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Rapid Risk Assessment: The risk of Zika virus to Canadians (first update)

The risk assessment is reviewed on a regular basis, and is updated as required.

Last reviewed: 11 April 2016
Last updated: 11 April 2016

What's New?

- In this update, we updated the likelihood of sexually-associated infection with ZIKV from **Very Low** to **Low**, based on new data on travel cases linked to sexual contact [1].
- We assessed several new scenarios not previously assessed, namely (i) the likelihood of sexual transmission under the specific assumption that the male partner was infected with ZIKV, (ii) the likelihood that native Canadian mosquito species could efficiently transmit ZIKV, and (iii) the impact of ZIKV infection assuming a severe outcome occurs.
- Finally, we increased our level of confidence for many statements in response to data or scientific publications made available since the last version's publication.

Summary

- An epidemic of mosquito-borne Zika virus (ZIKV) is occurring in many parts of the Americas and several other tropical/sub-tropical areas. The virus causes no or relatively mild illness in most adults. However, it also has been associated with more severe outcomes, e.g., Guillain Barré Syndrome (GBS), and associated with an increase in the likelihood of congenital abnormalities in the fetus.
- The mosquito implicated as the primary vector (*Aedes aegypti*) of ZIKV does not occur in Canada. Other implicated vectors (e.g., *Aedes albopictus*) are not known to be established in Canada. There are substantial barriers to long-term maintenance of ZIKV in Canada. Hence, risk of establishment of ZIKV in Canada is considered negligible. Local epidemic or endemic transmission is assessed as very unlikely (**Very Low** likelihood, with high confidence).
- Travel-related ZIKV infections have been reported among Canadian travellers. For the individual, it is estimated that travel to an affected area is associated with a medium chance of infection with ZIKV (**Medium** likelihood, with high confidence).
- Sexual transmission, from symptomatic male travellers to a sexual partner who has not travelled, has been reported. Because the likelihood of infection with ZIKV is considered low, so too is the likelihood of transmission via this route (**Low** likelihood, medium confidence). However, if a man does become infected with ZIKV, the likelihood of transmission to his sexual partner is assessed as **Medium** (low confidence).
- For most infected travellers, ZIKV will have little or no health impact (**Low** impact, with medium confidence). However, severe outcomes (e.g., GBS) might occur in some affected individuals (**High** impact, medium confidence).
- Based on recent evidence, we assess that there could be **Very High** impact (with medium confidence) to the unborn children of women who become infected with ZIKV while pregnant.
- Canadian recommendations for the prevention and management of ZIKV-disease (/publications/diseases-conditions-maladies-affections/committee-statement-treatment-prevention-zika-declaration-comite-traitement-prevention/index-eng.php) have been developed by the Committee to Advise on Tropical Medicine and Travel.

1. **Date of initial assessment**
   28 January 2016
2. **Date of last update**
   24 March 2016
3. **Risk identification**
   Individual and public health risk to Canadians associated with the 2015/16 ZIKV outbreak in the Americas.
4. **Prepared by**
   Public Health Agency of Canada, with expert consultation from the Department of National Defence, Force Health Protection
5. **Key information sources**
   See Reference list
6. **Review & update**
   This assessment will be revised as required, informed by a continuous review of outbreak data and the scientific literature. Triggers for a revision include substantial change in epidemiology, new scientific developments, or increased rates of severe outcomes.

Document information

In this Rapid Risk Assessment (RRA) document we assess the risk to Canadians posed by the ongoing Zika virus (ZIKV) epidemic. We separately consider the likelihood of infection with ZIKV and the impact of infection. We consider the likelihood of infection for (i) Canadians remaining in Canada (by assessing the likelihood of local mosquito-associated or sexual transmission), and (ii) Canadians travelling to countries with ongoing ZIKV activity. We then consider the impact of ZIKV infection. The terms "likelihood", "impact", and "confidence" are used in a specific sense, and are defined in Appendix 1.

Our assessments will change as more information becomes available, and this document will be updated accordingly.

Disease background information

Infectious agent

Zika virus disease is a mosquito-associated flaviviral disease caused by Zika virus (ZIKV). It is related to other *Flaviviridae*, including Japanese Encephalitis, West Nile, Yellow Fever, St. Louis Encephalitis, and Dengue viruses.

Transmission modes

The natural cycle of ZIKV involves mosquito vectors and vertebrate hosts, probably African primates [2] [3] [4]. There is limited documentation of non-primate reservoirs of ZIKV; serological evidence has been demonstrated in rodents [5], but their role (if any) in transmission is unknown. Once infected, a mosquito is thought to remain so for their lifetime [6]. Aside from mosquitos, blood transfusion-associated [7] [8] [9] and sexual transmission (via semen) has been documented. The latter includes several instances where symptomatic male travellers infected their partner, who had not travelled [10] [11] [1].

A significant concern with the current ZIKV outbreak is the potential for vertical transmission from mother to infant [12] [13] [14] [15] which, in Brazil and French Polynesia has been associated with a significant increase in congenital abnormalities including microcephaly [13] [14] [15] [16] [17] [18] [19].

Vector

Aedes aegypti is implicated as the primary vector of ZIKV (as well as Dengue and Yellow fever virus). This mosquito is largely restricted to tropical and subtropical regions, though more northern populations may occur in isolated refuges [20]. *Ae. albopictus* also has been implicated as a vector of ZIKV, though its role in the current outbreak is uncertain. This species is widely distributed outside the tropics [21], but is not known to be established in Canada.

Epidemiology

ZIKV was first identified in macaques in Uganda 1947, and then in humans in Uganda and Tanzania in 1952 [3] [22]. Over the next 50 years, few cases were reported and human ZIKV infection was restricted to Africa and parts of Asia. In 2007, the first major outbreak outside of these areas was reported on the island of Yap (Micronesia) in the southwestern Pacific Ocean [23]. Between 2013 and 2015, additional outbreaks occurred on islands and archipelagos in the Pacific region including a large outbreak in French Polynesia [24] [25]. An outbreak was also reported in Cape Verde [26]. More recently, the virus has caused widespread outbreaks across Central and South America, Mexico, and the Caribbean.

Clinical presentation

Asymptomatic infections appear to be the norm; only one in four or five people (20-25%) infected with ZIKV are believed to develop clinical symptoms [23] [27]. Disease is generally relatively mild, with symptoms that include: low-grade fever (usually <38.5°C), transient arthritis/arthralgia with possible joint swelling mainly in the smaller joints of the hands and feet, maculo-papular rash often spreading from the face to the body, conjunctival hyperaemia or bilateral non-purulent conjunctivitis, and general non-specific symptoms such as myalgia, asthenia, and headaches [23]. Less commonly, infection with ZIKV has been associated with serious complications such as Guillain Barré Syndrome (GBS) [a] [17] [28] and other neurologic complications [29] [30]. There have been a handful of reports of ZIKV-associated deaths in adults [14].

The incubation period (i.e. the amount of time between exposure and symptom onset) is thought to range from 3 to 12 days [31]. The disease symptoms are usually mild and last for 2 to 7 days. Most people recover fully without severe complications, and hospitalization rates are low [23]. Viremia (the period when ZIKV is measurably present in the blood) has been estimated as lasting 3 to 5 days following symptom onset [32] [33], although viral RNA has been detected in saliva [34] or urine [35] more than a week longer. Infection may go unrecognized or be misdiagnosed as dengue, chikungunya, or other viral infections causing fever and rash.

Event background information

Between 2013 and 2015, several significant outbreaks were noted on islands and archipelagos from the Pacific region including a large outbreak in French Polynesia [24] [25]. In 2015, ZIKV emerged in South America with widespread outbreaks reported in Brazil and Colombia. Locally acquired cases have been reported to WHO by many countries, mostly in the Americas (see the Agency's list of affected countries (/diseases-conditions-maladies-affections/disease-maladie/zika-virus/risks-countries-pays-risques-eng.php)). Evidence is accumulating that infection with ZIKV is associated with congenital abnormalities among children born to mothers infected during pregnancy, as well as with neurologic complications in a small proportion of infected persons. Information related to the ZIKV outbreak is rapidly evolving. For a summary of the most up-to-date information related to the ZIKV outbreak, readers are referred to the World Health Organization situation report (http://www.who.int/emergencies/zika-virus/en/).

Risk assessment

In this section, we consider i) the likelihood of infection with ZIKV for Canadians who have not travelled to an area where ZIKV is actively circulating, ii) the potential for local transmission (i.e., in Canada) of ZIKV, and iii) the likelihood of infection with ZIKV for travelling Canadians. We then separately consider the impact for individuals who become infected, first in the general case and then specifically for the unborn child of a woman infected while pregnant.

Likelihood of infection with ZIKV via blood and sexual transmission for Canadians who have not travelled

Human-to-human transmission of ZIKV can occur through several routes, including sexually [1] and via contaminated blood [8]. Individual Canadians who do not travel to areas of ongoing ZIKV outbreaks could be exposed to ZIKV in Canada via these routes.

Because ZIKV does not persist for long in the blood (typically 3-5 days following symptom onset) [32] [33], there is a narrow window for blood-based transmission. In general, almost all individuals should clear infection from their blood within 21 days (combining 12 days for incubation and an additional 9 days for blood viremia; personal communication, Dr. Scott Weaver, 24 January 2016). Given that Canadian blood safety agencies have enacted a 21-day donor deferral period following travel to ZIKV outbreak countries, the likelihood of transmission via this route is assessed as **Very Low** (with high confidence).

Several cases of sexual transmission from a symptomatic male to his sexual partner have been documented [1]. Indeed, it is thought that viable virus might persist in semen for at least several weeks after it has been cleared from the blood [8] [10] [11]. Because the likelihood of infection with ZIKV is considered low, so too is the likelihood of transmission via this route (**Low** likelihood, medium confidence). However, if a man does become infected with ZIKV, the likelihood of transmission to his sexual partner is assessed as **Medium** (low confidence). It is unknown if sexual transmission from asymptomatic but infected males to their partners is possible, or if infected females can transmit the virus to their partners.

Likelihood of local transmission in Canada

Here, we assess the likelihood of endemic or epidemic transmission of ZIKV in Canada. At the time of writing, there have been 32 confirmed cases of ZIKV in Canada, all resulting from travel to epidemic regions. Additional travel-associated cases are expected.

Local transmission would require the presence of a species of mosquito that can be infected with and transmit to human hosts ZIKV. *Ae. aegypti* is thought to be the principal vector in the current outbreak, with *Ae. albopictus* possibly playing a role. The distribution of *Ae. aegypti* is largely limited to tropical and subtropical areas and, while *Ae. albopictus* can occur in temperate regions, it also is limited by climate [21] [39] [40].

The likelihood that *Ae. aegypti* will become established in any area of Canada under current climatic conditions is estimated as **Very Low** (high confidence). This assessment is supported by a recent study [b] [21].

Ae. albopictus occurs in the United States, including the southern parts of some Eastern and upper Midwest states that border Canada. The likelihood that this species will become established in any area of Canada under current climatic conditions is considered **Low** (medium confidence [c]). This assessment is based on recent work [21] [39] [40] that estimated the current probability of this species occurring in most of Canada as at, or approaching, zero. However, one study did report that small areas in southern Ontario, southern Nova Scotia, as well as southern coastal British Columbia had low to moderate climatic suitability for this species [40].

Self-sustaining populations of the mosquitoes associated with the current ZIKV outbreak are not thought to occur in Canada. On this assumption of absence of *Ae. aegypti*, or absence of *Ae. albopictus* from all but a very few limited locations in Canada, there is **Very Low** likelihood (with high confidence) of epidemic spread and subsequent endemic establishment of ZIKV in Canada.

It is not known if mosquitoes that occur in Canada are capable of transmitting ZIKV nor, if they are, whether they could do so in their natural environment. However, the absence of reports of autochthonous transmission of ZIKV or other arboviruses associated with warm climates (e.g., dengue viruses, chikungunya virus) in Canada or similar climatic regions suggests that, even if native species could transmit ZIKV, they are very unlikely to support anything other than sporadic transmission (**Very Low** likelihood, high confidence).

Assumptions for assessments of likelihood of local transmission

We have made a number of assumptions in assessing the likelihood of local transmission:

1. Populations of *Ae. aegypti*, are not established in Canada. This assumption is supported by a robust assessment of the distribution of this vector species [21].
2. Populations of *Ae. albopictus* are not established in Canada, or occur with a geographic distribution too limited to support endemic transmission of ZIKV. This assumption is supported by robust assessments of the distribution [17] and climatic suitability of Canada [40] for this species as well as its absence (except for rare individual specimens in southeastern Canada) in recent mosquito surveillance for West Nile virus in Canada.
3. Other mosquito species occurring in Canada are not capable of maintaining cycles of Zika virus transmission. This assumption is based upon the absence of records of ZIKV from northern temperate regions of the world [41] [42] [43].
4. There are temperature limitations to transmission of ZIKV (e.g., effects of temperature on the extrinsic incubation period in mosquitoes) that limit endemic transmission to tropical and sub-tropical areas. This assumption is based on similar limits on transmission of dengue [41] [42] [43] [44] [45] [46].
5. There are no alternative (i.e. non-mosquito-borne) routes of ZIKV transmission, including sexual transmission [d], capable of maintaining epidemic or endemic transmission cycles in Canada.

Likelihood of ZIKV infection for travellers

At the time of writing, many countries have reported recent, locally-acquired ZIKV cases (/diseases-conditions-maladies-affections/disease-maladie/zika-virus/risks-countries-pays-risques-eng.php). Continued spread of ZIKV is expected [44] with the result that more areas will present a risk to Canadian travellers. To date, of approximately 1,150 individuals tested by the Canadian health care sector, 33 (~3%) have yielded positive results for ZIKV infection (personal communication, Dr. Theodore Kuschak, March 21 2016). All cases acquired ZIKV via recent travel to: Barbados (n=10), Brazil (n=1), Central America (Honduras, Panama, and Guatemala; n=1), Colombia (n=5), Dominical Republic (n=1), El Salvador (n=5), Guyana (n=1), Haiti (n=7), Nicaragua (1), and Venezuela (1). Thus, among Canadians

who have travelled to countries with active ZIKV transmission, the likelihood of infection is **Medium** (with high confidence). However, only a small minority of Canadians who have travelled to areas of risk have been tested. Hence, the true prevalence of ZIKV infection among Canadian travellers is uncertain, but is likely substantially lower than the estimated 3% among individuals who have been tested to date.

Factors that could affect the likelihood or impact of infection

The impact of traveller- and/or itinerary-specific factors on the likelihood or impact of ZIKV infection has not been well described. However, there are a number of plausible relationships:

- Conditions at higher elevations (≥ 2,000 m) are generally not supportive of viral replication in, or survival of, *Ae. aegypti* populations. Correspondingly, the relative likelihood of infection with ZIKV might be substantially lower for travellers (depending on how much time they spend at altitude compared to lower elevations) to such areas.
- All else held equal, the likelihood of infection is higher in countries/areas that are reporting high levels of ZIKV activity compared to those that are not.
- The likelihood of infection is likely lower for shorter travel durations and/or when staying in protected environments (e.g., well screened and air-conditioned accommodations, transiting through an airport in a risk area). This might also apply to situations where the traveller is staying in an isolated location, i.e. where there are relatively few residents who might support sustained transmission.
- Travellers with co-morbidities (often, these are associated with age) might be at increased risk for more serious ZIKV-associated outcomes.

Impact of ZIKV infection

For most travellers, ZIKV will have little or no health impact (**Low** impact, with medium confidence). This is because infection will be relatively infrequent, and, of those infected, only about 20-25% will develop illness, most of it mild [23] [27].

However, rare but severe outcomes have been reported [37]. Cases of GBS and other neurological syndromes [29] [30] have now been reported in twelve countries or territories affected by the current outbreak [48]. The most compelling evidence comes from a retrospective case-control study done with patients from French Polynesia ZIKV outbreak during 2013-2104 [28]. Among the 42 GB cases, all but one (98%) showed serologic evidence (anti-ZIKV IgM and IgG) of ZIKV infection, compared to 35 of 98 (36%) matched controls (Odds Ratio 59.7, 95% Confidence Interval 10.4 to ∞). Based on an estimated ZIKV attack rate of 66% among the population of French Polynesia the authors estimate the proportion of post-ZIKV infection GBS as approximately 1 GBS case per 4,000 ZIKV infections. This estimate would put

ZIKV among the higher-risk pathogens of those known to cause GBS, equal to or less than the risk posed by *Campylobacter jejuni* (1 to 2.6 GBS cases per 4,000 infections [46]), and less that the risk posed by cytomegalovirus (2.4 to 8.8 GBS cases per 4,000 infections [47]). However, while such evidence provides strong support for the role of ZIKV as a presumptive infection event preceding neurologic complications, a direct causal relationship has not been established.

Again, for most infected travellers, ZIKV will have little or no health impact (**Low** impact, with medium confidence). Severe outcomes (e.g., GBS) might occur in some affected individuals (**High** impact, medium confidence).

Impact of infection on unborn children of women who acquire ZIKV

The unborn children of women who become infected with ZIKV while pregnant are of special concern. This reflects the association of ZIKV with the significant increase in microcephaly in Brazil and French Polynesia. Locally-acquired ZIKV cases have been reported in Brazil since February 2015 [33]. Between 22 October 2015 and 12 March 2016, 6480 cases of microcephaly and/or central nervous system malformation were reported by Brazil (including 182 deaths) [48]. This is a sharp increase from previous years, but it is important to note that investigations have been concluded for only 2212 cases, of which just 863 were confirmed to be associated with ZIKV infection [48].

The co-occurrence of these two unusual events (the ZIKV outbreak and apparent increased rates of microcephaly) would be highly unexpected unless ZIKV were a contributing cause to microcephaly. In addition, in at least six cases, viral genome of ZIKV was detected by RT-PCR technique in samples from newborns and/or miscarriages [38]. Further, interim results from a cohort study in Brazil detected fetal anomalies in 12 of 42 ZIKV-positive women, and 0 of 16 ZIKV-negative women [49], which provides additional evidence of a causal link. Recent work, based on data from the French Polynesian outbreak, estimated the probability of congenital anomalies as about 1% of ZIKV infections during pregnancy (based on seropositivity during pregnancy), with simulation results that support first trimester infection as being most predictive of the observed rate of anomalies [50]. Of note, these studies reached different conclusions on the importance of timing of infection; the Brazilian study [49] observed poor outcomes following infection in any trimester, while the French Polynesian study [50] suggests that first trimester infection may be more detrimental. Further research is required to clarify this issue.

Aside from Brazil and French Polynesia, evidence of an association between ZIKV and congenital anomalies has not been reported from other countries affected by the current outbreak. One possible explanation for this is that the virus was first imported to the Americas in Brazil, as early as 2014 [53], and therefore precedes outbreaks in other affected countries such as Colombia and El Salvador. Highly-affected Colombia reports plans to enhance surveillance [52]. We note one report from the Brazil Ministry of Health analysing a small number of women in Pernambuco found that all mothers with newborn babies that had microcephaly belonged to low-income families [51], which suggests the involvement of other risk factors related to low-income households. It is plausible that other socioeconomic explanations (e.g. fewer resources devoted to surveillance, resulting in underreporting) explain why the association between ZIKV and congenital anomalies has not been observed elsewhere. More information is needed from other countries to determine the significance these findings.

In conclusion, there is mounting evidence to support the possible link between infection with ZIKV and infant microcephaly. Substantial effort is being directed towards clarifying the causal link, the effect of timing of infection on fetal development, and determining if there are other contributing risk factors (i.e. co-infection or serial infection with other viruses, nutritional status, or other environmental factors) [54]. Future scientific results could change this judgement substantially, but we estimate a **Very High** impact (with medium confidence) on the unborn child of a woman who acquires ZIKV while pregnant.

Biosafety information for laboratory workers

ZIKV is classified as a Risk Group 2 human pathogen, since this virus presents a moderate individual risk and a low community risk. Laboratory work involving ZIKV requires Containment Level 2 physical and operational requirements as outlined in the Canadian Biosafety Standard (http://canadianbiosafetystandards.collaboration.gc.ca/cbs-ncb/index-eng.php). The impact on the unborn children of pregnant women working in the laboratory with ZIKV could be **Very High** (with medium confidence; see Impact section), if she became infected.

The main risks for laboratory acquired infection include accidental auto-inoculation and exposure to specimens from viremic patients, experimentally-infected animals, or ZIKV cultures. Local risk assessments should take into consideration the activities taking place in the laboratory to determine if risk reduction strategies in place are sufficient. Pregnant women or women trying to get pregnant should be made aware of the potential risks for the fetus and take extra care when working in a laboratory where ZIKV is propagated or handled.

Conclusions and Risk mitigation

In summary, we conclude that the overall risk of infection to Canadians (while in Canada) is very low. This is driven by the **Very Low** likelihood of exposure in Canada through mosquito-based transmission. An exception is transmission from symptomatic males to their sexual partner (**Medium** likelihood, with low confidence). The overall likelihood of infection for a Canadian travelling to an outbreak area is **Low** (medium confidence), and the impact for most of those infected will be **Low** (medium confidence). However, for some of those who are infected, impact may be **High** (medium confidence) specifically because of the association with severe outcomes such as GBS. Although pregnant women or those who may soon become pregnant are assumed to be equally likely to be infected as are other travellers, the impact of such infection could be, for the unborn child, **Very High** (medium confidence).

Persons considering travel should consult the Agency's Travel Health Notice on ZIKV (http://travel.gc.ca/travelling/health-safety/travel-health-notices/143), and Canadian recommendations for the prevention and management of ZIKV-disease (/publications/diseases-conditions-maladies-affections/committee-statement-treatment-prevention-zika-declaration-comite-traitement-prevention/index-eng.php) developed by the Committee to Advise on Tropical Medicine and Travel.

What can be anticipated in the next 6 months

The Agency continues to closely monitor the situation. Changes in scientific information are continually monitored, and this review will be updated on an as-needed basis.

Footnotes

a Risk of GBS was estimated as ~ 1 per 4,000 infections in the French Polynesia outbreak.

b Also see section on assumptions for estimates of local transmission.

c We reduced our confidence estimate from high to medium based on the listed assumptions (and associated limitations)

d We note that if ZIKV were efficiently sexually transmissible, we would expect much wider geographic distribution than has been observed.

References

1 *Travel-Associated Zika Virus Disease Cases Among U.S. Residents — United States, January 2015–February 2016.* **Armstrong P, Hennessey M, Adams M, et al.** s.l. : MMWR Morb Mortal Wkly Rep, 2016, Vol. ePub: 18 March 2016.

2 *Zika Virus in the Americas — Yet Another Arbovirus Threat.* **Fauci, M.D and Morens, D.M.** s.l. : New England Journal of Medicine, 2016, Vol. Published online 2016/01/13.

3 *Sylvatic Transmission of Arboviruses Among Bornean Orangutans.* **Wolfe, N, et al., et al.** s.l. : Am. J. Trop. Med. Hyg., Vols. 64(5, 6), 2001, pp. 310–316.

4 *Zika virus. II. Pathogenicity and physical properties.* **Dick , G.** s.l. : Trans RSoc Trop Med Hyg, 1952, Vols. 46:521–34.

5 *A sero-epidemiological survey for certain arboviruses (Togaviridae) in Pakistan.* **Darwish, M, et al., et al.** s.l. : Trans R Soc Trop Med Hyg, 1983, Vols. 77(4):442-5.

6 *Current Zika virus epidemiology and recent epidemics.* **Ioos, S, et al., et al.** s.l. : Médecine et maladies infectieuses , 2014, Vols. 44 302–307.

7 *Seroprevalence of arboviruses among blood donors in French Polynesia, 2011-2013.* **Aubry M, Finke J, Teissier A, Roche C, Broult J, Paulous S, et al.** December, s.l. : International Journal of Infectious Diseases, 2015, Vol. 41.

8 *Potential for Zika virus transmission through blood transfusion demonstrated during an outbreak in French Polynesia, November 2013 to February 2014.* **Musso D, Nhan T, Robin E, Roche C, Bierlaire D, Zisou K, Shan Yan A, Cao-Lormeau VM, Broult** 2014, Eurosurveillance, pp. Volume 19, Issue 14.

9 Outbreak News Today. [Online] 2015. 3. http://outbreaknewstoday.com/transfusion-associated-zika-virus-reported-in-brazil-76935/.

10 *Probable non-vector-borne transmission of Zika virus, Colorado, USA. .* **Foy, B, et al., et al.** 2011, Emerging Infectious Diseases, pp. May;17(5):880-.

11 *Potential Sexual Transmission of Zika Virus.* **Musso, D, et al., et al.** 2015, Emerging Infectious Diseases, pp. Volume 21, Number 2—February 2015.

12 *Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014.* **Besnard , M, et al., et al.** 2014, Eurosurveillance, p. 19(13).

13 *Zika virus intrauterine infection causes fetal brain abnormality and microcephaly: tip of the iceberg?* **Melo, A, et al., et al.** s.l. : Ultrasound Obstet Gynecol, 2016, Vols. 47: 6–7.

14 **PAHO.** Epidemiological alert Neurological syndrome, congenital malformations, and Zika virus infection. Implications for public health in the Americas. [Online] 12 01, 2015. [Cited: 12 16, 2015.] http://www.paho.org/hq/index.php?option=com_topics&view=article&id=427.

15 **Brazil Ministry of Health.** Epidemiological report 7 Microcephaly. [Online] 1 6, 2016. [Cited: 1 6, 2016.] http://portalsaude.saude.gov.br/images/pdf/2016/janeiro/05/COES-Microcefalias---Informe-Epidemiol--gico-07---SE-52---04jan2016.pdf.

16 **PAHO.** Epidemiological Alert- Increase in Microcephaly in the northeast of Brazil. *PAHO.* [Online] 2015. [Cited: 12 16, 2015.] http://www.paho.org/hq/index.php?option=com_topics&view=readall&cid=7880&Itemid=41484&lang=en.

17 *Zika Virus as a Cause of Neurologic Disorders.* **Broutet N, Krauer F, Riesen M, Khalakdina A, Almiron M, Aldighieri S, Espinal M, Low N, Dye C.** March 9, s.l. : New England Journal of Medicine, 2016.

18 *Association between Zika virus and microcephaly in French Polynesia, 2013–15: a retrospective study.* **Cauchemez S, Besnard M, Bompard P, Dub T, Guillemette-Artur P, Eyrolle-Guignot D, Salje H, Van Kerkhove MD, Abadie V, Garel C, Fontanet A.** March 16, s.l. : The Lancet, 2016.

19 *Detection and sequencing of Zika virus from amniotic fluid of fetuses with microcephaly in Brazil: a case study.* **Calvet G, Aguiar RS, Melo AS, Sampaio SA, de Filippis I, Fabri A, Araujo ES, de Sequeira PC, de Mendonça MC, de Oliveira L, Tschoeke DA.** February 18, s.l. : The Lancet Infectious Diseases, 2016.

20 *Evidence for an Overwintering Population of Aedes aegypti in Capitol Hill Neighborhood, Washington, DC.* **Lima A, Lovin DD, Hickner PV, Severson DW.** 1, s.l. : American Journal of Tropical Medicine and Hygiene, 2016, Vol. 94.

21 *The global distribution of the arbovirus vectors Aedes aegypti and Ae. albopictus.* **Kraemer MU, Sinka ME, Duda KA, Mylne AQ, Shearer FM, Barker CM, Moore CG, Carvalho RG, Coelho GE, Van Bortel W, Hendrickx G, Schaffner F, Elyazar IR, Teng HJ, Brady OJ, Messina JP, Pigott DM, Scott TW, Smith DL, Wint GR, Golding N, Hay SI.** 08347, s.l. : Elife, Vol. 4.

22 *Zika virus. I. Isolations and serologicalspecificity.* **Dick, G, Kitchen, S and Haddow, A.** s.l. : Trans R Soc Trop Med Hyg, 1952, Vols. 46(5):509–20.

23 *Zika virus outbreak on Yap Island, Federated States of Micronesia.* **Duffy , M, et al., et al.** s.l. : New England Journal of Medicine, 2009, Vols. 360:2536–43.

24 *Emerging arboviruses in the Pacific.* **Cao-Lormeau, V and Musso, D.** s.l. : Lancet, 2014, Vol. Vol 384.

25 *Rapid spread of emerging Zika virus in the Pacific area.* **Musso, D, Nilles, E and Cao-Lormeau, V.** s.l. : Clin Microbiol Infect, 2014, Vols. published online June 7. DOI:10.1111/1469-0691.12707.

26 **World Health Organization.** Zika virus infection - Cape Verde. *World Health Organization .* [Online] 12 21, 2015. [Cited: 01 11, 2016.]

27 **ECDC.** ZIKA Fact Sheet for Health Professionals. [Online] 11 27, 2015. [Cited: 12 16, 2015.] 6. http://ecdc.europa.eu/en/healthtopics/zika_virus_infection/factsheet-health-professionals/Pages/factsheet_health_professionals.aspx.

28 *Guillain-Barré Syndrome outbreak associated with Zika virus infection in French Polynesia: a case-control study.* **Cao-Lormeau VM, Blake A, Mons S, Lastère S, Roche C, Vanhomwegen J, Dub T, Baudouin L, Teissier A, Larre P, Vial AL.** March 2, s.l. : The Lancet, 2016, Vol. Published online.

29 *Zika Virus Associated with Meningoencephalitis.* **Carteaux G, Maquart M, Bedet A, Contou D, Brugières P, Fourati S, Cleret de Langavant L, de Broucker T, Brun-Buisson C, Leparc-Goffart I, Mekontso Dessap A.** March 9, s.l. : New England Journal of Medicine, 2016, Vol. Published online.

30 *Acute myelitis due to Zika virus infection.* **Mécharles S, Herrmann C, Poullain P, Tran TH, Deschamps N, Mathon G, Landais A, Breurec S, Lannuzel A.** March 4, s.l. : The Lancet, 2016, Vol. Published online.

31 *Current Zika virus epidemiology and recent epidemics.* **Ioos S, Mallet HP, Leparc Goffart I, Gauthier V, Cardoso T, Herida M.** 7, s.l. : Eurosurveillance, 2014, Vol. 44.

32 *A diagnostic polymerase chain reaction assay for Zika virus.* **Balm MN, Lee CK, Lee HK, Chiu L, Koay ES, Tang JW.** 9, s.l. : Journal of medical virology, 2012, Vol. 84.

33 **ECDC.** Rapid Risk Assessment- Zika virus epidemic in the Americas: Potential association with microcephaly and Guillain-Barré syndrome. [Online] 12 10, 2015. [Cited: 12 10, 2015.] http://ecdc.europa.eu/en/publications/Publications/zika-virus-americas-association-with-microcephaly-rapid-risk-assessment.pdf.

34 *Detection of Zika virus in saliva.* **Musso D, Roche C, Nhan TX, Robin E, Teissier A, Cao-Lormeau VM.** s.l. : Journal of Clinical Virology, 2015, Vol. 68.

35 *Detection of zika virus in urine.* **Gourinat AC, O'Connor O, Calvez E, Goarant C, Dupont-Rouzeyrol M.** 1, s.l. : Emerging infectious diseases, 2015, Vol. 21.

36 *Zika virus infection complicated by Guillain-Barré syndrome – case report, French Polynesia December 2013.* **Oehler, E, et al., et al.** s.l. : Eurosurveillance, 2014, Vol. 2014;19(9):pii=20720.

37 **Pan American Health Organization / World Health Organization.** Epidemiological Update: Neurological syndrome, congenital anomalies and Zika virus infection. [Online] 1 17, 2016. [Cited: 1 19, 2016.] http://www.paho.org/.

38 **Brazil Ministry of Health.** Brazil Ministry of Health. *INFORME EPIDEMIOLÓGICO Nº 09– SEMANA EPIDEMIOLÓGICA(SE)02/2016 (10A16/01/2016) MONITORAMENTO DOS CASOS DE MICROCEFALIA NO BRASIL.* [Online] 1 16, 2016. [Cited: 1 22, 2016.] http://portalsaude.saude.gov.br/images/pdf/2016/janeiro/21/COES-Microcefalias---Informe-Epidemiol--gico-SE-02-2016.pdf.

39 *Projection of climatic suitability for Aedes albopictus Skuse (Culicidae) in Europe under climate change conditions.* **Fischer D, Thomas SM, Niemitz F, Reineking B, Beierkuhnlein C.** 1, s.l. : Global and Planetary Change, 2011, Vol. 78.

40 *Recent and projected future climatic suitability of North America for the Asian tiger mosquito Aedes albopictus .* **Ogden, N H, et al., et al.** 7, 532, s.l. : Parasites & Vectors, 2014.

41 *Zika virus outside Africa.* **EB, Hayes.** 9, s.l. : Emerging Infectious Diseases, 2009, Vol. 15.

42 *Zoonotic mosquito-borne flaviviruses: worldwide presence of agents with proven pathogenicity and potential candidates of future emerging diseases.* **Weissenböck H1, Hubálek Z, Bakonyi T, Nowotny N.** 3-4, s.l. : Veterinary Microbiology, 2010, Vol. 140.

43 *Zika virus: following the path of dengue and chikungunya?* **Musso D, Cao-Lormeau VM, Gubler DJ.** 9990, 2015, Vol. 386.

44 *Anticipating the international spread of Zika virus from Brazil.* **Bogoch II, Brady OJ, Kraemer MU, German M, Creatore MI, Kulkarni MA, Brownstein JS, Mekaru SR, Hay SI, Groot E, Watts A., Khan K.** 10016, s.l. : Lancet, 2016, Vol. 387.

45 *Modelling adult Aedes aegypti and Aedes albopictus survival at different temperatures in laboratory and field settings.* **Brady OJ, Johansson MA, Guerra CA, Bhatt S, Golding N, Pigott DM, Delatte H, Grech MG, Leisnham PT, Maciel-de-Freitas R, Styer LM.** 1, s.l. : Parasites & vectors, 2013, Vol. 6.

46 *Global temperature constraints on Aedes aegypti and Ae. albopictus persistence and competence for dengue virus transmission.* **Brady OJ, Golding N, Pigott DM, Kraemer MU, Messina JP, Reiner Jr RC, Scott TW, Smith DL, Gething PW, Hay SI.** 338, s.l. : Parasit Vectors, 2014, Vol. 7.

47 **ECDC.** Rapid Risk Assessment: Zika virus outbreak, French Polynesia 14 February 2014. *ECDC.* [Online] 2 14, 2014. [Cited: 1 22, 2016.] http://docs.google.com/viewer?url=http://ecdc.europa.eu/en/publications/Publications/Zika-virus-French-Polynesia-rapid-risk-assessment.pdf?time=0.

48 **World Health Organization.** Zika virus, Microcephaly and Guillain-Barré syndrome. [Online] March 17, 2016. [Cited: March 21, 2016.] http://apps.who.int/iris/bitstream/10665/204633/1/zikasitrep_17Mar2016_eng.pdf?ua=1.

49 *Zika virus infection in pregnant women in Rio de Janeiro—preliminary report.* **Brasil P, Pereira, Jr JP, Raja Gabaglia C, Damasceno L, Wakimoto M, Ribeiro Nogueira RM, Carvalho de Sequeira P, Machado Siqueira A, Abreu de Carvalho LM, Cotrim da Cunha D, Calvet GA.** March 4, s.l. : New England Journal of Medicine, 2016, Vol. Published online.

50 *Association between Zika virus and microcephaly in French Polynesia, 2013–15: a retrospective study.* **Cauchemez S, Besnard M, Bompard P, Dub T, Guillemette-Artur P, Eyrolle-Guignot D, Salje H, Van Kerkhove MD, Abadie V, Garel C, Fontanet A.** March 16, s.l. : The Lancet, 2016, Vol. Published online.

51 *A new mosquito-borne threat to pregnant women in Brazil.* **Truinfol, M.** s.l. : Lancet, 2015, Vols. December 23, 2015.

52 The risks to pregnant women due to the Zika virus. [Online] http:/www.elespectador.com/noticias/salud/los-risks-of-pregnant woman s-the-virus-of the-zika-article-609254.

53 *Zika Virus Transmission from French Polynesia to Brazil.* **Musso, D.** s.l. : Emerging Infectious Disease, 2015, Vols. Vol. 21, No. 10, October .

54 *Zika and microcephaly: Causation, correlation, or coincidence?* **Tetro, J.A.** Microbes and Infection : s.n., 2016, Vol. In press.

55 *Zika Virus Outbreak, Bahia, Brazil.* **Campos , G, Bandeira, A and Sardi, S.** 10, s.l. : Emerging Infectious Diseases, 2015, Vol. 21.

56 **PAHO.** Zika virus infection. *PAHO.* [Online] 1 2, 2016. [Cited: 1 5, 2016.]

57 *Quantitative risk assessment for authochthonous transmission of Chikungunya virus and Zika virus in Canada.* **Ng V, Faizil A, Mascarenhas M, Ogden N.** Forthcoming 2016.

58 *Is there a risk of chikungunya transmission in Canada?* **Ogden, N H, Lindsay , L R and Coulthart, M.** 41, 11-14, s.l. : Canada Communicable Disease Report, 2015.

59 **PAHO.** Epidemiological Alert May 7 2015 Zika virus infection. *PAHO.* [Online] 5 7, 2015. [Cited: 12 18, 2015.]

60 *Texas Lifestyle Limits Transmission of Dengue Virus.* **Reiter P, Lathrop S, Bunning M, Biggerstaff B, Singer D, Tiwari T, Baber L, Amador M, Thirion J, Hayes J,**

Seca C. 1, s.l. : Emerging Infectious Diseases, 2003, Vol. 9.

61 *Incidence of Guillain-Barré syndrome following infection with Campylobacter jejuni.* **McCarthy N, Giesecke J.** 6, s.l. : American Journal of Epidemiology, 2001, Vol. 153.

62 *Evidence of perinatal transmission of Zika virus, French Polynesia, December 2013 and February 2014.* **Besnard M, Lastere S, Teissier A, Cao-Lormeau V, Musso D.** 13, s.l. : Eurosurveillance, 2014, Vol. 19.

63 *Anticipating the international spread of Zika virus from Brazil.* **Bogoch II, Brady OJ, Kraemer MU, German M, Creatore MI, Kulkarni MA, Brownstein JS, Mekaru SR, Hay SI, Groot E, Watts A, Khan K.** s.l. : Lancet, Vol. [Epub ahead of print].

Appendix 1 – Definition of technical terms

Table 1: Working definitions for likelihood levels

Level	Definition
Very low	Could occur only under exceptional circumstances
Low	Could occur some of the time
Medium	Will occur some of the time
High	Is expected to occur in most circumstances

Table 2: Working definitions for impact levels

Level	Impact
Very low	Limited impact on the affected population Few extra costs for authorities and stakeholders
Low	Minor impact for a small population or at-risk group Some increase in costs for stakeholders
Medium	Moderate impact, as a large population or at-risk group is affected Moderate increase in costs for stakeholders
High	Major impact for a small population or at-risk group Significant increase in costs for stakeholders
Very high	Severe impact for a large population or at-risk group Serious increase in costs for stakeholders

Table 3: Working definitions for confidence levels

Level	Definition	Examples of information/evidence
Low	Little or poor-quality evidence, significant uncertainty, conflicting views amongst experts, no experience with similar incidents. Further research is likely to have significant impact on the results of the assessment. Further research is very likely to change the results of the assessment and the confidence in the assessment and the information used.	Individual case reports Grey literature Individual, non-expert opinion
Medium	Adequate quality of evidence, including consistent results, reliable source(s), and assumptions made on analogy. Agreement between experts or opinions of two trusted experts. Further research may necessitate some changes to the assessment. Further research is likely to have an impact on the confidence in the assessment and information used. It may change the results of the assessment.	Non-peer-reviewed published studies/reports Observational studies Surveillance reports Outbreak reports Individual, expert opinion
High	Good-quality evidence, multiple reliable sources, verified, multiple expert opinions concur, experience with previous and similar events. Further research is unlikely to change the results of the assessment. Further research is unlikely to change the confidence in the assessment.	Peer-reviewed published studies where design and analysis reduce bias (i.e. systematic reviews, RCT, outbreak report). Textbooks regarded as definitive sources. Expert group risk assessment, or specialized expert knowledge, or consensus opinion of experts.

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Government of Canada activities and initiatives

Canada Child Benefit

(http://www.budget.gc.ca/2016/tool-outil/ccb-ace-en.html?utm_source=CanCa&utm_medium=Priority&utm_content=Calculator&utm_campaign=Budget16)

Calculate your Canada Child Benefit amount.

An innovative and clean economy

(http://www.budget.gc.ca/2016/docs/bb/brief-bref-en.html#section02?utm_source=CanCa&utm_medium=Carousel&utm_content=Tile&utm_campaign=Budget16)

Protecting the environment and growing the economy go hand in hand.

Have your say on climate change today!

(http://canada.ca/en/services/environment/weather/climatechange/climate-action.html)

Share your ideas on how to address climate change