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Coming to a Shore Near You: Zika and other Emerging Infectious Diseases

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EIDs – Two Major Categories

Newly emerging:
Newly recognized in human hosts

Re-emerging – have historically infected humans:
Appear in new locations
Appear in drug-resistant forms
Reappear after control/elimination

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But don't forget the following:

- MERS-CoV
- Chikungunya virus
- Influenza H7N9
- Ebola virus in West Africa
- Avian influenza H5N2 and others
- Zika virus
- Yellow fever (Angola, Brazil)

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Factors in the Emergence of Infectious Diseases

<p>1992</p> <ul style="list-style-type: none"> • Microbial adaptation and change • Economic development and land use • Human demographics and behavior • International travel and commerce • Technology and industry • Breakdown of public health measures 	<p>2003</p> <ul style="list-style-type: none"> • Microbial adaptation and change • Human susceptibility to infection • Climate and weather • Changing ecosystems • Human demographics and behavior • Economic development and land use • International travel and commerce • Technology and industry • Breakdown of public health measures • Poverty and social inequality • War and famine • Lack of political will • Intent to harm
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PublicHealthOntario.ca Source: [JOM \(2003\)](#) 5

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Challenges of Newly Emerging Infections

Need to rapidly learn about:

- Transmission, e.g. incubation period, communicability
- Clinical presentations and consequences
- At-risk populations
- Treatments
- Prevention, e.g. vaccines
- IP&C measures

Risk assessment
Communication
Education, training

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Our globally inter-connected reality


- The frontlines of infectious disease surveillance and response are not border-crossings/ports-of-entry.
- They are:
 - Primary care/urgent care
 - Emergency departments/hospitals
- EMS
- Community care
- LTC

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Transmission and Incubation Period

- Transmitted by *Aedes aegypti* mosquitos
- Incubation period - 3 to 12 days (may be up to 14 days)
- Usually causes a mild, self limiting illness
 - Maculopapular rash
 - Low grade fever
 - Conjunctivitis
 - Arthralgia



Source: <http://www.theguardian.com/2015/11/deaths-from-dengue-rise-to-three-in-yucatan-three-cases-of-zika-reported-in-mexico/>

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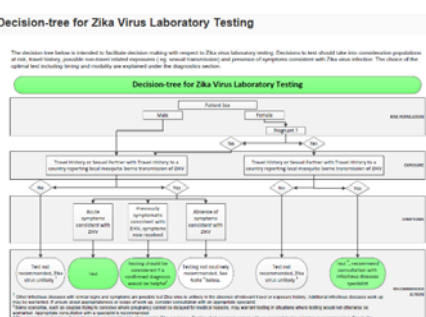
Acute Zika Virus Infection: Clinical Management

- Supportive management
 - No antiviral therapy available for Zika virus infection.
 - Rest, fluids to avoid dehydration
 - Antipyretics, analgesics
- Do not take aspirin and other non-steroidal anti-inflammatory drugs (NSAIDs) until dengue ruled out, and do not use them in pregnant patients.
- Avoid mosquito bites until a week after symptom onset (to prevent spread to others)

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Decision-tree for Zika Virus Laboratory Testing

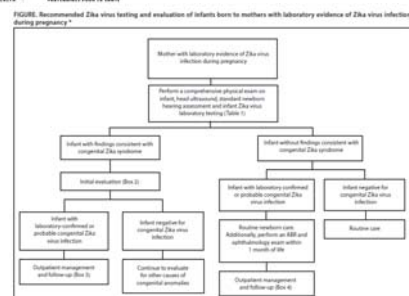


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Source: <http://www.cdc.gov/mmwr/volumes/55/wr/mm5512a2.htm>

FIGURE 2. Recommended Zika virus testing and evaluation of infants born to mothers with laboratory evidence of Zika virus infection during pregnancy*



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Source: <http://www.cdc.gov/mmwr/volumes/55/wr/mm5512a2.htm>

BOX 2. Initial clinical evaluation and management of infants with laboratory evidence of Zika virus infection and abnormalities consistent with congenital Zika syndrome

- Consultation with:
 - Neurologist for determination of appropriate neuroimaging and additional evaluation.
 - Infectious disease specialist for diagnostic evaluation of other congenital infections (e.g., syphilis, toxoplasmosis, rubella, cytomegalovirus infection, lymphocytic choriomeningitis virus infection, and herpes simplex virus infection).
 - Ophthalmologist for comprehensive eye exam and evaluation for possible cortical visual impairment prior to discharge from the hospital or within 1 month of birth.
 - Endocrinologist for evaluation for hyperthalamia or pituitary dysfunction.
 - Clinical geneticist to evaluate for other causes of microcephaly or other anomalies if present.
- Consider consultation with:
 - Otolaryngologist, physician, or physical therapist for the management of hypernatremia, club foot or arthrogryposis-like conditions.
 - Pulmonologist or occupational therapist for concerns about apnea.
 - Lactation specialist, nutritionist, gastroenterologist, or speech or occupational therapist for the management of feeding issues.
- Perform auditory brainstem response to assess hearing.
- Perform complete blood count and metabolic panel, including liver function tests.
- Provide family and supportive services.

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Testing Modalities Available

- Molecular detection: real-time RT-PCR (PHOL)
 - Blood/urine up to 14 days post-symptom onset
 - Combined with CHIKV and dengue PCRs if symptomatic
- Serology (NML)
 - ELISA IgM
 - Plaque reduction neutralization titre (PRNT)
- Antigen detection
 - Immunohistochemistry (CDC only)
 - Immunochromatographic tests
- Virus Culture

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Zika virus IgM serology

- Zika virus IgM reactive specimens are considered indicative of a recent **flavivirus** infection.
- IgM antibodies against Zika, dengue, West Nile and other flaviviruses have strong cross reactivity in serological assays
- Current assays cannot reliably distinguish between Zika and dengue virus infections.
 - IgM reactive specimens will be further investigated by neutralization assays (PRNT).

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Asian lineage detected in French Polynesia, 2014 and Suriname, 2015

Complete Coding Sequence of Zika Virus from a French Polynasia Outbreak in 2013

First Complete Genome Sequence of Zika Virus (Flaviviridae, Flavivirus) from an Autochthonous Transmission in Brazil

Sources: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4047448/>
<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC477745/>

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Worldwide spread of Zika virus

How the Zika virus spread

SOURCE: WHO and Lancaster University, Feb.1

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Zika Virus in the Americas – Why now, why here?

- International spread eastward over past 10-12 years
- Immunologically naïve populations
- Ample competent mosquito vectors, especially *Ae. aegypti* + *Ae. albopictus*
- Socio-economic determinants:
 - Poverty
 - Population density
 - Housing
 - Healthcare/public health systems capacity/access
- Viral mutations – changes to transmissibility and/or virulence?
- Co-factors?
 - Previous/concurrent flavivirus infections, especially dengue
 - Environmental exposures
 - Bovine-like diarrheal virus (BVDV)

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Challenges in Assessing/Understanding Emerging Zika Epidemiology

- Healthcare/public health system capacity in areas most affected
- Competing priorities in Zika-affected areas
- Concurrent epidemics of dengue fever and chikungunya virus infections
- Non-specific nature of clinical signs and symptoms:
 - Fever, rash, conjunctivitis, arthralgias

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Challenges in Assessing/Understanding Emerging Zika Epidemiology

- Short period of viremia + capacity to detect via PCR
- Cross-reactivity of serological tests for antibodies with other flaviviruses:
 - Dengue
 - Yellow fever
 - West Nile virus
- High proportion of asymptomatic infections
- Evolving understanding of routes of transmission/clinical consequences

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Figure 1. Countries and territories in the Americas with confirmed autochthonous (vector-borne) Zika virus cases, 2015 - 2017.

Updated as of 27 April 2017

Countries with confirmed autochthonous cases of Zika virus

- First Case: 2015 (1)
- First Case: 2016 (2)
- First Case: 2017 (3)
- No autochthonous confirmed cases to date

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Figure 2. Distribution of suspected and confirmed Zika cases by epidemiological week and sub-region. Region of the Americas, 2016 – 2017 (as of EW 16).15

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Figure 3. Distribution of suspected and confirmed Zika cases by EW. Bolivia (Plurinational State of), Brazil, Ecuador, and Peru, EW 25 of 2015 to EW 16 of 2017.

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Figure 3. continued...

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PublicHealthOntario.ca Source: <http://www.haaretz.com/israel-news/science/1.699193>

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Articles

Congenital Zika virus syndrome in Brazil: a case series of the first 1501 livebirths with complete investigation

Gonery V A França, Lavinia Schuler-Faccini, Wanderlei F Oliveira, Claudio M P Henriques, Eduardo H Carmo, Yaraide D Paul, Marli L Neves, Maria C Castro, Suzanne Senoya, Mardelga F Silva, Fernando C Barros, Cesar G Victora

Summary
Background In November, 2015, an epidemic of microcephaly was reported in Brazil, which was later attributed to congenital Zika virus infection. 7830 suspected cases had been reported to the Brazilian Ministry of Health by June 4, 2016, but little is known about their characteristics. We aimed to describe these newborn babies in terms of clinical findings, anthropometry, and survival.

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Articles

Association between Zika virus infection and microcephaly in Brazil, January to May, 2016: preliminary report of a case-control study

Thales Vélho Barreto de Araújo, Laura Cunha Rodrigues, Ricardo Assis de Alencar Ximenes, Demétrio de Barros Miranda-Filho, Ulisses Ramos Montenegro, Ana Paula Lopes de Melo, Sandra Valença, Maria de Fátima Pessoa Miranda de Albuquerque, Wagner Vieira Soares, Cynthia Braga, Simão Pinho Brandão Filho, Marli Tereza Carlini, Evagosto Viçoso, Denisse Di Camillo, Soraia Cruz, Claudio Mouton de Paula, Henrique Loureiro Gonçalves Albuquerque Barros, Fátima Magalhães de Sá, Catarina, Rafael Duarte, Everton Torres Azevedo Marques Junior, Celma Maria Turchi Martini, on behalf of investigators from the Microcephaly Epidemic Research Group, the Brazilian Ministry of Health, the Pan American Health Organization, Instituto de Medicina Integral Professor Fernando Figueira, and the State Health Department of Pernambuco

Summary
Background The microcephaly epidemic, which started in Brazil in 2015, was declared a Public Health Emergency of International Concern by WHO in 2016. We report the preliminary results of a case-control study investigating the association between microcephaly and Zika virus infection during pregnancy.

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Early Growth and Neurologic Outcomes of Infants with Probable Congenital Zika Virus Syndrome

We report the early growth and neurologic findings of 48 infants in Brazil diagnosed with probable congenital Zika virus syndrome and followed to age 1–8 months. Most of these infants had microcephaly (86.7%) and craniofacial disproportion (95.8%). The clinical pattern included poor head growth with increasingly negative z-scores, pyramidal/extrapyramidal symptoms, and epilepsy.

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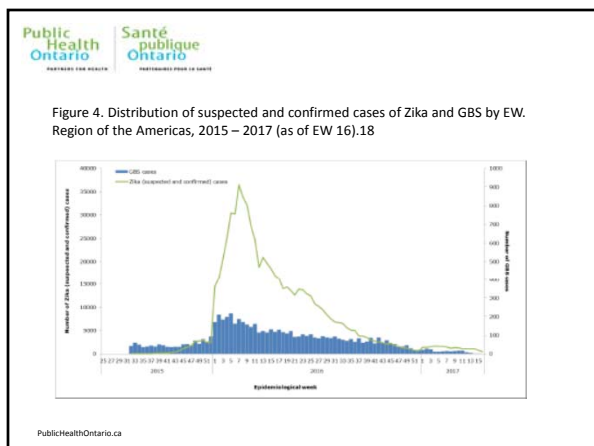
CDC Centers for Disease Control and Prevention

EMERGING INFECTIOUS DISEASES

Volume 22, Number 1 – January 2017

Guillain-Barré Syndrome and Healthcare Needs during Zika Virus Transmission, Puerto Rico, 2016

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NEWS

Zika virus is a global public health emergency, declares WHO

Anno Gulland
London

Zika virus and microcephaly: why is this situation a PHEIC?

When the Director-General of WHO declared, on Feb 1, 2016, that recently reported clusters of the WHO Regional Office in the Americas on the Zika virus outbreaks and other neurological disorders are a Public Health Emergency of International Concern (PHEIC), it dengue and chikungunya viruses. During one country

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Media centre

Fifth meeting of the Emergency Committee under the International Health Regulations (2005) regarding microcephaly, other neurological disorders and Zika virus

2015-11-16

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The EC originally recommended a PHEIC in February 2016 on the basis of an extraordinary cluster of microcephaly and other neurological disorders reported in Brazil, following a similar cluster in French Polynesia and geographic and temporal association with Zika virus infection which required urgent and coordinated and research. Because research has now demonstrated the link between Zika virus infection and microcephaly, the EC felt that a robust longer-term technical mechanism was now required to manage the global response.

As a result, the EC felt that Zika virus and associated consequences remain a significant enduring public health challenge requiring intense action but no longer represent a PHEIC as defined under the IHR. Many aspects of this disease and associated consequences still remain to be understood, but this can best be done through sustained research. The EC recommended that this should be escalated into a sustained programme of work with dedicated resources to address the long-term nature of the disease and its associated consequences.

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Articles

Potential for Zika virus introduction and transmission in resource-limited countries in Africa and the Asia-Pacific region: a modelling study

Issa I Bogoch*, Oliver J Brady*, Mark UCK Ekwame*, Matthew Gorman, Marisa Coovadia, Shannon Burt, Alexander G Wally, Simon I Higgs, Manisha A Kulkarni, John J Bromberg, Karim Khan

Summary

Background As the epidemic of Zika virus expands in the Americas, countries across Africa and the Asia-Pacific region are becoming increasingly susceptible to the importation and possible local spread of the virus. To support public health readiness, we aim to identify regions and times where the potential health, economic, and social effects from Zika virus are greatest, focusing on resource-limited countries in Africa and the Asia-Pacific region.

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Case Counts in the US

Zika virus disease is now a nationally notifiable condition. Cases are reported to CDC by state, territorial, and local health departments using standard case definitions. This webpage contains provisional data reported to ArboNET for **January 1, 2015 - April 26, 2017**.

US States

- 5,264 Zika virus disease cases reported
- 4,963 cases in travelers returning from affected areas
- 224 cases acquired through presumed local mosquito-borne transmission in Florida (N=218) and Texas (N=6)
- 77 cases acquired through other routes, including sexual transmission (N=46), congenital infection (N=29), laboratory transmission (N=1), and person-to-person through an unknown route (N=1)

US Territories

- 36,575 Zika virus disease cases reported
- 143 cases in travelers returning from affected areas
- 36,432 cases acquired through presumed local mosquito-borne transmission
- 0 cases acquired through other routes*

*Sexually transmitted cases are not reported for US territories because with local transmission of Zika virus it is not possible to determine whether infection occurred due to mosquito-borne or sexual transmission.

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Outcomes of Pregnancies with Laboratory Evidence of Possible Zika Virus Infection in the United States

Outcomes for Completed Pregnancies in the United States and District of Columbia, 2016-2017

*As of April 11, 2017

Completed pregnancies with or without birth defects

1,367

Includes aggregated data reported to the US Zika Pregnancy Registry*

Liveborn infants with birth defects*

58

Includes aggregated data reported to the US Zika Pregnancy Registry*

Pregnancy losses with birth defects**

7

Includes aggregated data reported to the US Zika Pregnancy Registry*

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Source: <http://www.cdc.gov/zika/public-health-partners/zaps.html>

COVID-19

Zika Active Pregnancy Surveillance System (ZAPSS) in Puerto Rico

What clinicians need to know and do

Background

The first confirmed case of Zika virus in Puerto Rico was reported on December 16, 2016. On December 16, 2016, the Puerto Rico Health Department (PRHD) issued a public health emergency declaration for Zika virus infection. PRHD is currently conducting a surveillance system for Zika virus infection in pregnant women and their fetuses and newborns.

Zika Active Pregnancy Surveillance System (ZAPSS) Sistema de Vigilancia Activa de Zika en Embarazadas (ZAVIE)

The Puerto Rico Department of Health (PRDH) and the Centers for Disease Control and Prevention (CDC) have developed the ZAPSS. ZAPSS is a surveillance system for Zika virus infection in pregnant women and their fetuses and newborns. ZAPSS is a surveillance system for Zika virus infection in pregnant women and their fetuses and newborns. ZAPSS is a surveillance system for Zika virus infection in pregnant women and their fetuses and newborns.

Clinical Participation for the Surveillance System

Clinicians who are involved in the surveillance system, PRDH and CDC, request that clinicians:

1. Report all pregnant women who are pregnant or have been pregnant in the last 12 months, regardless of whether they are currently pregnant or have been pregnant in the last 12 months.
2. Report all birth defects to the Puerto Rico Department of Health (PRDH) and the Centers for Disease Control and Prevention (CDC).
3. Report all pregnancy losses to the Puerto Rico Department of Health (PRDH) and the Centers for Disease Control and Prevention (CDC).
4. Report all pregnancy losses to the Puerto Rico Department of Health (PRDH) and the Centers for Disease Control and Prevention (CDC).

Where to get more information

For general information, go to www.cdc.gov/zika. For more information, please contact PRDH at prdh@prh.gov or www.prh.gov.

To notify the PRDH of any birth defects and pregnancy losses, please contact the PRDH at prdh@prh.gov or www.prh.gov.

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Vital Signs: Update on Zika Virus–Associated Birth Defects and Evaluation of All U.S. Infants with Congenital Zika Virus Exposure — U.S. Zika Pregnancy Registry, 2016

Megan R. Reynolds, MPH¹; Abbey M. Jones, MPH¹; Emily E. Peterson, MD²; Ellen H. Lee, MD³; Marion E. Rice, MPH^{1,4}; Andrea Bingham, PhD⁵; Sacha R. Ellington, MSFH⁶; Nicole Ewert, MS⁷; Sarah Reagan-Scott, MD⁸; Tinsale Odoyofo, MD⁹; Catherine M. Brown, DVM¹⁰; Saavey Martin, MS¹¹; Nina Ahmad, MD¹²; John Blanton, PhD¹³; Jennifer Macdonald, MPH¹⁴; Carolyn Gould, MD¹⁵; Anne D. Fine, MD¹⁶; Kara D. Foley, MPH¹⁷; Heather Lake-Burger, MPH¹⁸; Christina L. Hillard, MA¹⁹; Naomi Hall, PhD²⁰; Maha M. Yazdy, PhD²¹; Kamelha Shughra, MPH²²; Jamie N. Sommer, MS²³; Aly Adamski, PhD²⁴; Meghan Reynolds, MPH²⁵; Shannon Pade-Dorritan, MPH²⁶; Jyoti Gupta, MPH²⁷; Kimberly Newsome, MPH²⁸; Madhvi Bhat-Sastry, PhD²⁹; Sally Slavitski, DVM³⁰; Jennifer L. White, MPH³¹; Cynthia A. Moore, MD, PhD³²; Carrie K. Shapiro-Mendoza, PhD³³; Lytle Peterson, MD³⁴; Colton Boyle, PhD³⁵; Denise J. Jamieson, MD³⁶; Dana Mosney-Delman, MD³⁷; Margaret A. Honein, PhD³⁸; U.S. Zika Pregnancy Registry Collaboration

On April 4, 2017, this report was posted as an MMWR Early Release on the MMWR website (<https://www.cdc.gov/mmwr>).

Abstract

Background In collaboration with state, tribal, local, and territorial health departments, CDC established the U.S. Zika Pregnancy Registry (USZPR) in early 2016 to monitor pregnant women with laboratory evidence of possible recent Zika virus infection and their infants.

Methods This report includes an analysis of completed pregnancies (which include live births and pregnancy losses, regardless of gestational age) in the 50 U.S. states and the District of Columbia (DC) with laboratory evidence of possible recent Zika virus infection reported to the USZPR from January 15 to December 27, 2016. Birth defects potentially associated with Zika virus infection during pregnancy include brain abnormalities and/or microcephaly, eye abnormalities, other consequences of central nervous system dysfunction, and neural tube defects and other early brain malformations.

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Results During the analysis period, 1,297 pregnant women in 44 states were reported to the USZPR. Zika virus–associated birth defects were reported for 51 (5%) of the 972 fetuses/infants from completed pregnancies with laboratory evidence of possible recent Zika virus infection (95% confidence interval [CI] = 4%–9%); the proportion was higher when restricted to pregnancies with laboratory-confirmed Zika virus infection (24/250 completed pregnancies [10%, 95% CI = 7%–14%]). Birth defects were reported in 15% (95% CI = 8%–26%) of fetuses/infants of completed pregnancies with confirmed Zika virus infection in the first trimester. Among 895 liveborn infants from pregnancies with possible recent Zika virus infection, postnatal neuroimaging was reported for 221 (25%), and Zika virus testing of at least one infant specimen was reported for 585 (65%).

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Surveillance of Zika virus

Learn how Zika virus is monitored

On this page

- Zika virus (not detected in Canada)
- How Zika virus is monitored in Canada
- How many cases are there of Zika virus around the world?
- For more information

Has Zika virus been detected in Canada?

As of April 6, 2017, there are 488 travel-related cases and 2 laboratory-confirmed cases, including 20 pregnant women reported in Canada (United States of America, U.S., with possible mosquito-borne transmission of Zika virus)

The increase in case count for the reporting period is related to reporting delays and is not a reflection of an increase in newly identified cases.

The data will be updated monthly. The next update will be made on Thursday, May 4, 2017.

Zika virus detected in Canada, as of April 6, 2017

Acquired through sexual transmission	Travel related
3	485

Reports of pregnancies

Number of pregnancies reported among Zika-infected women	Fatal and liveborn outcomes	
	No. Zika-related anomalies observed	Zika-related anomalies observed
28	2	2

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Public Information

Zika Virus

Zika virus infection is caused by a virus which is spread by the bite of infected mosquitoes and has no other means of transmission. There are the same mosquito that spread Dengue, Chikungunya and yellow fever viruses. These mosquitoes are not established in Canada and are not well suited to our climate.

Zika virus has been reported in Africa and parts of Asia since the 1950s and in the southeastern United States in 2014 to 2015. Zika virus emerged in South America, first reports, the virus has spread throughout southern and Central and South America, Mexico, and the Caribbean.

There has been reports of a series of fetal deaths (miscarriages) in southern and central Africa which is hard to explain than expected when compared to babies of the same age and age in babies of mothers who were infected with Zika virus (miscarriages).

It is recommended that pregnant women and those considering becoming pregnant discuss their travel plans with their health care provider to assess their risk and consider postponing travel to areas where the Zika virus is circulating, if travel cannot be postponed, then strict mosquito bite prevention measures should be followed to protect themselves against bites.

Prevalence Reporting

Laboratory-confirmed travel-related cases of Zika virus in Ontario¹ as of April 6, 2017

Number of laboratory-confirmed cases	Countries of Travel ²
20 ¹	Aruba, Antigua and Barbuda, Barbados, Belize, Brazil, British Virgin Islands, Guyana, Haiti, Cuba, Dominican Republic, Ecuador, El Salvador, Guatemala, Honduras, Jamaica, Haiti, Honduras, Jamaica, Netherlands, French West Indies, Mexico, Nicaragua, Panama, Puerto Rico, Saint Kitts and Nevis, Saint Lucia, St. Martin / St. Eustache, St. Vincent & the Grenadines, Turkey and Costa Rica, Trinidad and Tobago, Venezuela

¹Note: Four of the 208 laboratory-confirmed cases of Zika virus in Ontario are non-travel related.

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Zika virus

Pregnancy, traveling, causes, symptoms, virus, treatment, prevention, surveillance, guidance for professionals

Recent notices

- Travel health notice: Zika virus (2016) update, March 14, 2017
- Zika virus virus in Canada, April 6, 2017

Services and information

Prevalence
What you need to know if you are pregnant or planning a pregnancy

Causes
The source of Zika virus and how it's spread

Signs
What the signs are and when to seek help

Prevention
How to prevent Zika virus

Treatment
What travelers need to know about Zika virus

Surveillance
What to look for and what to do if you become ill

Guidance
Clinical information, diagnosis and treatment for Zika virus

Surveillance
Zika virus monitoring

Contributors

- Health Canada
- Public Health Agency of Canada

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Government of Canada / Gouvernement du Canada

Recommendations on the Prevention and Treatment of Zika Virus for Canadian health care professionals

An Advisory Committee Statement (ACS) Committee to Advise on Tropical Medicine and Travel (CATMAT)

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Surveillance report of Zika virus among Canadian travellers returning from the Americas

Andrea K. Boggild MD, Jennifer Gerbald MHC, Michael Libman MDCM, Cedric P. Yansouni MD, Anne E. McCarthy MD, Jan Hajek MD, Wayne Ghoguelin MD, Yasmin Mirzazadeh MD, Jean Vézette MD, Susan Kuhn MD, Pierre J. Flouffe MD, Samanta Chakrabarti MD, David O. Freedman MD, Kevin C. Kain MD

■ Cite as: CMAJ 2017 March 6;189(10):1624-30. doi:10.1503/cmaj.162434

CMAJ/Pediatrics author interview at <https://soundcloud.com/soundcloudcmaj/162434-ve>

Visual abstract available at www.cmaj.ca/lookup/suppl/doi:10.1553/cmaj.162434/-DC1

ABSTRACT

BACKGROUND: Widespread transmission of Zika virus in the Americas has occurred since late 2015. We examined demographic and travel-related characteristics of returned Canadian travellers with Zika infection acquired in the Americas to illuminate risk factors for acquisition and the clinical spectrum.

METHODS: We analysed demographic and travel-related data for returned Canadian travellers who presented to a Canadian site between October 2015 and September 2016 for care of Zika virus acquired in the Americas. Data were collected with use of the Sentinel surveillance health work data platform.

RESULTS: During the study period, 1118 travellers presented to a Canadian site after returning from the Americas; 41 (3.7%) of whom had Zika infection. Zika infection from the Americas was diagnosed at Canadian sites as either dengue (n = 41) over the study period in the first half of the study period. Zika virus burden was borne by people visiting friends and relatives in South America, in the latter half, coincident with the increased spread of Zika throughout the Caribbean and Central America. Zika virus occurred more often in tourists in the Caribbean. Forty (98%) of the travellers with Zika infection acquired it through probable mosquito exposure, and 1 had confirmed sexual acquisition. Congenital transmission occurred in 2 of 3 pregnancies. Two (5%) of those with Zika had symptoms resembling those of Guillain-Barré syndrome, 1 of whom also had Zika viral meningitis.

INTERPRETATION: Even in this small cohort, we observed the full clinical spectrum of acute Zika virus, including abnormal and neurologic outcomes. Our observations suggest that complications from Zika infection are underestimated by data arising exclusively from populations where Zika is endemic. Travellers should adhere to mosquito-avoidance measures and barrier protection during sexual activity.

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Severe microcephaly

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Co-investigators
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 Aidem Moore, MD, The Hospital for Sick Children, Toronto

Collaborators
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 Joanne Tataryn, DVM, Public Health Agency of Canada, Saskatoon

Background
 Microcephaly is an anomaly of the central nervous system. It is a condition in which an infant's head is significantly smaller than the head of other children of the same age and sex. Sometimes detected at birth, microcephaly usually results from the brain developing abnormally in the womb or not growing as it should after birth. There are many known causes of microcephaly, including genetic disorders, exposures to known drugs or toxins, hypoxic injury, and congenital infections. There are a variety of outcomes associated with microcephaly, however, many affected children experience developmental delays, ranging from mild to severe. Children with microcephaly also present with a constellation of other health concerns, often requiring intensive, significant, and life-long medical, educational and social supports.

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Congenital Zika syndrome (CZS) in infants in Canada

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Background
 Zika virus is primarily transmitted to humans via the bite of an infected *Aedes* mosquito, but can also be transmitted following unprotected sexual contact and, very rarely, via blood and other body fluids. The majority of people infected with Zika virus are asymptomatic, or develop mild illness; however, Zika virus has been shown to be neurotropic, particularly to the developing fetus, causing severe neurologic disease that manifests in infants. In October 2015, an increased incidence of microcephaly was noted in northeastern Brazil and further investigations noted an increase in other neurologic disorders among newborns born to mothers with Zika virus infection. In February 2016, the World Health Organization (WHO) declared the Zika virus-related cluster of microcephaly and other neurologic disorders to be a public health emergency of international concern.

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Sexual Transmission of Zika Virus

- Substantial evidence of symptomatic male→female/male transmission
- Limited evidence of transmission from:
 - Asymptomatic males
 - Females→males/females
 - Sex toys
- What is still unknown/uncertain?
 - Persistence of/pattern of shedding of infectious virus in semen
 - Persistence of/pattern of shedding in vaginal fluids/cervical secretions
 - Differences in the above in symptomatic vs. asymptomatic cases

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Prevention of Sexual Transmission

- Abstinence
- Male/female condoms:
 - For vaginal, oral and anal sex
 - For entirety of sexual contact
 - Dental dams for oral to vagina/anal contact
- Condoms for males with symptomatic or asymptomatic illness:
 - Six months post-symptom onset
 - Based on earlier evidence of virus persistence in semen + precaution factor
 - Recent evidence of PCR positivity for 180+ days post-symptom onset

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Prevention of Sexual Transmission

- Symptomatic or asymptomatic females require 8 weeks of transmission precautions:
 - Shorter duration of viral persistence in vaginal fluids/cervical secretions
- Avoid sharing of sex toys

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Other Potential Exposures/Modes of Transmission

- Urine:
 - No reports of transmission
 - Use of routine practices
- Breastmilk:
 - No reports of transmission
 - No restrictions on breastfeeding
- Saliva/tears:
 - No reports of transmission
 - Use of routine practices
- Blood screening/blood supply:
 - CBS donor deferral for 21 days

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Reportability of Zika Virus Infection

- Zika virus infection not designated reportable in Ontario
- Limited data elements from PHO laboratories collected by/shared with CMOH/PHAC
- Why isn't Zika reportable?
 - Limited PH actions requiring reporting/collection of personal health info
 - Prevention of sexual transmission via public education vs. case/contact follow-up
 - Priorities for lab testing → dependence on clinical diagnosis/reporting
 - Non-specific clinical signs and symptoms → ? Zika, ? chikungunya, ? dengue, ? other
 - High proportion of asymptomatic infections
- Pregnancy complications/CZS reporting/assessment via PHAC/CPS voluntary system

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Inactivation and Environmental Stability of Zika Virus

...inactivation and environmental stability of Zika virus... (text continues with scientific details)

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Morbidity and Mortality Weekly Report

Preliminary Findings from an Investigation of Zika Virus Infection in a Patient with No Known Risk Factors — Utah, 2016

Caroline Bunn^{1,2}, Angela Dross, MD³, Harry Svingo, PhD⁴, Amy Faraji, PhD⁵, Mike Rubin, MD⁶, Bassi Rizk, MD⁶, Wandy Garcia⁷, Margaret Corneo, MD⁸, Shannon Niswam, MD⁹, Elizabeth Espgal Kross-Lozel, PhD⁹, Jacqueline Crump¹⁰, Mary Hill, MPH¹¹, Annette Atkinson, MD¹², Dallas Pittman¹³, Kimberly Christensen¹⁴, Melissa Dismond, MPH¹⁵, J. Erin Staples, MD¹⁶, Allyn Nakadima, MD¹⁷

On September 13, 2016, this report was posted as an MMWR Early Release on the MMWR website (<http://www.cdc.gov/mmwr>).

On July 12, 2016, the Utah Department of Health (UDOH) was notified by a clinician caring for an adult (patient A) who was evaluated for fever, rash, and conjunctivitis that began on July 1. Patient A had not traveled to an area with ongoing Zika virus transmission; had not had sexual contact with a person who recently traveled; and had not received a blood transfusion, organ transplant, or mosquito bites (1). Patient A provided care over several days to an elderly male family contact (the index patient) who contracted Zika virus abroad. The index patient developed septic shock with multiple organ failure and died in the hospital on June 25, 2016. The index patient's blood specimens obtained 2 days before his death had a level of

Nineween family contacts, including patient A, were identified and interviewed, and provided blood or urine specimens for testing. Thirteen family contacts reported hugging and kissing the index patient's face. Five family contacts reported being present while the index patient's stool, urine, or vomitus was being cleaned. Patient A reported hugging and kissing the index patient, in a similar fashion to other family contacts, and assisted hospital personnel in holding the index patient while his stool was being cleaned, but did not have direct contact with stool. Other than patient A, all family contacts were negative for Zika virus infection by RT-PCR or MAC-ELISA on specimens obtained roughly 2–3 weeks after last exposure. Health care workers who provided care to the index patient and residents living within a 200-meter radius of the two

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CDC Centers for Disease Control and Prevention

SEARCH

CDC A-Z INDEX

Zika Virus

- Interim Guidance for Managing Occupational Exposures to Zika Virus for Healthcare Personnel
- Introduction
- Zika virus is primarily spread by the bite of an infected Aedes species mosquito. Sexual and maternal-fetal transmission have also been well documented.
- Transmission via transfusion of blood products has been reported in the United States, but to date, transmission of Zika virus via blood transfusion has not been reported in the United States. There is currently no clinical evidence that Zika virus is transmitted through the air.
- In June 2016, there was 1 reported case of possible Zika virus transmission from an infected patient to family members in the United States; the exact mechanism of transmission and whether transmission occurred in the home or in a healthcare setting are unclear. There have been no reports of transmission of Zika virus from infected patients to healthcare personnel (HCP) or to other patients in healthcare settings. However, transmission related to occupational exposure to Zika virus has occurred in laboratory workers, including one in 2016 in which a research laboratory worker became infected via a needlestick injury.
- To prevent occupationally acquired infections and reduce the possibility of spreading infectious diseases, including Zika virus, in healthcare settings, HCP should adhere to Standard Precautions that all patients care activities (2015 Guidelines for Infection Prevention: Preventing Transmission of Infectious Agents in Healthcare Settings) (2). (3) (4) (5) (6) (7) (8) (9) (10) (11) (12) (13) (14) (15) (16) (17) (18) (19) (20) (21) (22) (23) (24) (25) (26) (27) (28) (29) (30) (31) (32) (33) (34) (35) (36) (37) (38) (39) (40) (41) (42) (43) (44) (45) (46) (47) (48) (49) (50) (51) (52) (53) (54) (55) (56) (57) (58) (59) (60) (61) (62) (63) (64) (65) (66) (67) (68) (69) (70) (71) (72) (73) (74) (75) (76) (77) (78) (79) (80) (81) (82) (83) (84) (85) (86) (87) (88) (89) (90) (91) (92) (93) (94) (95) (96) (97) (98) (99) (100)

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Managing Occupational Exposures

- No documented evidence to date of transmission to HCWs, one lab transmission via needlestick injury
- Use of routine practices
- If exposed, within 8 wks of source patient exposure?
- If risk factors, testing of source patient
- Initial testing/counselling re. Zika symptoms
- If transmission occurs, pregnancy/sexual transmission follow-up
- No exclusion from work

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Rapid risk assessment: Zika virus

August 12, 2016

Summary

Event information summary:

Zika virus (ZIKV) infection is a mosquito-borne illness that is usually mild and resolves without treatment. This outbreak was first documented in Brazil in early 2015. Since then, ZIKV infection has spread rapidly throughout Central and South America and the Caribbean, with local transmission recently documented in two counties in Florida. The [World Health Organization \(WHO\)](#) has concluded that ZIKV is a causative agent of congenital malformations and neurological complications.

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Figure 1: Core questions in risk assessment for communicable diseases

Assessing likelihood of transmission:

- Is human exposure and transmission likely within Ontario?
- Is the population highly susceptible?
- Is the agent highly infectious?

Assessing probability of impact:

- Is the agent likely to cause severe disease?
- Will a significant proportion of the population be affected?
- Are effective treatments and/or control measures available?

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Rapid Risk Assessment: The risk of Zika virus to Canadians (third update) – Appendix 1

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 information used.	Individual case reports Grey literature Individual, non-expert opinion
Medium	Adequate quality of evidence, including consistent results, reliable sources(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) Testimonials regarded as definitive sources Expert group risk assessment, or specialized expert knowledge, or consensus opinion of experts

PublicHealthOntario.ca Source: <http://www.healthycanadians.gc.ca/publications/leaves-and-conditions/maladies-et-affections/zika-virus-virus-mosquito-eng.php> 58

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Zika Virus

Laboratory

Testing Information
[Zika virus test information sheet](#)

Resources

[Zika Virus Infection: Information and guidance for health care providers](#)
[Rapid Risk Assessment: Zika Virus](#)
[And \(Grand\) Rebirth: Zika Virus Infection: Surveillance, Research, Diagnosis and Pregnancy Management—Canada Developmental March 22, 2016](#)

Related Links

Ministry of Health and Long-Term Care
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→ [Zika Virus Prevention](#)

Pan American Health Organization
→ [Zika Virus Infection](#)

World Health Organization
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→ [Zika Virus and Pregnancy](#)
→ [Zika Virus](#)

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Zika Virus Infection: Information and guidance for health care providers

(Updated October 5, 2016)

Public Health Ontario has been working with the Ontario Ministry of Health and Long-Term Care, the Public Health Agency of Canada (PHAC) and other partners on monitoring and assessing the epidemiology, clinical impacts, prevention and control of Zika virus (ZIKV) infection. Where possible, PHO refers to the latest advice from the Committee to Advise on Tropical Medicine and Travel (CATMAT). PHO also refers to the Centers for Disease Control and Prevention (CDC), Pan American Health Organization (PAHO) or the European Centre for Disease Prevention and Control (ECDC) when more up-to-date guidance is available.

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PAHO and Zika Risk Communication

- With uncertain health risks, what is known, what not?
- Timely, transparent, accurate, accessible information
- Coordinating messages across health organizations
- Prioritize the messages → those with greatest impact
- Adapt information for different audiences
- Avoid over-interpretation and over-confidence
- Things will change as more is learned
- Link with/mobilize community leaders/educators
- Keep media informed

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Journal of Clinical Virology 81 (2016) 66–71

Contents lists available at ScienceDirect

Journal of Clinical Virology

journal homepage: www.elsevier.com/locate/jcv

Simultaneous detection of Zika, Chikungunya and Dengue viruses by a multiplex real-time RT-PCR assay

Kanti Pabbaraju^{a,*}, Sallene Wong^a, Kara Gill^a, Kevin Fonseca^{a,b}, Graham A. Tipples^{a,c}, Raymond Teiller^{a,b}

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Zika Virus Commercial Assays

altona DIAGNOSTICS

Press Release

altona Diagnostics launches worldwide first commercially available CE-IVD real-time PCR test for detection of Zika Virus

Hamburg, January 27, 2016 The RealStar® Zika Virus RT-PCR Kit 1.0 is an in vitro diagnostic assay based on real-time Reverse Transcription-Isogenetic Chain Reaction (RT-PCR) technology, for the identification of Zika virus. RealStar® kits are reliable CE-IVD marked assays for detection and quantification of various viruses, bacteria and parasites. The assays meet all requirements of the MD Directive 98/79/EC. With the development of the RealStar® Zika Virus RT-PCR kit 1.0, altona Diagnostics enlarges its panel of CE-IVD marked ready-to-use kits for tropical pathogens.

RealStar®
Zika Virus RT-PCR Kit 1.0
01/2016

fast-track DIAGNOSTICS
TRUE POSITIVES. TRUE NEGATIVES.

Manual
FTD Zika virus

WHO PREQUALIFICATION TEAM: DIAGNOSTICS

World Health Organization

32 reactions (batching no. FTD-77-32)
64 reactions (batching no. FTD-77-64)

Invitation to manufacturers of in vitro diagnostics for Zika virus to submit an application for emergency use assessment and listing by WHO (originally issued 10 February 2016)

Source: http://www.who.int/diagnostics_laboratory/eval-zika-virus/160211invitation_to_mv_of_zika_virus_diagnostics_v2.pdf?ua=1

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Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Editorial

Zika virus outbreak and the case for building effective and sustainable rapid diagnostics laboratory capacity globally

New and re-emerging pathogens with epidemic potential have threatened global health security for the past century. As with the recent Ebola Virus Disease (EVD) epidemic, the Zika Virus (ZIKV) outbreak has yet again surprised and overwhelmed the international health community with an unexpected event for which it might have been better prepared.

ZIKV was first identified in Uganda in 1947, was also found in Gabon in 2007 and may be endemic in much of tropical Africa without receiving much attention. The current ZIKV epidemic facing the Americas, was declared a "Public Health Emergency of International Concern (PHEIC)" by the World Health Organization on 1st February 2016.¹ Preceding the declaration of a Global Public Health Emergency by 4 days was the release of the United Nations report "Protecting Humanity from Future Health Crises. Report of the High-level Panel on the Global Response to Health Crises".

The present ZIKV outbreak again exposes an unprepared global public health system.

Survivance of infections is based on reporting cases of illness, often syndromic reporting of CNS or pulmonary infections among others, but unexplained brief febrile illnesses are rarely reported, even in pregnant women. In addition, assigning a possible diagnosis to syndromic surveillance requires suitable laboratory tests to be readily available for the causative agent and require a considerable laboratory capacity. During the first six months of the Ebola virus disease (EVD) epidemic in West Africa, the weak diagnostic laboratory capacity in the affected countries was an important factor in the rapid spread of the outbreak.² As a result of intense international efforts, over 20 laboratories were established to provide rapid in-country testing for Ebola virus. These laboratories included both mobile and temporary laboratories equipped to do molecular diagnostic testing and several laboratories to provide local genomic sequencing of the virus to help in contact tracing. However, since the laboratories were mostly run by Non-Governmental Organizations and volunteers from overseas public health laboratories, most of these efforts provided only a temporary solution, rather than a long-term sustainable solution. Furthermore these laboratories were focused on a single, known infection.

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PLOS | NEGLECTED TROPICAL DISEASES

FROM INNOVATION TO APPLICATION

OpenZika: An IBM World Community Grid Project to Accelerate Zika Virus Drug Discovery

Sean Ekins^{1,2}, Alexander L. Perryman³, Carolina Horita Andrade⁴

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Abstract

The Zika virus outbreak in the Americas has caused global concern. To help accelerate this fight against Zika, we launched the OpenZika project. OpenZika is an IBM World Community Grid Project that uses distributed computing on millions of computers and Android devices to run docking experiments, in order to dock tens of millions of drug-like compounds against crystal structures and homology models of Zika proteins (and other related flavivirus targets). This will enable the identification of new candidates that can then be tested in vivo, to advance the discovery and development of new antiviral drugs against the Zika virus. The docking data is being made openly accessible so that all members of the global research community can use it to further advance drug discovery studies against Zika and other related flaviviruses.

OPEN ACCESS

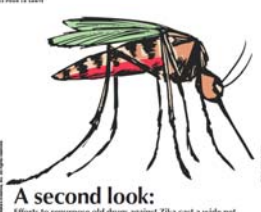
© Ekins S, Perryman AL, Horita Andrade C (2016) OpenZika: An IBM World Community Grid Project to Accelerate Zika Virus Drug Discovery. PLoS Negl Trop Dis 10(5): e0151717. doi:10.1371/journal.pntd.0151717

PublicHealthOntario.ca Source: Ekins S, Perryman AL, Horita Andrade C (2016) OpenZika: An IBM World Community Grid Project to Accelerate Zika Virus Drug Discovery. PLoS Negl Trop Dis 10(5): e0151717. doi:10.1371/journal.pntd.0151717

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Source: <http://www.nature.com/journal/2226/full/nrn016-024.html>



A second look: Efforts to repurpose old drugs against Zika cast a wide net

By Ellie Kincaid

It's not just the mosquito that's spreading Zika virus, it's the old drugs we've been using to fight other diseases. A new study from the University of California, San Diego, shows that many of the drugs we've used to fight malaria, dengue, and other tropical diseases might be worth a second look as potential treatments for Zika.

The study, published in the journal *Nature Reviews Microbiology*, found that a wide range of drugs, including some that have been used for decades, could potentially block the Zika virus from infecting cells. The researchers tested over 100 different drugs and found that many of them were effective at blocking the virus.

The study is a promising first step in the search for new treatments for Zika. It shows that there are many old drugs that we've forgotten about that might be worth a second look. It also shows that there are many new drugs that we've developed that might be worth a second look as potential treatments for Zika.

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Cell Host & Microbe
A Screen of FDA-Approved Drugs for Inhibitors of Zika Virus Infection

Abstract
In response to the current global health emergency posed by the Zika virus (ZIKV) outbreak and its link to microcephaly and other neurological conditions, we performed a drug repurposing screen of ~6,000 compounds that included approved drugs, clinical trial drug candidates and pharmacologically active compounds; we identified compounds that either inhibit ZIKV infection or suppress infection-induced caspase-3 activity in different neural cells. A pan-caspase inhibitor, emricasan, inhibited ZIKV-induced increases in caspase-3 activity and protected human cortical neural progenitors in both monolayer and three-dimensional organoid cultures. Ten structurally unrelated inhibitors of cyclin-dependent kinases inhibited ZIKV replication. Niclosamide, a category B anthelmintic drug approved by the US Food and Drug Administration, also inhibited ZIKV replication. Finally, combination treatments using one compound from each category (neuroprotective and antiviral) further increased protection of human neural progenitors and astrocytes from ZIKV-induced cell death. Our results demonstrate the efficacy of this screening strategy and identify lead compounds for anti-ZIKV drug development.

Authors: Hoshino Y, Serrano RA, Park CS, Shrestha T, Pineda J, ...

Journal: Cell Host & Microbe

DOI: 10.1016/j.chom.2016.07.004

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Articles
Identification of small-molecule inhibitors of Zika virus infection and induced neural cell death via a drug repurposing screen

Authors: Miao Xu^{1,2,3,4}, Emily M Lee^{1,3,4}, Zhenyong Wei^{4,5,6}, Yichen Cheng⁶, Wei-Kai Huang^{1,6}, Xuyu Qian^{1,6}, Indira TCW^{1,6}, Jennifer Kuznetsov⁴, Sarah C Ogden⁴, Christy Hammack⁴, Fadi Jacob^{1,6}, Ha Nam Nguyen^{1,6}, Misha Klein^{1,6}, Catherine Hanna¹, Paul Shinn¹, Chase Albert¹, Samuel G Michael¹, Anton Simonov¹, Wenshan Huang¹, Kimberly M Christian^{1,3}, Alison Gust^{1,6}, Kirsten J Hermandes^{1,6}, Ruli Huang¹, Menghang Xia¹, Guo-li Ming^{1,2,3,4,5,6,7}, Wei Zheng^{1,6}, Honglin Song^{1,2,3,4,5,6,7} & Hengli Tang^{1,7}

Journal: Nature Medicine

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From Drug Re-Purposing to Clinical Treatments

- In-vitro studies re. mechanism of action, toxicity
- Prioritization among drug candidates
- Phase 1, 2 and 3 clinical trials:
 - Clinical end-points: infection, transmission, protection of fetus?
 - Dose, route, duration of treatment?
 - Capacity to set-up/undertake vs. competing priorities?
- Drug approvals
- Manufacturing, distribution, clinical guidelines
- Phase 4 post-marketing capacity

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ZIKA research

Published primary research studies and protocols

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Rank	Status	Study
1	Recruiting	Phase I, Randomized, Double-blind, Placebo-Controlled Dose De-escalation Study to Evaluate Safety and Immunogenicity of Alum Adjuvanted Zika Virus Purified inactivated Vaccine (ZPV) in Adults in a Flavivirus Endemic Area Condition: Zika Virus Infection Interventions: Other: Placebo; Biological: Zika Virus Purified inactivated Vaccine (ZPV)
2	Recruiting	A Phase 1, First-in-human, Double-blind, Randomized, Placebo-controlled Trial of a Zika Virus Purified inactivated Vaccine (ZPV) With Alum Adjuvant in Healthy Flavivirus-naïve and Flavivirus-Primed Subjects Condition: Zika Virus Infection Interventions: Biological: IJARO; Biological: YF via YTD Strain; Biological: Zika Virus Purified inactivated Vaccine (ZPV)
3	Recruiting	Understanding Excretion and Infectivity of Zika Virus in Semen During and After Infection Condition: Zika Virus Intervention: Other: Semen analysis and semen PCR for Zika virus

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Rank	Status	Study
1	Recruiting	Phase I, Randomized, Double-blind, Placebo-Controlled Dose De-escalation Study to Evaluate Safety and Immunogenicity of Alum Adjuvanted Zika Virus Purified inactivated Vaccine (ZPV) in Adults in a Flavivirus Endemic Area Condition: Zika Virus Infection Interventions: Other: Placebo; Biological: Zika Virus Purified inactivated Vaccine (ZPV)
2	Recruiting	A Phase 1, First-in-human, Double-blind, Randomized, Placebo-controlled Trial of a Zika Virus Purified inactivated Vaccine (ZPV) With Alum Adjuvant in Healthy Flavivirus-naïve and Flavivirus-Primed Subjects Condition: Zika Virus Infection Interventions: Biological: IJARO; Biological: YF via YTD Strain; Biological: Zika Virus Purified inactivated Vaccine (ZPV)
3	Recruiting	Understanding Excretion and Infectivity of Zika Virus in Semen During and After Infection Condition: Zika Virus Intervention: Other: Semen analysis and semen PCR for Zika virus

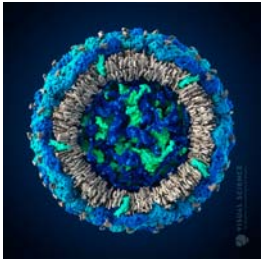
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ZIKV Vaccines

Options for vaccine development:

- Inactivated whole virus
- Subunit vaccines
- Live attenuated →
 - ?? with pregnant women
- Chimeras, using existing viral platforms
- DNA vaccines → virus-like particles



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Source: http://www.who.int/immunization/research/nextsteps_workshops/WHO_Zika_vaccine_TPP.pdf

WHO/UNICEF Zika Virus Vaccine Target Product Profile for Emergency use: July 2016

World Health Organization | unicef

WHO Zika Virus (ZIKV) Vaccine Target Product Profile (TPP):
Vaccine to protect against congenital Zika virus syndrome for use during an emergency

The purpose of this document:

This document is a TPP that describes the preferred and minimal product characteristics for vaccines aimed at protecting against congenital ZIKV syndrome during the ongoing Public Health Emergency of International Concern (PHEIC), or future emergency situations. With that public health objective, this TPP is primarily aimed at vaccines for use in women of childbearing age, with men as a secondary target population if resources permit. The TPP has been drafted by an independent WHO working group of subject matter experts with diverse areas of expertise, and focuses on the product attributes. It has undergone public consultation, and discussion in various fora. As the TPP is based on currently available information in the context of emerging data on ZIKV epidemiology and pathogenesis, the TPP should be considered as living document, and it may undergo adaptation, as knowledge on ZIKV evolves.

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Issues in ZIKV Vaccine Development

Challenges of developing/testing a vaccine for women in reproductive years/pregnant:

- outcomes of Zika in pregnancy not fully characterized
- ethical challenges – risks vs. benefits mother/fetus, consent
- research design – vaccination prior to/early pregnancy
- baseline outcome rates (e.g. miscarriage), across geographies

Potential vaccine complications:

- association of GBS with ZIKV infection
- antibody-dependent enhancement with previous dengue infections
- phase 3 and 4 detection/monitoring

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Issues in ZIKV Vaccine Development (cont'd)

- Testing in animal models, phase 1, 2 and 3 studies
- WHO Emergency Assessment and Listing procedure for the use of experimental products during an epidemic:
 - accelerated assessment process
 - ensure products meet acceptable levels of quality, safety and efficacy, even if evaluation fast-tracked
- Regulatory approvals, manufacturing and distribution
- Funding, education, infrastructure, delivery, Phase 4 capacity

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Source: <https://www.rnh.gov.on.ca/news-releases/rnh-begins-testing-investigational-zika-vaccine-humans>


NEWS RELEASES

Friday, August 5, 2016

NIH begins testing investigational Zika vaccine in humans

The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, has launched a clinical trial of a vaccine candidate intended to prevent Zika virus infection. The early-stage study will evaluate the experimental vaccine's safety and ability to generate an immune system response in participants. At least 50 healthy volunteers aged 18-55 years of diverse ethnicities in the United States, including the NIH Clinical Center in Bethesda, Maryland, are expected to participate in the trial. Scientists at NIAID's Vaccine Research Center (VRC) developed the investigational vaccine – called the NIAID ZIKV virus investigational ZIKV vaccine – earlier this year.

The study is part of the U.S. government response to the ongoing outbreak of Zika virus in the Americas. According to the Centers for Disease Control and Prevention, more than 50 countries and territories have active Zika virus transmission in the United States and its territories, more than 4,500 Zika virus cases have been reported. Although Zika infections are usually asymptomatic, some people experience mild illness lasting about a week. However, Zika virus infection during pregnancy can cause a serious birth defect called microcephaly, as well as other severe health effects of the brain and other organs. There are no vaccines or specific therapies to prevent or treat Zika virus disease.



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World Health Organization

Immunization, Vaccines and Biologicals

WHO vaccine pipeline tracker

WHO Vaccine Pipeline Tracker

Candidate vaccine name	Developer / Collaborators	Disease / Pathogen	
BBV-011	Novartis (contracted) LSI	ZIKV	Health
	Biologicals Institute	ZIKV	Health
	Novartis (contracted) LSI	ZIKV	Recent
	Biologicals Institute, Mérieux (Vaccine)	ZIKV	Recent
	Novartis (contracted) LSI, UTM and ICI/CHS	ZIKV	LSI, Rec
Ruban ZIKV	Ruban	ZIKV	Health
Ruban attenuated ZIKV	Ruban	ZIKV	LSI, Rec
ZIKV	Emergent Biologics	ZIKV	Rec, Rec

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What's the risk of Zika coming to your city?

NATIONAL CENTER FOR ZIKV EPIDEMIOLOGIC RESEARCH US map showing cities at risk of local Zika transmission.

PublicHealthOntario.ca Source: <http://www.statnews.com/2016/03/16/us-cities-local-zika-transmission/>

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Source: <http://news.nationalgeographic.com/2016/02/160225-zika-virus-brazil-mosquitoes-microcephaly-pictures/>

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Mosquito Vector Control

- Personal protection measures → acceptability? compliance? effectiveness?
- Larviciding → myriad breeding sites
- Adulticiding:
 - Magnitude of applications
 - *Aedes* lives/feeds indoors
 - Reduction of adult mosquito populations
 - Impact on disease transmission/impacts?
 - Cost/sustainability

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Sources:
http://memoria.abc.com.br/agenciabrasil/sites/_agenciabrasil/files/imagecache/300x225/gallery_assist/29/gallery_assist664106/prev/13062010-FOTO11217.jpg ;
http://memoria.abc.com.br/agenciabrasil/sites/_agenciabrasil/files/gallery_assist/27/gallery_assist737964/Demoticao_RJ_0382.jpg

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Mosquito Vector Control (cont'd)

- Eradication of breeding sites:
 - El Nino and rainfall patterns
 - Scale of what would be required, given *Aedes* breeding capacity
 - Huge community capacity/compliance
- Release of genetically-modified adult male mosquitoes:
 - WHO-supported
 - Evidence of impact on mosquito populations
 - Impact on incidence and complications, especially pregnancy-related?
 - Scale up, sustainability, cost-effectiveness?
 - Potentially part of the answer, not THE answer

Emergence of/need to monitor for insecticide resistance

- Resistance to permethrins – impregnated clothing

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STAT | Reporting from the frontlines of health and medicine

Ambitious experiment plans to release bacteria-bearing mosquitoes at large scale

STAT | Reporting from the frontlines of health and medicine

Two major public-health organizations, along with the United States and Britain, announced on YouTube that scientists experiment to combat mosquito-borne Zika by releasing the insects with deadly bacteria.

Source: <https://www.statnews.com/2016/02/26/mosquitoes-will-battle-bacteria-virus/>

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 Source: Zika: CDC Interim Response Plan, August 2016

ZIKA

CDC Interim Response Plan

CDC and partners will support and assist states in the key activity areas listed below as different stages in this continuum are reached.

Stage	Phase Level ¹	Transmission Risk Category
Pre-incident	0	Preparedness — vector present or possible in the state
	1	Mosquito Season — <i>Aedes aegypti</i> or <i>Aedes albopictus</i> mosquito biting activity. Introduced travel-related, sexually, or other bodily fluid transmitted cases
Suspected/Confirmed Incident	2	Confirmed Local Transmission — single, locally acquired case, or cases clustered in a single household and occurring <2 weeks apart
Incident/Response	3	Confirmed Multiperson Local Transmission — Zika virus illnesses with onsets occurring ≥2 weeks apart but within an approximately 1 mile (1.5 km) diameter

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Local Zika virus transmission, Florida

- Local transmission started in June 2016
- 285 confirmed cases in 2016
- Aedes aegypti* responsible
- Intensive management program put in place

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Zika virus management, Florida

South Miami Beach Zika Activities Timeline

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Local Zika virus transmission, Texas

- First evidence of local transmission at end of November 2016
- 6 confirmed cases
- Likely *Aedes aegypti* is vector
- Intensive management program initiated
- Active testing of residents near index case

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As Zika Season Nears, States Brace for an End to CDC Funding

DATE: 08/11/16 BY: JESSICA KAPLAN, THE ASSOCIATION FOR PUBLIC HEALTH CRISIS RESPONSE

State programs that track Zika infections and Zika-related birth defects around the country are in jeopardy as public health officials have been told not to count on federal funds for those efforts after July.

In meetings at the Centers for Disease Control and Prevention in Atlanta last week, federal officials told state health departments that Zika funding would be discontinued by the end of the year. Instead, according to representatives of six states that attended the meetings, state health officials say they could have the ability to prepare for a manageable wave of new infections, or to provide services for babies already struggling with Zika-related birth defects.

The potential loss of federal funding comes as health officials are bracing for this summer's mosquito season, and as the dangers associated with the mosquito-borne disease are finally becoming clearer. After the disease emerged in Brazil in 2015, it was discovered that the urban areas would virus caused neurological defects in developing fetuses. A CDC report released this month concluded that one in 10 pregnant women with Zika gave birth to a child with serious birth defects, another CDC study found that a Zika infection increased the chance of delivering a baby with certain birth defects, as well.

Over the course of 2016, the virus spread to at least 58 countries and territories, outbreaks occurred in Puerto Rico, the U.S. Virgin Islands,

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Aedes albopictus – pre 2016, Ontario

- 2005 – Ottawa, August 28
- 2005 – Peel, September 1
- 2005 – Toronto, August 10
- 2012 – Windsor-Essex, June 12
- Likely detected from adventitious individuals hitching ride in vehicles from south
- WNV surveillance not designed to detect these mosquitoes, but if there is a local population, our traps will detect it

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Aedes albopictus detected in Ontario

- Late September and early October 2016
- Adult mosquitoes collected in CDC traps at single location in Windsor (index site)
- Mid-October, intense collection of eggs, larvae and pupae from container habitats near index site
- BGS traps set up to collect adults, designed specifically for *Aedes albopictus* and *Aedes aegypti*
- Results:
 - Immature forms reared to adulthood identified as *Aedes albopictus* and *Aedes aegypti*
 - Female and male adult *Aedes albopictus* collected by BGS traps

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Aedes sampling, Windsor: 2016

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Sampling for *Aedes* mosquitoes, Windsor: 2016

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Sampling for *Aedes* mosquitoes with BGS trap, Windsor: 2016

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Guidance For Managing Ethical Issues In Infectious Disease Outbreaks

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Source: <http://thelancet.com/journal/issue/Volume7/ISSN216-1091/1010008-3>

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Source: www.thelancet.com/lancogh

Editorial

The right(s) approach to Zika

“The face of Zika is not often seen in the air-conditioned shopping malls of upscale Rio neighbourhoods or on the beaches of Ipanema. Rio has its fair share of cases, but so far the heaviest burden has been borne by the northeast region of Brazil, where poverty, poor infrastructure, and lack of access to health services are rampant, and the penetration of *Aedes aegypti* is high. A large proportion of the population in that region is of African descent—indeed, the face of Zika is often that of a darker-skinned person. And because most cases are asymptomatic, and the most dramatic signs of the disease appear through congenital Zika syndrome, the face of Zika is that of a woman or a small child. That is at least what we are able to outline, because in spite of the need for disaggregated epidemiological data to understand transmission patterns and evaluate interventions in vulnerable populations, there is no reliable count of Zika cases by sex and ethnicity.”

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Source: <https://www.thieme-connect.com/products/ejournals/abstract/10.1055/s-0036-1593411>

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DOI: 10.1055/s-0036-1593411

Editorial

Thieme Publications Ltda Rio de Janeiro, Brazil

Zika Virus Outbreak and the Poor Brazilian Family Planning Program

A epidemia de Zika e a insuficiência do programa de planejamento familiar no Brasil

Mirna Bastos Brito, Jan S. Fraser

Wacize Barreto de Medeiros e Saúde Pública, Salvador, BA, Brazil
University of New South Wales, School of Women's and Children's Health and Royal Hospital for Women, Sydney, Australia

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A gendered human rights analysis of Ebola and Zika: locating gender in global health emergencies

SARA E. DAVIES AND BELINDA BENNETT*

Globally, gender remains a key determinant of health.¹ Alcohol consumption, violence, deaths related to road injuries and sexually transmitted infections may be accounted for by the intersecting gendered inequalities and gender norms that determine the health of both men and women. Any attempt to address the gendered dimensions of health faces complex challenges that go beyond sex-specific health needs based on biological difference to understandings of health as socially and economically determined.²

PublicHealthOntario.ca Source: [InternationalAffairs.92.1\(2016\).1045-1060](http://InternationalAffairs.92.1(2016).1045-1060) 101

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Source: <http://www.thelancet.com/pdfs/journal/issue/ISSN216-1091/1010008-3.pdf>

Zika virus and global health security

A recent poll found that 77% of the US public is not seriously concerned about Zika virus.¹ Congress went on summer recess without authorizing President Obama's US\$1.8 billion emergency Zika appropriation request. By Aug 30, 2016, the US Centers for Disease Control and Prevention had spent \$194 million of the \$222 million allocated to respond to the 'Zika virus outbreak.'² WHO's \$22 million strategic plan for response, to be implemented until December, 2017, grossly underestimates the resources required. Still worse, WHO has raised only \$14.2 million in direct contributions for a worldwide response.³ WHO's emergency contingency fund has a negative balance of \$31.5 million, spent daily among ongoing health threats.⁴ Consequences of

Case Act. These policies make reproductive, maternal, and health services unaffordable or inaccessible. Poor women often face long waits for Zika virus testing, maternal, and other health services.

Up to 6% of Zika-virus-infected pregnant women will miscarry or have stillborn deliveries.⁵ Actual rates might be even higher. Surviving infants have as much as a 13% chance of Zika-virus-related microcephaly and associated mental, ocular, and hearing impairments.⁶ Recent studies suggest that Zika virus infection can cause severe joint damage and gastrointestinal, cardiac, and digestive complications among affected infants.⁷ Many could be impaired in less obvious ways, with disabilities appearing later in a child's development.

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Zika and Global Health Security – Some Facts

WHO strategic response plan needs until end-2017	\$122 million!!!
International funds raised by WHO to mid-August 2016	\$14.5 million
WHO emergency contingency fund for all health threats	\$31.5 million
World Bank estimates of economic losses, Latin America, to date	\$3.5 billion
World Bank offsetting loans to mid-August 2016	\$155 million
CDC spending on Zika response activities by end-August 2016	\$194 million of \$222 million allocated


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International Federation of Red Cross and Red Crescent Societies

UNDP

A SOCIO-ECONOMIC IMPACT ASSESSMENT OF THE ZIKA VIRUS IN LATIN AMERICA AND THE CARIBBEAN: with a focus on Brazil, Colombia and Suriname



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The United Nations Development Programme (UNDP) in partnership with the International Federation of Red Cross and Red Crescent Societies (IFRC)

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UNDP Report Conclusions

- The current Zika epidemic will have a long-term impact, and countries will incur high direct and indirect costs as a result.
- There is a profound equity challenge at the core of the Zika epidemic. The impact is disproportionate on the poorest countries of the region, as well as on the poorest and most vulnerable groups, especially poor women in peri-urban communities.
- Regional and national preparedness and response strategies require strengthening and must involve communities.

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UNDP Report Recommendations

Given that Zika is likely to become endemic, budgetary plans should be established accordingly.

Integrate efforts aimed at multiple mosquito-borne viruses, allowing room to tailor approaches to each disease's unique effects.

Put equity considerations at the forefront of Zika strategies and provide adequate social protection mechanisms for those affected.

Promote public policies that support gender equality and promote sexual and reproductive health and rights, targeting affected communities.

Develop a multi-sectoral approach to mosquito-borne diseases both nationally and regionally.

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ESSAY

Make Data Sharing Routine to Prepare for Public Health Emergencies

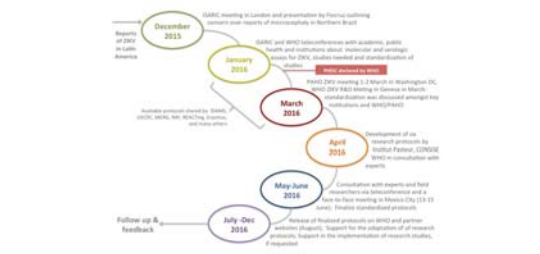
Jean-Paul Chretien^{1*}, Caitlin M. Rivers², Michael A. Johansson³

¹ Integrated Surveillance Section, Armed Forces Health Surveillance Branch, Defense Health Agency, Silver Spring, Maryland, United States of America, ² Epidemiology and Disease Surveillance, US Army Institute of Public Health, Aberdeen Proving Ground, Maryland, United States of America, ³ Dengue Branch, Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, San Juan, Puerto Rico, United States of America

Source: Chretien J-P, Rivers CM, Johansson MA (2016) Make Data Sharing Routine to Prepare for Public Health Emergencies. PLoS Med 13(8): e1002109. doi:10.1371/journal.pmed.1002109

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December 2015: IHRIC meeting in London and presentation by Patrick Gunning (summary of reports of microcephaly in Northern Brazil)

January 2016: IHRIC and WHO consultations with academic, public health and institutions about molecular and serologic assays for ZIKV; studies started and identification of the outbreak

March 2016: IHRIC ZIKV meeting 1-3 March in Washington DC; IHRIC ZIKV F&C meeting in Geneva in March; standardization was discussed amongst the institutions and WHO/IFRC

April 2016: Development of an research protocols by Institut Pasteur, CNRS/IRD in consultation with experts

May-June 2016: Consultation with experts and field researchers on identification and a first in-house meeting in Valencia City (19-21 April); finalised operational protocols

July-Dec 2016: Review of finalized protocols on IRD and partner institutes globally; support for the adaptation of research protocols; support in the implementation of research studies; a response

Follow up & feedback

Figure 1. Timeline for the development and implementation of standardized research protocols for ZIKV

PublicHealthOntario.ca Source: WHO/Institut Pasteur Draft 108

Our globally inter-connected reality

- The frontlines of infectious disease surveillance and response are not border-crossings/ports-of-entry.
- They are:
 - **Primary care/urgent care**
 - **Emergency departments/hospitals**
- EMS
- Community care
- LTC