developments since the ninth RRA update in October 2016 [7].

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ECDC acknowledges the valuable contributions of all experts. Although experts from the WHO reviewed the risk assessment, the views expressed in this document do not necessarily represent the views of WHO. All experts have submitted declarations of interest and a review of these declarations did not reveal any conflicts of interest.

Disease background information

Zika virus disease is caused by an RNA virus transmitted to humans by *Aedes* mosquitoes, especially by the *Aedes aegypti* species. More information about Zika virus disease is available in the ECDC <u>factsheet for health professionals</u> and the <u>previous risk assessments</u> [1,8-18].

Epidemiological developments

Since the ninth Zika virus disease epidemic risk assessment was published on 28 October 2016, the Zika virus epidemic appears to have been slowing down in the Americas and the Caribbean regions [19]. New information about Zika virus circulation has been documented in South East Asia. Between 26 October 2016 and 9 March 2017 [20,21], the main developments can be summarised as follows:

- seventy countries have reported evidence of mosquito-borne Zika virus transmission since 2015, including three new countries since 26 October 2016, Palau, Montserrat and Angola;
- the United Kingdom reported one incidence of sexual transmission of Zika virus and overall, 13 countries have reported evidence of person-to-person sexual transmission;
- thirty-one countries and territories have reported cases of microcephaly and other central nervous system (CNS) malformations potentially associated with Zika virus infection to WHO, including eight since 26 October 2016 (Argentina, Bolivia, Guadeloupe, Mexico, Nicaragua, Saint Martin, Trinidad and Tobago, and Vietnam);
- four additional countries (Bolivia, Curaçao, Trinidad and Tobago, and Saint Martin) have reported at least one case of Guillain-Barré (GBS) syndrome potentially associated with Zika virus infection.

South America

The large and intense epidemic waves of Zika virus observed during the first half of 2016 are over in several countries in South America: Colombia, Brazil, Suriname and Venezuela [22]. Nevertheless, most of the countries in South America have still been reporting Zika suspected and confirmed cases within the past three months. In the absence of systematic testing, the assessment of the current level of transmission remains challenging. However, Zika virus transmission is expected to be significantly lower than that seen during the initial outbreak waves in the region.

In Argentina, the Ministry of Health in Chaco Province reported a confirmed case of Zika virus infection on 22 February 2017. The patient is a woman living in Presidencia Roque Sáenz, Peña city (Chaco Province) but with recent travel history to Formosa Province which is the probable site of infection [23]. As of week 9, 2017, Formosa Province had reported six cases of Zika virus infection [24]. In addition, Salta Province reported the first two cases of Zika virus infection in week 6 and 7 of 2017 [25].

The austral winter in 2016 is likely to have decreased vector activity in the southern parts of the transmission area e.g. northern Argentina and Paraguay and in regions with a mountainous climate (e.g. Peru and Colombia). However, these areas may have experienced an increase in transmission during the current austral summer, as exemplified by the local transmission in some areas of northern Argentina.

Central America and Mexico

The pattern of transmission during 2016 is different to that in South American countries. An increase in transmission was observed during the first months of 2016. Later, some countries experienced a second wave during the period June to August 2016 (e.g. Panama, Honduras and Guatemala) [22]. During late summer in the Northern Hemisphere, as the climatic conditions became more suitable for vector activity, the epidemic front moved northwards, with outbreak waves developing in Belize and Mexico.

In 2016, Mexico reported 7 560 confirmed cases [26] and its first confirmed case of congenital syndrome associated with Zika virus infection in February 2017 [27]. During the first ten weeks of 2017, 97 confirmed Zika cases have been detected in Baja California, Guerrero, Hidalgo, Jalisco, Morelos, Nayarit, Nuevo Leon, Oaxaca, Puebla, Quintana Roo, San Luis Potosí, Sinaloa, Tabasco, Tamaulipas, Veracruz and Yucatán states [28]. During the 2016–2017 winter, mosquito activity has diminished in Mexico, especially in the northern part and in areas with temperate climate at altitude. However sporadic cases are still being detected.

The Caribbean

Despite the heterogeneity of information and the different introduction dates of the Zika virus into countries and territories, it is apparent that the Caribbean region is experiencing a decreasing trend in suspected and confirmed cases since the last risk assessment on 28 October 2016.

In the Greater Antilles (Cuba, Hispaniola island, Puerto Rico, Jamaica and the Cayman Islands), epidemic waves occurred at different times. In the first half of 2016, the outbreak peaked in February in Haiti, then in the Dominican Republic in May and in Jamaica in June. The most recent infected traveller returning to the EU/EEA from Cuba was reported to the European Surveillance System (TESSy) with onset of symptoms during the second week of 2017.

Martinique, Guadeloupe and French Guiana reported the last confirmed Zika case in week 5, week 1 and 7 of 2017, respectively. The positivity rate of laboratory testing has been <1% since the beginning of the year in Guadeloupe, 2–7% in French Guiana from mid-January onwards and 1% in Martinique, indicating a low to very low viral circulation. The latest confirmed Zika cases in Saint Martin and Saint Barthélemy were reported in week 5 and 6 of 2017 [29].

For countries and territories between the British Virgin Islands and Aruba, and Trinidad and Tobago (Lesser Antilles), the start of the epidemic waves occurred at different times across the islands, ranging from the first half of 2016 in Martinique, Dominica, Aruba and Barbados to the second half of the year, as reported in Saint Barthélemy, Saint Martin and Sint Maarten.

Sporadic cases are expected to be reported following an outbreak wave, the extent of which will depend on Zika virus infection immunity within the community.

United States of America

In 2017, as of 20 March, Florida had reported two locally acquired asymptomatic cases of Zika virus infection. Both cases had multiple exposure in Miami-Dade County in 2016 and infection may have occurred in 2016. However, cases are reported according to their date of laboratory confirmation in 2017 [30].

On 28 November 2016, the Texas Department of State Health Services reported the first locally acquired case of Zika virus infection in a resident of Cameron County, Texas [31]. Five additional cases were reported in the three weeks following the initial case. On 25 January 2017, a pregnant woman in Texas was confirmed with Zika virus infection. It has not been confirmed whether the infection is linked to her travel to Cameron County or to a sexual transmission [32].

Africa

On 20 January 2017, Angola reported its first two cases of Zika virus infection [33]. The first case was a French traveller who presented with a symptomatic Zika virus infection confirmed by seroneutralisation after returning from Angola in September 2016. The second case is a resident with no recent travel history who was confirmed by polymerase chain reaction (PCR) at the end of December 2016 [34]. On 1 February 2017, Angola reported the first case of microcephaly potentially associated with Zika virus infection in a woman who is possibly the third Zika case in the country [35].

In Tanzania, a rumour of Zika virus infections among the local population was reported in December 2016 [36]. According to media, a survey in 533 people in 2016 found 15.6% positive for Zika virus infection. However, media quoting the Ministry of Health reports that the information has not been confirmed and further investigations are required to validate the results [37].

Asia

On 27 August 2016, Singapore reported its first locally acquired case of Zika virus infection. Since then and until the end of 2016, around 500 locally acquired Zika virus infections had been recorded in Singapore. The majority of these (379) were reported in the three weeks following the initial case [38]. As of 28 March 2017, eight additional cases have been reported so far during 2017 (last confirmed case reported week 13) [38].

According to media quoting the local authorities on 15 November 2016, Thailand reported over 600 confirmed Zika cases in 2016 [39]. On 27 February 2017, New Zealand reported one case of Zika virus infection in a returning traveller from Thailand [40].

On 3 November 2016, Vietnam reported the first case of microcephaly potentially associated with Zika virus infection [41]. Around 200 cases of Zika virus have been detected in Vietnam in less than three months, the majority of which have been in Ho Chi Minh City [42,43]. According to media, additional cases have been reported in the southern part of the country (Southern Dong Nai province) [44]. In Malaysia and the Philippines, new locally acquired cases have been reported in December 2016 and February 2017 respectively [45,46].

New insights on virus circulation in southern Asia have been published, supporting the hypothesis that Zika virus circulation was taking place in the region, notably in Cambodia (2007–2008–2009 and 2015) and in the People's Democratic Republic of Lao where 17 cases were reported in Lao residents of Vientiane between June 2012 and September 2013 [47-49].

Other

In the South Pacific region, American Samoa reported 1 004 suspected cases including 58 laboratory confirmed cases from 1 January to 1 December 2016 [50].

The Maldives initiated testing for Zika virus in October 2016, following several reports of Zika-positive individuals who had returned from the Maldives. Since then, two have tested positive out of more than 500 Maldivians who have been tested for Zika virus in 2016 [51].

Europe (as of week 10, 2017)

No locally acquired cases by vector-borne transmission have been reported by EU/EEA countries in continental Europe as of week 10, 2017. Since week 26, 2015, 21 countries have reported 2 130 travel-associated Zika virus infections through the European Surveillance System (TESSy). The latest week of exposure reported was week 50, 2016. France reported 54% of the cases, Spain 14% and the UK 9%. During the same period, eight countries reported 108 Zika cases among pregnant women.

As of 7 March 2017, six European countries reported 20 sexual transmission events in TESSy, all from male partners to females where gender was reported: France (12), Italy (2), Netherlands (2), Spain (2), Portugal (1) and the United Kingdom (1). Reported exposures took place in Brazil (2), Guatemala (1), Maldives (2), Martinique (1), Puerto Rico (1) and Thailand (1).

ECDC provides regular updates on the Zika virus epidemic via its Zika outbreak <u>webpage</u> [52] and a monthly <u>epidemiological update</u> [53] which is also available in the <u>ECDC Communicable Disease Threats Report</u> [54].

Country classification scheme

A revised scheme has been developed by WHO, in collaboration with the US CDC and ECDC, to categorise the epidemiological profile of vector-borne Zika virus transmission in countries and territories [55].

The following four categories have been defined:

- Category 1: Area with new introduction or re-introduction with ongoing transmission.
- Category 2: Area either with evidence of virus circulation before 2015 or area with ongoing transmission that is no longer in the new or re-introduction phase, but where there is no evidence of interruption.
- Category 3: Area with interrupted transmission and with potential for future transmission.
- Category 4: Area with established competent vector (*Aedes aegypti*) but no known documented past or current transmission. Areas where *Aedes albopictus* mosquitoes are the only potential vectors are not included as there is no evidence that they can ensure sustained Zika virus transmission on their own.

WHO has published the classification with a list of countries in each category, available at http://www.who.int/emergencies/zika-virus/situation-report/10-march-2017/en/ [55]. ECDC has updated the map showing the epidemiology of Zika infections worldwide on its website to reflect the new WHO classification (Figure 1).

The following adjustments were made to reflect the risk to travellers more accurately:

- While WHO lists countries or territories as one entity, ECDC classifies sub-national level areas for some large countries.
- The areas of category 2 countries experiencing a 'new documented intense transmission' are represented
 with a red hatching pattern. Hatched areas are areas where ten or more confirmed/probable/suspected
 cases have been documented in the last three months or where two or more
 confirmed/probable/suspected cases have been documented in the last three months in at least two
 locations.
- Countries and areas in category 4, with potential for transmission based on the presence of a suitable vector, and a border with a category 2 area have been listed as category 4a. This indicates a higher risk of transmission because of the proximity with a category 2 area, sharing the same ecological characteristics, or experiencing virus transmission following past virus circulation (endemic areas). Other countries and areas have been listed as category 4b.

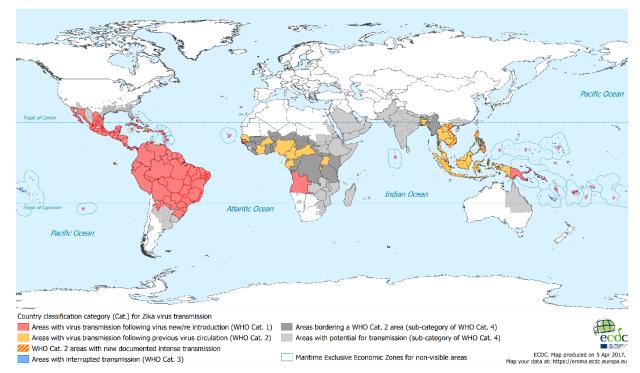


Figure 1. Distribution of areas by type of Zika virus transmission, worldwide, as of 27 March 2017

Note. The 'new documented intense transmission' attribute is defined as a category 2 area with ten or more confirmed/probable/suspected cases in the last three months or two or more confirmed/probable/suspected cases in the last three months in at least two locations.

A regularly updated list areas/countries and maps are available on ECDC's webpage (Current Zika transmission).

Main scientific developments

Since the ninth update of the rapid risk assessment on 28 October 2016, ECDC has published a review of scientific findings based on published scientific literature. The main findings regarding Zika virus research are set out below.

Pathogenesis

Knowledge on molecular and cellular mechanisms and pathogenesis has significantly increased in the past three months. Ming et al. have performed a comprehensive review of the progress made in stem cell-based Zika virus research since the emergence of the Zika virus in 2015 [56].

Congenital Zika syndrome

Brasil et al. report consolidated results of the prospective cohort on pregnancy outcomes from Rio de Janeiro [57,58]. Zika diagnosis was based on RT-PCR assay. Adverse outcomes were defined as miscarriages, stillbirths, infants anomalies detected during infant clinical assessments, imaging or both. Zika virus-positive pregnancies with symptomatic Zika symptoms presented 46% of adverse pregnancy outcomes compared to 11.5% for Zika virus-negative pregnancies. Neurological examinations revealed various neurological symptoms and imaging studies confirmed a broad spectrum of CNS impairments. Adverse outcomes were identified as late as 34 weeks into gestation.

The first report of the US Zika Pregnancy Registry showed that the risk of birth defects was similar for symptomatic (10/167, 6%) and asymptomatic infections (16/271, 6%) [59]. There was a higher risk of birth defects in women who were infected around the preconception period or during the first trimester.

According to the findings of an expert review, the risk of congenital brain abnormalities could be approximately 50 times higher in mothers who had Zika virus infection in pregnancy compared with those who did not [60]. The expert panel recognised that Zika virus alone may not be sufficient to cause either congenital brain abnormalities or GBS but agreed that the evidence was sufficient to recommend enhanced public health measures.

Guillain-Barré syndrome

A systematic review produced by Krauer et al. and the WHO Zika Causality Working Group stated that the most likely explanation of GBS occurrence during the recent Zika virus outbreak is that Zika virus infection is able to trigger GBS [60]. A case series on the comprehensive clinical and laboratory investigation of GBS cases, potentially associated with Zika virus infection in Colombia, resolutely supports the association between Zika virus infection and acute inflammatory demyelinating polyneuropathy [61].

Transmission

Zika virus RNA in semen has been detected beyond six months after onset of symptomatic Zika virus infection in longitudinal follow-up studies of men [62,63], with intermittent detection for more than 12 months [L. Barzon, personal communication]. A recent prospective cohort study involving 55 men from whom semen samples were repeatedly tested for ZIKV-RNA reported the median time until loss of RNA detection of 34 days (95% CI, 28 to 41) and the maximum duration of RNA detection of 125 days after symptoms onset; 4% of the subjects are still under follow-up [64]. The same study reports that the virus was successfully isolated from 6/20 (30%) semen specimens; information on timing of isolation in relation to the onset is not yet reported. Zika virus RNA was detected up until day 77 after the onset of symptoms in the ejaculate of vasectomised patients [65,66] and in seminal plasma from a man with azoospermia [67]. This finding suggests that apart from spermatocytes, other cells could be infected with Zika virus (in this study probably mainly inflammatory cells).

The isolation of Zika virus from semen through cell culture was possible up to 21 days post symptom onset, complying with the timeline for sexual transmission events which have been reported mostly within three weeks of onset of symptoms.

The longest reported duration of virus RNA in vaginal swabs is 14 days after onset of symptoms [68]. In addition, a study from France reported for the first time the isolation through cell culture of infectious Zika virus from vaginal samples of a woman with well controlled HIV-infection on day three post onset of Zika symptoms [69]. A second swab on day 10 was negative, suggesting a short duration of infectivity of women with acute Zika virus infection through their genital secretions [69]. A study on 50 symptomatic women found that only one woman (2%) had ZIKV-RNA in vaginal secretions (at day 3 after onset) [64]. These findings indicate a short duration of infectivity for women with acute Zika virus infection through their genital secretions.

Limited data are available on the presence of viable virus, viral load or kinetics in saliva and other bodily fluids that may be exchanged during sexual contact. Zika RNA has been detected in saliva 29 and 49 days after onset [66,70] and Zika virus has been isolated in cell culture from an oral sample taken six days after onset of symptoms. A study on rhesus macaques documented Zika virus transmission via the oropharyngeal mucosa after direct application of a high-dose of Zika virus but the results suggest the risk posed by oral secretion from individuals with a typical course of Zika virus infection is low [71].

A modelling study suggests that the persistence duration of the virus in semen appears to be insufficient for a sustained transmission in settings where vector-borne transmission is absent [72].

Proportion of asymptomatic blood donors

Gallian at al. showed that among 4 129 consecutive blood donations tested by Zika RNA NAT in Martinique during the first half of 2016, 76 donations (1.84%) were positive [73]. Post-donation information from 75 of these positive donors revealed that 34 (45.3%) remained asymptomatic, and 41 (54.7%) reported symptoms.

Serosurveys conducted at the end of the outbreak and 18 months later in French Polynesia (2013–2014) showed lower-than-expected disease estimate prevalence rates (49%) and asymptomatic/symptomatic case ratios (1:1) in the general population based on a cluster sample method. However, there was a significantly higher prevalence rate (66%) and asymptomatic/symptomatic ratio (1:2) in schoolchildren [74].

WHO has published the Zika Virus Research Agenda with the aim of identifying critical areas of research and supporting harmonisation of research in countries using standardised research protocols to generate the evidence needed to strengthen public health guidance [75].

ECDC threat assessment for the EU

On 18 November 2016, WHO's Director-General accepted the recommendations of the fifth meeting of the Emergency Committee on Zika virus, microcephaly and other neurological disorders and declared an end to the Public Health Emergency of International Concern (PHEIC).

Since it began in 2015, the current Zika epidemic has been unprecedented in terms of size and public health impact compared to previous reported outbreaks. Furthermore, the epidemiology of this emerging vector-borne disease remains a significant concern for public health. According to WHO, the global risk assessment has not changed and vigilance needs to remain high in countries and territories where the *Aedes* mosquitoes are established. However, after the epidemic wave of 2016, transmission declined in several countries of the Americas and Caribbean, significantly reducing the level of exposure compared with the epidemic peak period. As expected, with the decrease in intensity of Zika virus transmission after the 2016 wave, the number of travel-associated cases of Zika also decreased in the EU.

There is a consensus that Zika virus infection during the first and second trimester of pregnancy is associated with an increased risk of central nervous system (CNS) malformations and microcephaly. The risk of CNS malformations when the infection occurs during the third trimester of pregnancy is still unclear. Therefore, Zika virus infection should be considered as a risk throughout the duration of pregnancy, as supported by recent findings during the follow-up of

pregnant women in a cohort from Rio de Janeiro [58]. The recent findings from the pregnancy cohort in Rio de Janeiro not only demonstrated that microcephaly is a birth defect associated with Zika virus infection during pregnancy but also showed that a congenital Zika syndrome includes a broader spectrum of CNS malformations [58]. The risk of adverse events may be higher in symptomatic infections, but paucisymptomatic cases are probably common and associated risk for adverse pregnancy outcomes in such cases still remains under investigation.

To date, there is still insufficient data to provide a robust estimate of the risks of adverse pregnancy outcomes by gestational age and the role of possible co-factors. It is conceivable that co-factors, such as the mother's age, nutritional status, genetic predisposition, socio-economic status, environmental exposures and previous or concomitant infections, such as previous infection with other flaviruses (e.g. dengue) can influence the possibility of Zika transplacental transmission and congenital malformations. The reasons for the large difference observed in the frequency of adverse outcomes of pregnancy among Zika infection women in the Rio de Janeiro cohort and US registry is unknown. Several hypotheses can be proposed: i) variation in measurement of pregnancy outcomes and birth defects; ii) demographic and human genetic differences of the pregnant women and iii) difference in comorbidity rate or co-exposure to factor(s) enhancing/reducing the risk of adverse pregnancy outcome after Zika virus infection. A variation in the virus strain is not expected to play a role as pregnancies under follow-up in both cohorts have probably had exposure to the same Zika virus lineage Asia II [76]. Around 88% of Zika-affected pregnant women in the Rio de Janeiro cohort had prior dengue virus infection, which is expected to be higher than the pregnant women enrolled in the US registry cohort (data not reported). Further investigations could confirm if previous dengue infection is a risk factor for Zika transplacental transmission and congenital malformations.

Vector-borne transmission remains the primary route of transmission. Sexual transmission does occur and while, according to modelling studies, it increases the risk of infection and epidemic size and duration, it may not initiate or sustain an outbreak alone [72,77]. Comprehensive data on Zika virus kinetics in bodily fluids and the significance of prolonged detection of viral RNA, especially in semen, is still required to assess the risk of sexual transmission at population level and under case-based circumstances.

It is not expected that local vector-borne transmission will take place in continental Europe because the seasonal conditions for Zika virus transmission by vectors are unfavourable during early spring season.

Definition of potentially infectious person

A potentially infectious person is defined as:

- a person who resides in a category 1 or 2 area; OR
- a woman who has visited a category 1 or 2 area in the past eight weeks; OR
- a man who has visited a category 1 or 2 area in the past six months; OR
- a woman who has had unprotected sex in the past eight weeks with a potentially infectious person, as defined above; OR
- a man who has had unprotected sex* in the past six months with a potentially infectious person, as defined above
- a male resident in category 3 areas with transmission interrupted less than six months ago.

Travel-related risk for EU citizens

Travellers to affected areas (category 1 and 2) are at risk of becoming infected through mosquito bites. Infection during pregnancy can cause congenital microcephaly and other brain defects, therefore pregnant women constitute a high-risk group for serious adverse outcomes of Zika virus infection.

Based on the Zika virus country classification scheme, ECDC assesses the corresponding level of risk for travellers as presented in Table 1. The categories would support defining travel recommendations based on available evidence and local risk factors.

Table 1. Correspondence between risk for travellers and adapted WHO classification schema

Areas	Risk to travellers
WHO category 1 areas	High risk
WHO category 2 areas with new intense transmission (red hatched areas)	
WHO category 2 areas with no new intense transmission	Moderate
WHO category 4 areas bordering WHO category 2 areas (category 4a)	Low
WHO category 3 areas	Very low
WHO category 4 areas, not bordering a category 2 area (category 4b)	

^{*} Protected sex is defined as sexual contact during which appropriate barrier methods are correctly and consistently used in order to reduce the risk of sexually transmitted infections and sexually transmissible infections, such as Zika virus. Barrier methods include: male or female condoms for penetrative sex, including sex toys, and male or female condoms or dental dams for oral—genital or oral—anal sexual contact. To increase their effectiveness they should be used consistently and correctly, for the entire duration of sexual contact (United Nations position statement on condoms and the prevention of HIV, other sexually transmitted infections and unintended pregnancy, 7 July 2015).

Risk of importation and transmission in EU Outermost Regions and Overseas Countries and Territories

Residents in category 1 or 2 EU Outermost Regions (OMRs) and Overseas Countries and Territories (OCTs) with active vectors are at risk of exposure to Zika virus. *Aedes aegypti* mosquitoes are present in the EU OCTs and OMRs in the Americas and the Caribbean, and most of them have reported autochthonous transmission.

The risk of spread is related to the susceptible (naïve) populations, presence of competent vectors and permissive climate. EU OMRs and OCTs outside of the Caribbean where mosquito vectors are present, such as Madeira and Mayotte (category 4) with *Aedes aegypti*, or La Réunion with *Aedes albopictus* as the main mosquito vector, are at risk of local transmission should the virus be introduced [78]. The likelihood of vector-borne transmission in Madeira is considered very low due to unfavourable conditions for vector activity during the winter period.

Risk of importation and transmission within continental Europe

The probability of transmission of Zika virus infection is extremely low in the EU during early spring 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. However, there is no evidence to date of this mosquito species being able to sustain a Zika virus outbreak on its own.

According to the Interim Risk Assessment issued by the WHO Regional Office for Europe, the capacity to contain Zika virus transmission at an early stage is good for the countries of the WHO European Region overall [79].

Risk of sexual transmission

Since 28 October 2016, no major scientific developments have been reported which would indicate the need to amend the recommendations for prevention of sexual transmission published in the previous Rapid Risk Assessment - Zika virus disease epidemic (Ninth update, 28 October 2016).

A detailed description of current evidence related to sexual transmission is available in the <u>recent scientific findings</u> <u>based on literature reviews</u>.

The risk has not changed compared to the previous Rapid Risk Assessment - Zika virus disease epidemic.

Risk of Zika virus transmission via substances of human origin

Assessing the risk of Zika virus transmission through SoHO remains difficult due to the scarcity of data on virus transmission through transfusion and the absence of relevant data among the donors and recipients of other types of SoHO. Zika-virus-positive blood donations in affected and non-affected areas have been reported after the implementation of universal screening in the US [80,81]. In Martinique, the finding of a higher proportion of symptomatic cases among infected blood donors [73] than in the general population suggests that the ratio of asymptomatic/symptomatic infections may vary depending on local conditions [82].

In cooperation with a working group of experts from EU/EEA Member States, ECDC is currently updating the scientific advice document 'Zika virus and safety of substances of human origin - A guide for preparedness activities in EU'. The update covers the risk of Zika virus infection in SoHO donors exposed through sexual contact and changes to ECDC's country classification.

A temporary deferral (28 days) from donation for blood donors and living donors of non-reproductive tissues and cells is being considered for the update of 'Zika virus and safety of substances of human origin - A guide for preparedness activities in EU', despite recent findings showing that Zika virus RNA can be detected in whole blood up to 81 days post-symptom onset [68]. In another study, viral RNA has been detected 101 days post symptom onset in the whole blood of vasectomised travellers returning from Martinique [66]. The virus has not been isolated and infectivity not proven from such Zika virus RNA-positive whole blood samples [83]. This longer period of detection of the viral RNA in whole blood is consistent with similar findings for both West Nile virus [84] and dengue viruses [84], and has been attributed to the adsorbed viral RNA on the erythrocytes in the whole blood. These data raise the question of whether testing using plasma-based NATs to detect the Zika virus infection in humans is effective. The impact for transfusion recipients of transfused blood testing positive for Zika virus RNA based on whole blood or red blood cell samples, but testing negative with plasma testing is currently being investigated [86]. The suggested 28-day deferral for blood donors and living donors of non-reproductive tissues and cells who have had sexual contact with a person infected with Zika virus, or travelled to affected areas up to six months prior to sexual contact with a male or within two months prior to sexual contact with a female is also in line with current evidence and is made in order to harmonise the quide with ECDC and CDC advice for sexual precautions. The suggested deferral period for SoHo donation will be revised as and when new evidence becomes available.

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