Zika: Resources at Your Fingertips

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In 2016, the World Health Organization (WHO) declared Zika a public health emergency of international concern. Outbreaks occurred over the globe, including in the U.S. By the end of that same year, WHO cancelled the declaration, but the concern for hot spots remains. This document is primarily intended to inform planning in jurisdictions experiencing a Zika virus disease outbreak or anticipating a surge in cases resulting from exposures during travel in locations with active disease transmission. Not all content is relevant outside these circumstances, but planners are encouraged to maintain awareness of current Zika virus transmission patterns and emerging outbreaks to rapidly identify increasing risk and enable timely implementation of the considerations outlined in this document.

This document provides Zika virus disease resources and an overview of public health and healthcare system considerations and implications that are applicable to professionals in those systems, emergency management stakeholders, and other audiences. **Appendix A** contains resources from the U.S. Department of Health and Human Services (HHS) Office of the Assistant Secretary for Preparedness and Response (ASPR) and relevant contact links. **Appendix B** includes citations with annotations for additional relevant resources and Zika Guidance. Finally, individuals can review the ASPR TRACIE (Technical Resources, Assistance Center, and Information Exchange) Zika Topic Collection, which provides a wide array of materials and resources for further research.

This document and its hyperlinks/guidance references are current as of February 17, 2022. Changes to resources and guidance since the last update are indicated in RED FONT and all changes or additions since the original publication include the date of inclusion or update. Information on Zika is constantly evolving; therefore, if you are a clinician treating a patient, please check the Centers for Disease Control and Prevention (CDC) Zika virus site for the most current information and clinical guidance.

Quick Links

What is Zika Virus?

Zika virus is transmitted through the bite of an infected *Aedes* species mosquito. It is a single-stranded RNA virus of the genus Flavivirus (the same family as dengue). Zika virus disease is usually mild – data show that most people infected will not become symptomatic. Symptoms (fever, rash, joint pain, and conjunctivitis) typically resolve in a few days to a week without any medical intervention. The illness is rarely severe though Zika virus disease has been linked to rare cases of Guillain-Barré syndrome.

More concerning is the confirmed linkage between Zika virus infection in pregnant women and microcephaly and other severe fetal brain defects. (Updated May 9, 2016) This linkage and the spectrum of potential Zika-mediated neurologic syndromes continues to be investigated. Women who contract Zika virus during pregnancy are at risk, though the timing and magnitude of the risk continue to be defined. Microcephaly is a birth defect where a baby's head is smaller than expected when compared to babies of the same sex and age. Babies with microcephaly typically have smaller brains that might not have developed properly. Zika virus' effects on neurological function may result in a spectrum of neurological disorders, not simply causing brain damage leading to microcephaly in utero or Guillain-Barré in pediatric and adult patients.

Due to the clusters of microcephaly and other neurological syndromes potentially linked to the spread of Zika virus, the World Health Organization (WHO) declared the situation a Public Health Emergency of International Concern (PHEIC) February 1, 2016. The Emergency Committee convened by WHO on November 18, 2016 determined that Zika virus and associated consequences no longer met the definition for a PHEIC, but the demonstrated link between Zika virus infection and microcephaly required sustained research to address the long-term nature of the disease and its consequences. (Updated January 27, 2017) Zika virus infection is a Nationally Notifiable Condition, so healthcare providers must notify their local/State health departments according to the laws or regulations for reportable diseases in their jurisdiction. (Updated January 27, 2017) Access the Clinicians/Healthcare Providers section of this document for information on Preparedness, Testing, and Patient Care.

Why is Zika Virus Disease a Public Health and Healthcare Systems Concern?

Zika virus is an emerging pathogen and our understanding of it is still evolving. The major reason that Zika virus disease is a public health concern is due to the implications for women in endemic areas or traveling to endemic areas who are pregnant or considering pregnancy and the potential neurological sequela that may present in some patients. (Updated May 9, 2016) Zika virus has been identified in fetal and placental tissues of fetuses with severe congenital abnormalities although little is known about the specific rates of transmission or the risks and timing of congenital malformations. (Updated May 9, 2016) Though the brain damage and associated microcephaly have attracted the most attention, it is likely that Zika causes a broader spectrum of neurologic disease, which is still being investigated. The WHO published a Bulletin titled, Defining the Syndrome Associated with Congenital Zika Virus Infection, which outlines the spectrum of abnormalities that may be associated with Zika virus infection. This spectrum includes microcephaly, craniofacial disproportion, spasticity, seizures, irritability, and brainstem dysfunction including feeding difficulties, ocular abnormalities, and findings on neuroimaging such as calcifications, cortical disorders, and ventriculomegaly. (Updated June 6, 2016) A review of published studies through September 2016 on Zika-related birth defects identified five features unique to congenital Zika virus infection or rarely seen in other congenital infections: severe microcephaly with partially-collapsed skull, thin cerebral cortices with subcortical calcifications, macular scarring and focal pigmentary retinal mottling, congenital contractures, and marked early hypertonia and symptoms of extrapyramidal involvement. (Updated November 14, 2016) A study of infants with probable congenital Zika virus syndrome found that additional symptoms emerged with age and suggested that Zika-affected babies may continue to fall behind in development compared to those not affected. (Updated October 7, 2016) Early evidence does not suggest a greater health risk than the general population to pediatric populations who acquire Zika virus disease postnatally; however, the study results emphasize the importance of counseling sexually active adolescents on Zika risks and prevention. (Updated October 7, 2016)

As there is no specific treatment or “cure” for Zika virus disease and symptoms of acute infection are usually mild and self-resolving, the most important steps for public health emergency managers relate to prevention, mitigation, and risk communication. Healthcare providers should familiarize themselves with the signs and symptoms of Zika virus infection, take travel histories of their patients and the sexual partners of pregnant women, and follow CDC guidance on diagnostic testing for Zika virus in pregnant women and monitoring of pregnant women with evidence of Zika virus infection. Women in endemic areas face difficult choices about conceiving with no clear endpoint aside from vaccine availability or the end of the epidemic, and those who have visited or have a partner who has visited an endemic area may have to carefully consider their options, test, and take precautions for months afterwards.

Where is Zika Virus Found?

Zika virus was discovered in the Zika forest in Uganda in 1947. Prior to 2015, Zika virus was found in Africa, Southeast Asia, and the Pacific Islands. The largest outbreak to that point occurred in French Polynesia during 2013-2014. A retrospective analysis of this outbreak conducted by French Polynesian health authorities after cases of microcephaly were identified in Brazil found increases of cases of microcephaly.

In May 2015, the Pan American Health Organization (PAHO) issued an alert for the first confirmed patient in Brazil. A significant increase in reported cases of microcephaly occurred simultaneous to spread of the virus in Brazil. Many countries in Central and South America, the Caribbean, West Africa, Pacific Islands, and the United States reported local transmission of the virus. (Updated August 5, 2016) In July 2016, the CDC and the state of Florida confirmed the first local Zika virus transmission by mosquitoes in the continental U.S., in addition to the cases reported in travelers returning from affected countries. (Updated August 5, 2016) There has been no local transmission of Zika virus in the continental U.S. since 2017 and no confirmed Zika virus disease cases in U.S. territories since 2019. (Updated February 17, 2022) The CDC tracks domestic Zika cases and provides current case counts and geographic spread of cases. (Updated August 13, 2018) Travelers should maintain awareness of areas with outbreaks and take appropriate precautions. (Updated February 17, 2022)

What are the Mosquito Vectors for Zika Virus and Where are They Found?

Figure 1 shows locations within the continental U.S. where *Aedes aegypti* and Figure 2 shows locations where *Aedes albopictus* mosquitoes, the primary vectors of Zika, dengue, and chikungunya viruses, are found. These *Aedes* mosquitoes have been found in 30 states and the District of Columbia, including the southeastern U.S., up the east coast to New York, and west to Indiana, Ohio, and Kentucky. These are areas at potential risk of local transmission of Zika virus (and also areas of potential transmission of dengue, chikungunya, and other diseases spread by *Aedes* mosquitoes). Aedes mosquitoes that spread Zika virus are aggressive daytime biters, but they can also bite at night. Aedes mosquitos breed in small collections of water and seldom venture far from where they were born, making control particularly difficult. Outside of the continental U.S., *Aedes* mosquitoes have been found in the following states and territories: Hawaii, Puerto Rico, American Samoa, Guam, Northern Mariana Islands, and the U.S. Virgin Islands. Zika is spread from an infected mosquito to a person to a mosquito. The virus can spread to new areas where *Aedes* mosquitoes are known to exist when an infected, viremic traveler from an endemic area is bitten by a mosquito and that person transmits the virus to the mosquito, causing a new transmission chain to begin. Sustainment of that transmission depends on many variables, however, and does not guarantee that local transmission will continue. Once a mosquito is infected with Zika virus, it will remain infected for life. A mosquito lifespan is up to 30 days. (Updated May 9, 2016)

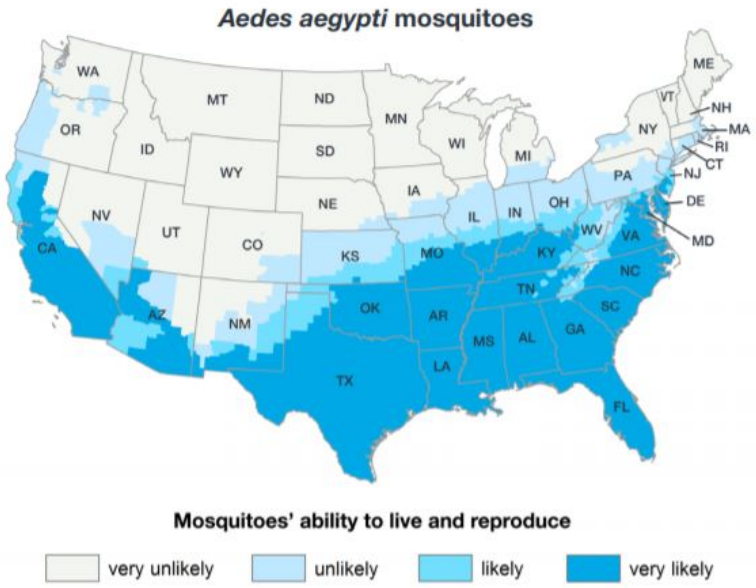

Figure 1. Estimated range of Aedes aegypti mosquitoes in the contiguous United States. Graphic courtesy of CDC. (Current as of February 16, 2018.)

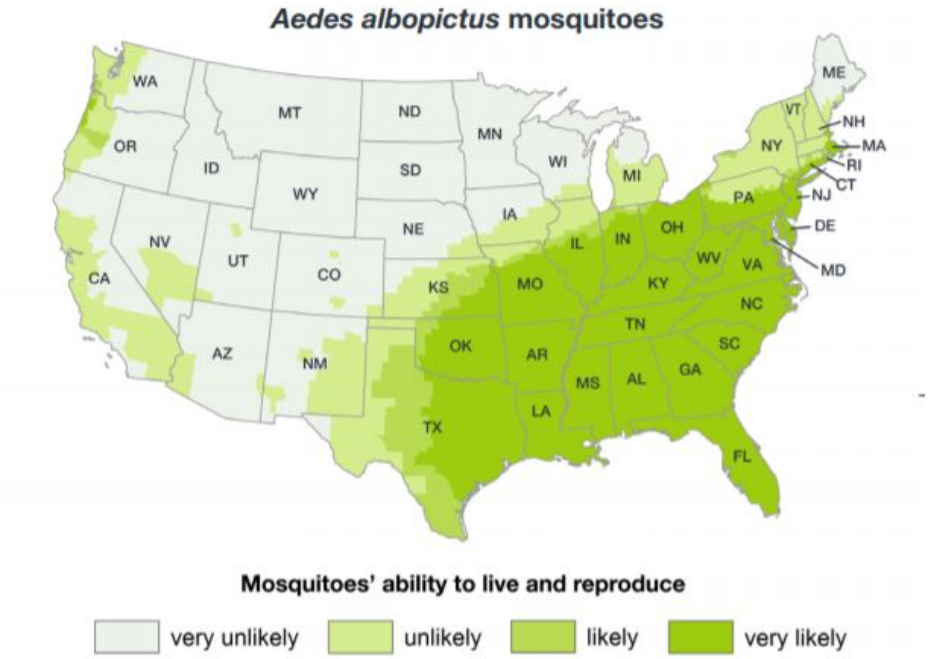

Figure 2. Estimated range of Aedes albopictus mosquitoes in the contiguous United States. Graphic Courtesy of CDC. (Current as of February 16, 2018.)

Can Zika Virus be Transmitted Person to Person?

There is evidence that Zika virus can be sexually transmitted (male to female [Updated April 8, 2016], male to male [Updated May 9, 2016], and female to male [Updated September 2, 2016]), and transmitted from a mother to her fetus during pregnancy. A case suggests possible sexual transmission from an asymptomatic male to female. (Updated September 2, 2016) Although there is no evidence Zika virus can be transmitted through casual contact or through air, local healthcare providers and the CDC completed an investigation of a possible case of non-sexual person-to-person transmission in Utah. (Updated October 7, 2016)

There are indications that it is possible to transmit Zika through a blood transfusion (Updated October 7, 2016), so providers should, as always, use standard precautions for personal protection when dealing with blood and blood products. On March 13, 2017, the CDC issued a special notice because analysis of locally-acquired cases in Florida revealed that blood and tissue safety in Broward and Palm Beach Counties may also be at increased risk due to Zika virus transmission in nearby Miami Dade County. While the risk is considered to be very low, tissue donors – particularly semen donors – are currently not tested for Zika, making this finding an important consideration factor for women and their partners trying to conceive, healthcare providers, and blood and tissue collection establishments. (Updated March 20, 2017) However, due to the lack of recent disease transmission in the U.S., the FDA withdrew its guidance requiring blood establishments to test donations for Zika virus in 2021. (Updated February 17, 2022)

Current guidelines for prevention of sexual transmission are as follows (Updated February 17, 2022):

- Couples planning to conceive:
  - Men should wait at least 3 months after symptom onset or last possible Zika exposure to attempt to conceive.
  - Women should wait at least 8 weeks after symptom onset or last possible Zika exposure to attempt to conceive.
  - Couples undergoing fertility treatment with their own gametes and embryos should follow the same guidelines.
- Couples who are not pregnant or planning to become pregnant, but who want to maximally reduce their risk of sexual transmission:
  - Men should practice abstinence or use condoms consistently and correctly for at least 3 months after symptom onset or last possible Zika exposure.
  - Women should abstain or use condoms consistently and correctly for at least 8 weeks after symptom onset or last possible Zika exposure.

Possible exposure is living in or traveling to a geographic area with active Zika transmission or sex without a condom with a partner who lives in or has traveled to such an area.

Earlier studies found that Zika virus has been detected in semen up to eight weeks after the onset of febrile illness and very high concentrations of live virus have been detected in semen at 2 weeks. (Updated October 7, 2016) Additional studies suggest that Zika virus remains in semen longer than other bodily fluids. (Updated September 29, 2017) Zika virus RNA has been found in semen as long as 188 days after symptom onset. (Updated October 7, 2016) Other studies have found that while Zika virus RNA can be detected in semen months after illness, prolonged shedding of infectious Zika is rare. (Updated February 17, 2022)

To avoid Zika transmission from a mother to her fetus, pregnant women should:

- Avoid travel to areas where Zika virus has been newly introduced or reintroduced and local mosquito-borne transmission is ongoing, where the virus was present before 2015 and there is no evidence that transmission has stopped, and where the virus is likely to be circulating but has yet to be documented. (Updated March 20, 2017)
- Prevent mosquito bites if they must travel to or reside in such areas.
- Abstain from sex or use a condom with a partner who has possible exposure to Zika.

How do Clinicians Test for Zika Virus Disease?

The CDC provides combined testing guidance for Zika and dengue viruses due to the similar transmission and disease symptoms associated with these mosquito borne flaviviruses for patients with clinically compatible illness living in or with recent travel to an active transmission area where there is a risk for both viruses. Exposure to dengue and Zika virus infections are mostly asymptomatic. The incubation period from infection until disease onset ranges from two to fourteen days. The virus RNA is detectable in the serum two days before onset of illness to one week after the onset. (Updated February 17, 2022)

Asymptomatic non-pregnant women: Previous recommendations for asymptomatic non-pregnant women remain the same with testing not recommended for Zika virus or dengue. Zika virus testing should not be part of preconception screening. (Updated February 17, 2002)

Asymptomatic pregnant women: For asymptomatic pregnant women living in or with recent travel to the U.S. and its territories, routine Zika testing is not currently recommended. For asymptomatic pregnant women who traveled to a high-risk transmission area with Zika outside the U.S. and its territories, testing is not routinely recommended but Nucleic Acid Amplification Testing (NAAT) may be considered up to 12 weeks after travel. Serologic testing for Zika virus is not recommended for asymptomatic pregnant women as IgM antibodies can persist for months to years following infection and provide limitations in determining whether the Zika virus infection occurred during or before pregnancy. Notable cross-reactivity is observed between dengue IgM and Zika IgM antibodies in serologic tests. This can cause a Zika IgM false positive due to a recent dengue infection. A shared decision-making model should be considered where patients and providers make decisions together about testing. (Updated February 17, 2002)

Symptomatic pregnant women: For symptomatic pregnant women with recent travel to areas with active dengue transmission and at risk for Zika virus infection, specimens should be collected as soon as possible after the onset of symptoms up to twelve weeks after onset. NAAT testing on a serum specimen should be performed for dengue and Zika at the same time along with a Zika virus NAAT on a urine specimen and only IgM testing for dengue. IgM Zika virus testing is not recommended for symptomatic pregnant women due to the persistence of IgM antibodies lingering for month to years following an infection. If the Zika virus NAAT is positive on a single specimen, then a repeated test should be performed on newly extracted RNA from the same specimen to rule out a false positive NAAT. A positive NAAT test or IgM antibody test for dengue is adequate for diagnosing the infection and no additional testing is required. Symptomatic pregnant women who have had sex with someone who lives in or recently traveled to a high transmission area with risk of Zika virus infection should have specimens taken from the onset of symptoms up to twelve weeks. Only Zika NAAT should be performed and if positive on a single specimen, a repeated NAAT should be performed on newly extracted RNA from the same specimen to rule out a false positive. Pregnant women with a confirmed prenatal ultrasound finding consistent with Zika virus who live in or traveled to areas of high-risk transmission for Zika during pregnancy should have Zika NAAT and IgM testing performed on maternal serum and NAAT on maternal urine. If the NAATs are negative and the IgM is positive a Plaque Reduction Neutralization Test (PRNT) should be performed against Zika virus and dengue. If as part of the clinical care an amniocentesis is performed, a Zika virus NAAT test of the fluid should be done, and results explained within the context of the limitations of amniotic fluid testing. There is an unknown factor on how sensitive or specific RNA NAAT testing of amniotic fluid is in determining congenital Zika virus infection or what proportion of infants born after infection will have abnormalities. There is also consideration for testing placental and fetal tissues. (Updated February 17, 2002)

Symptomatic non-pregnant persons: For symptomatic non-pregnant persons with suspected dengue or Zika virus, NAATs should be performed and are the preferred method of diagnosis. IgM can identify other infections and is valuable for diagnosing diseases but, as noted, cross-reactivity can complicate interpretation of results. Recommendations are to refer to specific dengue testing and guidance for this group. (Updated February 17, 2002)

Viremia levels decline over time and can lead to inaccurate reporting of illness onset. A negative NAAT does not eliminate either dengue or Zika virus. If IgM antibody testing is positive for dengue or Zika virus without a positive NAAT or Non-structural Protein (NS1) antigen test a definitive diagnosis is required to determine clinical or epidemiologic purposes with a confirmatory PRNT performed against dengue, Zika, and other flaviviruses endemic to the region. For suspected patients with dengue or Zika virus infection, molecular testing can confirm infections. NAATs can delineate specific viruses but can also provide false-negative and false positive results. Patients with clinical dengue should be monitored with appropriate management of care. Pregnant women diagnosed with laboratory confirmed Zika and their infants should be monitored and evaluated for adverse outcomes to include Congenital Zika Syndrome (CZS). (Updated February 17, 2002)

The U.S. Food and Drug Administration authorized four diagnostic tests for Zika virus. Several other tests for detecting Zika virus antibodies are available under Emergency Use Authorizations (EUAs). (Updated February 17, 2022)

How is Zika Virus Disease Treated?

There is no specific treatment for Zika virus disease. Supportive care and symptom management are the best options. No vaccination currently exists. It is important to note that Zika virus disease is transmitted by the same mosquitoes that spread chikungunya and dengue viruses; therefore, all three diseases should be considered in any patient with consistent signs and symptoms. The mainstay of disease management is prevention. Pregnant women should be referred to their provider for further evaluation and treatment. For more information about Zika virus disease, including guidance for clinicians, visit the CDC Zika virus website.

What Research and Development is Underway Related to Zika Virus Disease?

The U.S. government supports numerous research and development efforts related to Zika virus and how it affects various populations. The development and approval of a safe and effective vaccine is expected to take several years. Early research on potential treatments for Zika includes using an existing antiviral drug screening program for other flaviviruses to test drug compounds for activity against Zika; screening a library of approved drugs for activity against Zika; creating a rodent model on which to test antiviral compounds; and developing monoclonal antibodies capable of neutralizing Zika.

Internationally, the WHO published a Zika Virus Research Agenda that identifies areas of research the organization may be uniquely qualified to implement or coordinate. The WHO summarized its effort to harmonize its research protocols with those of PAHO, Institut Pasteur, and the networks of Fiocruz, Consortium for the Standardization of Influenza Seroepidemiology, and the International Severe Acute Respiratory and Emerging Infection Consortium. This harmonization effort includes the development of draft standardized research protocols for case-control, prospective longitudinal cohort, and cross-sectional seroprevalence studies of various populations.

What Support is Available to Communities Preparing for and Responding to Zika Virus Disease?

In September 2016, the federal government approved funding of $1.1 billion for Zika preparedness and response. In addition to supporting federal Zika-related efforts and vaccine and diagnostic development, a portion of these funds was awarded by several federal agencies to state, territorial, and local governments; health centers and healthcare providers; and public health organizations to address health and social support needs in affected geographic

locations and to strengthen capabilities in areas such as vector control and laboratory capacity. (Updated February 17, 2022)

What Effect Do Hurricanes and Tropical Storms Have on Zika?

The risk of Zika virus disease is not expected to increase in the immediate aftermath of natural disasters, but preventive efforts are necessary to reduce the long-term risk. Adult mosquitoes are likely to be killed by the high winds brought by hurricanes and tropical storms. Populations of floodwater mosquitoes – those species that lay eggs in soil that periodically floods – are likely to spike in the days and weeks following flooding conditions, but these tend to be nuisance species that do not carry Zika virus, West Nile virus, and dengue. In the longer term, standing water provides breeding grounds for those species that do transmit infectious diseases. In locations where flooding has occurred and standing water is present, particularly where Zika virus and mosquito-borne infections are endemic, residents should take steps to limit exposure to mosquitoes, particularly if their living quarters were compromised. Local officials should encourage the use of insect repellants; remove sources of standing water; continue surveillance of mosquito populations and vector-borne illnesses; and maintain or establish vector control programs. (Updated September 29, 2017)

Key Points for Consideration and Resources by Profession

All Professions

Case Numbers

- Cases in the United States [CDC] (Updated February 17, 2022)
- Data and Statistics on Zika and Pregnancy [CDC] (Updated February 17, 2022)

Prevention

- There is currently no vaccine. Senior federal officials outlined three potential strategies for investigators to consider when conducting clinical trials on Zika vaccine candidates. (Updated October 7, 2016)
- Because Zika infection is a cause of severe congenital disease, pregnant women (and those anticipating becoming pregnant in the next few months) who live in or cannot avoid travel to endemic areas should strictly follow steps to prevent mosquito bites. (Updated February 17, 2022)
- If a pregnant woman has a sex partner who lives in or has traveled to an area with Zika virus transmission, they should use a condom every time they have sexual intercourse or should not have sexual intercourse during the pregnancy. (Updated May 9, 2016)

Transmission

- The primary mode of transmission of Zika virus is a bite from an infected mosquito.
- Perinatal and sexual transmission, as well as transmission via blood transfusion, have been reported.

- The incubation period is 2-7 days.

Presentation and Treatment

- Most people infected with Zika virus will not become symptomatic. (Updated May 9, 2016)
- Illness is usually mild, lasting several days to a week.
- Acute onset of fever with maculopapular rash (flat, red area on skin covered by small bumps), arthralgia (joint pain), and/or conjunctivitis (inflammation of the inner surface of the eyelid and outermost layer of the eye) may occur.
- Myalgia (muscle pain) and headache are also reported.
- There is no "cure" or treatment specific to Zika virus disease.
- Symptoms of acute Zika virus infection can be treated with supportive care.
- Hospitalization for acute Zika virus infection is uncommon.
- Deaths are rare.

Clinicians/Healthcare Providers

Preparedness

- Monitor outbreak information and changes or updates to CDC medical management guidance and from public health departments or healthcare coalitions. (Updated August 13, 2018)
- Contact the state health department to facilitate testing. Ensure a plan is in place for transporting laboratory samples to designated labs for confirmatory testing. As of July 1, 2016, public health laboratories in all 50 states can provide testing using RT-PCR, IgM ELISA, and PRNT assays. (Updated January 27, 2017)
- Review this Zika Virus Planning Considerations for Healthcare Facilities and Coalitions document to identify anticipated hospital and healthcare system planning issues. (Updated September 2, 2016)
- Resources:
    - Fact Sheets and Posters. [CDC] (Updated September 29, 2017)
    - Information for Healthcare Providers. [CDC] (Updated September 29, 2017)
    - Training Resources for Health Professionals. [CDC] (Updated August 13, 2018)
    - Zika in the ED: How Emergency Care Staff Can Take Action Webinar. [CDC] (Updated January 27, 2017)
    - Zika Sustainment Strategy Presentations. [CDC] (Updated August 13, 2018)
    - Zika Virus: A Primer for Nurses. [CDC] (Updated July 26, 2017)
    - Zika Virus: Information for Clinicians PowerPoint. [CDC] (Updated July 7, 2016)

Testing

- Maintain awareness of evolving laboratory guidance about when to test for Zika virus based on presence of symptoms, pregnancy status, and travel history. (Updated February 17, 2022)

- Resources:
    - Collecting and Submitting Placental and Fetal Tissue Specimens for Zika Virus Testing. [CDC] (Updated February 17, 2022)
    - Collecting and Submitting Specimens at Time of Birth for Zika Virus Testing. [CDC] (Updated February 17, 2022)
    - Dengue and Zika Virus Diagnostic Testing for Patients with a Clinically Compatible Illness and Risk for Infection with Both Viruses. [CDC] (Updated February 17, 2022)
    - Evaluation and Testing for Zika Virus. [CDC] (Updated February 17, 2022)
    - Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection – United States, October 2017. [CDC] (Updated February 17, 2022)
    - Testing for Zika Virus. [CDC] (Updated February 17, 2022)
    - 3 Zika Tests Explained. [APHL] (Updated October 7, 2016)

Patient Care – General

- Do **not** give NSAIDS—for example acetyl-salicylic acid (aspirin) and ibuprofen—until dengue infection can be ruled out. These drugs thin the blood and can increase the risk of bleeding. Fever and pain can be addressed with acetaminophen. (Updated May 9, 2016)
- Continue to collect travel histories during healthcare assessments for: (1) symptoms suggestive of mosquito-borne illness, and (2) all pregnant patients and their sexual partners. (Updated May 9, 2016)
- Advise patients to strictly follow steps to prevent mosquito bites during the first week of illness to help prevent others from getting sick from local mosquito transmission. (Updated May 9, 2016)
- Counsel male and female patients of reproductive age on preventive behaviors.
- Resources:
    - Clinical Guidance for Healthcare Providers for Prevention of Sexual Transmission of Zika Virus. [CDC] (Updated February 17, 2022)
    - Guidance for Organ Donation and Transplantation Professionals Regarding the Zika Virus. [UNOS] (Updated April 8, 2016)
    - Providing Family Planning Care for Non-Pregnant Women and Men of Reproductive Age in the Context of Zika. [OPA] (Updated January 27, 2017)
    - Symptoms, Testing, & Treatment. [CDC]
    - Tool for the Diagnosis and Care of Patients with Suspected Arboviral Diseases. [PAHO] (Updated June 12, 2017)
    - WHO Guidelines for the Prevention of Sexual Transmission of Zika Virus. [WHO] (Updated February 17, 2022)
    - WHO Toolkit for the Care and Support of People Affected by Complications Associated with Zika Virus. [WHO] (Updated September 29, 2017)

Patient Care – Pregnant Women and Women of Reproductive Age

- Discuss Zika infection with women of reproductive age residing in or planning travel to areas with Zika virus transmission risk. (Updated February 17, 2022)
- Assure access to barrier contraception for patients and partners at potential risk. (Updated May 9, 2016)
- Counsel pregnant women in mosquito avoidance.
- Screen pregnant women for exposure to Zika virus. A marked increase in the number of babies born with congenital neurologic damage was reported in areas experiencing Zika virus disease outbreaks and a causal link from Zika virus infection to neurological syndromes including microcephaly and Guillain-Barré syndrome has been confirmed (updated May 9, 2016). Pregnant women presenting with Zika virus disease symptoms should be evaluated according to the Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Exposure - United States (Including U.S. Territories), July 2017. (Updated July 26, 2017)
- Resources:
    - Estimating Contraceptive Needs and Increasing Access to Contraception in Response to the Zika Virus Disease Outbreak. [CDC] (Updated April 8, 2016)
    - Gaps in Contraception Access and Zika: Interactive Map. [ASPR] (Updated September 2, 2016)
    - Interim Guidance for Care of Obstetric Patients During a Zika Virus Outbreak. [ACOG & SMFM] (Updated September 29, 2017)
    - Maternal-Fetal Health Planning Resource. [ASPR TRACIE] (Updated August 5, 2016)
    - Pregnancy and Zika. [CDC] (Updated February 17, 2022)
    - Preventing Transmission of Zika Virus in Labor and Delivery Settings Through Implementation of Standard Precautions. [CDC] (Updated April 8, 2016)
    - Promoting Stress Management for Pregnant Women during the Zika Virus Disease Outbreak. (Updated June 6, 2016) Spanish Version. [ASPR ABC] (Updated July 7, 2016)
    - Psychosocial Support for Pregnant Women and for Families with Microcephaly and other Neurological Complications in the Context of Zika Virus: Interim Guidance for Healthcare Providers. [WHO] (Updated September 2, 2016)
    - US Zika Pregnancy and Infant Registry. [CDC] (Updated February 17, 2022)
    - Zika Active Pregnancy Surveillance System (ZAPSS). [CDC] (Updated August 13, 2018)
    - Zika Grand Rounds Facilitation Guide: Pregnancy. [CDC] (Updated January 27, 2017)

Patient Care – Infants and Children

- Use this case definition to evaluate infants for congenital neurologic changes. (Updated August 13, 2018) Because it is difficult to predict at birth what problems babies will have, babies with specific findings or likely in utero exposure need close follow-up through regular check-ups with a doctor or other healthcare provider to track their growth and development. (Updated May 9, 2016)
- Be prepared to strengthen antenatal care and ensure availability of fetal ultrasound capability as well as antenatal counseling and support.
- Resources:
    - Care for Babies Affected by Zika. [CDC] (Updated February 17, 2022)
    - Caring for Infants and Children. [CDC] (Updated February 17, 2022)
    - CDC Urges Follow-up Evaluation of Babies Born to Women with Zika Virus Infection during Pregnancy. [CDC] (Updated August 13, 2018)
    - Evaluation and Testing for Zika Virus. [CDC] (Updated February 17, 2022)
    - Facts about Microcephaly. [CDC] (Updated August 13, 2018)
    - Follow-Up Care. [CDC] (Updated August 13, 2018)
    - Guidance for Review of Zika-Related Fatalities. [National Center for Fatality Review and Prevention] (Updated June 12, 2017)
    - Implementing CDC Guidance for Infant Neuroimaging and Infant and Placental Zika Virus Testing. [CDC] (July 26, 2017)
    - Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection. [CDC] (Updated February 17, 2022)
    - Measuring Infant Head Circumference: An Instructional Video for Healthcare Providers. [CDC] (Updated November 14, 2016)
    - New Zika Guidance Highlights the Need for Pediatricians to be Vigilant. [AAP] (Updated February 17, 2022)
    - Psychosocial Support for Pregnant Women and for Families with Microcephaly and other Neurological Complications in the Context of Zika Virus: Interim Guidance for Healthcare Providers. [WHO] (Updated February 17, 2022)
    - Resource Guide for States and Communities Caring for Infants and Children Affected by Zika Virus. [HRSA] (Updated January 27, 2017)
    - Support for Families of Newborns Affected by Zika. [CDC] (Updated August 13, 2018)
    - Supporting Children with Special Health Care Needs Planning Resource. [ASPR TRACIE] (Updated September 2, 2016)
    - Webcast Recordings: Clinical Evaluation and Management of Infants with Congenital Zika Infection. [CDC] (Updated August 13, 2018)
    - WHO Toolkit for the Care and Support of People Affected by Complications Associated with Zika Virus. [WHO] (Updated February 17, 2022)

- Zika Grand Rounds Facilitation Guide: Pediatrics. [CDC] (Updated January 27, 2017)
- Zika in Infants and Children. [CDC] (Updated February 17, 2022)

Patient Care – GBS/Neurological

- Maintain awareness of the link between Zika virus and Guillain-Barré syndrome. Cases of Guillain-Barré have been reported, which could result in the need for intensive care and mechanical ventilation – unlikely to reach levels of significant impact on the healthcare system, but localized surges requiring specialized care could be possible. In endemic areas, intensive care may not be available. (Updated May 9, 2016)
- Be prepared for a possible increase in demand for specialized care for patients with Guillain-Barré syndrome – while unlikely to result in a surge in demand for critical care resources, the potential for Guillain-Barré syndrome and other neurologic sequelae should be prepared for in a diligent and determined manner. The potential for a cluster of cases certainly exists, while the availability of clinicians with expertise in the management of Guillain-Barré syndrome may be limited, especially in certain geographic locations. (Updated May 9, 2016)
- Resources:
  - Guillain-Barré Syndrome and Other Neurological Deficits Planning Resource. [ASPR TRACIE] (Updated September 2, 2016)

Emergency Management/ Public Health Preparedness/ Healthcare System Emergency Management Professionals

General Preparedness and Response

- Monitor outbreak information and changes or updates to CDC medical management guidance.
- Ensure a plan is in place for transporting laboratory samples to designated labs for testing. Ensure healthcare facilities have plans and policies in place that state under what situations testing is indicated. Widespread testing is NOT recommended.
- Review this Zika Virus Planning Considerations for Healthcare Facilities and Coalitions document to identify anticipated hospital and healthcare system planning issues. (Updated September 2, 2016) Key roles of healthcare coalitions include:
  - Sharing guidance from federal, state, and local authorities, including updates.
  - Identifying local/regional experts (specifically, neurology, maternal fetal medicine, neonatology) who can interpret guidance and serve as regional discussant/subject matter experts.
  - Coordinating with public health departments on testing indications and process.
  - Coordinating public information about Zika virus disease.
- Engage Medical Reserve Corps and other voluntary organizations.
- Resources:
  - Epidemiologic Investigation Toolkit for Investigating Possible Local Mosquito-Borne Transmission of Zika Virus. [CDC] (Updated February 17, 2022)

- Resource Guide for States and Communities Caring for Infants and Children Affected by Zika Virus. [HRSA] (Updated January 27, 2017)
- Tribal Zika Response. [CDC] (Updated June 12, 2017)
- WHO Toolkit for the Care and Support of People Affected by Complications Associated with Zika Virus. [WHO] (Updated September 29, 2017)
- Zika Virus Planning Considerations for Healthcare Facilities and Coalitions. [ASPR TRACIE] (Updated September 2, 2016)

Worker Health and Safety

- Advise workers on preventive actions to avoid exposure to Zika virus.
- Resources:
  - Healthcare Exposure to Zika and Infection Control. [CDC] (Updated September 29, 2017)
  - Human Resources Flexibilities and Authorities for Federal Employees Affected by the Zika Virus. [OPM] (Updated October 7, 2016)
  - Interim Guidance for Managing Occupational Exposures to Zika Virus for Healthcare Personnel. [CDC] (Updated June 12, 2017)
  - Interim Guidance for Protecting Workers from Occupational Exposure to Zika. [OSHA & NIOSH] (Updated September 29, 2017)
  - Interim Guidance for Protecting Workers from Occupational Exposure to Zika Virus Fact Sheet. [OSHA & NIOSH] (Updated May 9, 2016)
  - Laboratory Safety when Working with Zika Virus. [CDC] (Updated June 12, 2017)
  - Mosquito-Borne Diseases. [NIOSH] (Updated May 9, 2016)
  - Prevent Mosquito–borne Diseases: Cruise Line Employees. [NIOSH] (Updated July 7, 2016)
  - Preventing Transmission of Zika Virus in Labor and Delivery Settings Through Implementation of Standard Precautions. [CDC] (Updated April 8, 2016)
  - Protecting the Health and Safety of Workers in Emergency Vector Control of Aedes Mosquitoes. [WHO] (Updated May 9, 2016)
  - The Zika Virus: Answers to Employers' FAQs. [EHS Today] (Updated May 9, 2016)
  - The Zika Virus: What Employers Should Not Do. [SHRM] (Updated May 9, 2016)

Risk Communication

- Provide clear instructions to the community about mosquito abatement and avoiding mosquitoes, particularly during biting hours.
- Educate the community on the purchase and proper use of EPA-registered insect repellents containing one of the following active ingredients: DEET, picaridin, IR3535, oil of lemon eucalyptus, permethrin, or para-menthane-diol.
  - When used as directed, EPA-registered insect repellents are proven safe and effective, even for pregnant and breastfeeding women.

    - Insect repellent containing DEET should not be used on infants younger than 2 months of age and repellents containing oil of lemon eucalyptus should not be used on children under 3 years. (Updated September 2, 2016)
    - Follow instructions on treating clothing with permethrin. (Updated October 7, 2016)
- Share information with the community about signs and symptoms of Zika virus disease and when to seek medical evaluation or treatment.
- Publicize travel advisories, targeting travelers, especially women who are pregnant or considering pregnancy.
- Monitor reports of local transmission of Zika virus.
- Correct misinformation and rumors with science-based educational materials and outreach activities.
- Resources:
    - Controlling Mosquitoes at Home. [CDC] (Updated June 12, 2017)
    - Fact Sheets and Posters. [CDC] (Updated September 29, 2017)
    - Mosquito Control and Bite Prevention Educational Flipbook. [CDC] (Updated October 7, 2016)
    - Mosquito Control: Do Your Part. [CDC] (Updated August 13, 2018)
    - Roadmap for Parents of Babies Infected with Zika Before Birth Who Appear Healthy. [CDC] (Updated August 13, 2018)
    - Roadmap for Parents of Babies with Congenital Zika Syndrome. [CDC] (June 12, 2017)
    - Zika Travel Information. [CDC] (Updated September 29, 2017)
    - Zika Virus and Pregnancy Fact Sheet. [March of Dimes] (Updated October 7, 2016)
    - Zika Virus and Pregnancy. [Mother to Baby] (Updated February 17, 2022)
    - Zika Virus Disease and Your Eyes. [Prevent Blindness] (Updated October 7, 2016)
    - Zika Virus Infection: Step-by-Step Guide to Risk Communication and Community Engagement. [PAHO] (Updated January 27, 2017)
    - Zika, Dengue and Chikungunya Prevention Toolkit. [International Federation of Red Cross and Red Crescent Societies] (Updated January 27, 2017)

Vector Control

- Collaborate with environmental health entities on community-based vector control/ bite prevention education.
    - Community/Facility
        - Eliminate standing water and maintain brush.
        - Apply insecticide spray to outdoor areas as feasible.
        - Make netting and other prevention items available as appropriate.
    - Individuals
        - Use insect repellent (as appropriate) and advise to follow label instructions.

        - Place netting over sleeping areas (e.g., beds, cribs) when screens are not available.
        - Avoidance of exposure is best and pregnant women/those considering pregnancy should delay travel to endemic areas when possible.
        - Refer to CDC guidance on prevention for more specific steps. (Updated April 8, 2016)
- Consider bed netting, insect spray, or other mosquito prevention equipment for facilities and workers if local cases are detected in endemic areas with open-air homes/hospitals.
- Monitor recommendations related to disinsection.
- Resources:
    - A Visual Guide to Modified Mosquitoes. [Scientific American] (Updated January 27, 2017)
    - Information on Aerial Spraying. [CDC] (Updated August 13, 2018)
    - Insect Repellant Use and Safety. [CDC]
    - Mosquitoes and Hurricanes. [CDC] (Updated September 29, 2017)
    - Mosquitoes and the Diseases They Transmit. [Texas A&M AgriLife Extension] (Updated September 29, 2017)
    - Regulation of Intentionally Altered Genomic DNA in Animals – Draft Guidance. [FDA] (June 12, 2017)
    - Resources for Mosquito Control Professionals. [CDC] (Updated February 17, 2022)
    - Surveillance and Control of *Aedes aegypti* and *Aedes albopictus* in the United States. [CDC] (Updated May 9, 2016)

Surveillance

- Establish or enhance surveillance (in people and mosquitoes).
- Conduct regular surveillance of and testing for mosquitoes. The use of GIS mapping of mosquito locations and abatement programs can show effectiveness and impact. (Updated May 9, 2016)
- Screen patients for travel history to an area with ongoing Zika transmission.
    - Zika virus disease affected patients
    - Birth defect surveillance
    - Neurologic and autoimmune syndrome surveillance
    - Border screening is not an effective method of controlling vector-borne diseases and is not recommended for Zika management.
- Resources:
    - Surveillance and Control of *Aedes aegypti* and *Aedes albopictus* in the United States. [CDC] (Updated May 9, 2016)
    - US Zika Pregnancy Registry. [CDC] (Updated August 13, 2018)
    - Zika Active Pregnancy Surveillance System (ZAPSS) [CDC] (Updated August 13, 2018)

Blood/Organ/Tissue Donation

- Maintain awareness of guidance related to blood, organ, and tissue donation.
- Resources:
    - Guidance for Organ Donation and Transplantation Professionals Regarding the Zika Virus. [UNOS] (Updated April 8, 2016)
    - Information for Blood Establishments Regarding FDA's Determination that Zika Virus is no Longer a Relevant Transfusion-Transmitted Infection. [FDA] (Updated February 17, 2022)

Veterinary/Animal Care Preparedness

- Maintain awareness of research and guidance related to Zika virus in animals.
    - Animals do not appear to be involved in the spread of Zika virus.
    - While Zika virus was first discovered in a monkey with a mild fever in the Zika Forest of Uganda in the 1940s, the current prevalence of Zika virus in monkeys and other nonhuman primates is not known.
    - At this time there have been no reports of other animals becoming sick with Zika or of being able to spread Zika to people or other animals.
- Resources:
    - Zika Virus and Animals. [CDC] (Updated August 13, 2018)

Large-Scale Events, Population Movement, and Travel

- Prepare for major national and international events in Zika-affected areas.
- Screen patients for travel history to an area with ongoing Zika transmission.
- Resources:
    - Travelers Can Protect Themselves from Zika. [CDC] (Updated January 27, 2017)
    - Zika Virus Country Classification Scheme. [WHO] (Updated March 20, 2017)

Administrative Preparedness

- Review emergency authorities and statutes for any relief necessary.
- Resources:
    - Declaration Under the Public Readiness and Emergency Preparedness Act for Zika Virus Vaccines. [Federal Register] (Updated August 13, 2018)
    - Emergency Legal Preparedness and Zika Virus: Primer. [The Network for Public Health Law] (Updated January 27, 2017)
    - Executive Orders and Emergency Declarations for the West Nile Virus: Applying Lessons from Past Outbreaks to Zika. [CDC] (Included March 9, 2016.)
    - Human Resources Flexibilities and Authorities for Federal Employees Affected by the Zika Virus. [OPM] (Updated October 7, 2016)

Recovery

- Continue surveillance and mosquito abatement, as appropriate.
- Evaluate any long-term health impacts to the community.

Plans and State- and Locally-Developed Resources

Please note these plans are public health plans concentrating on vector management and risk communications but do not reflect many of the clinical issues nor involvement by coalition partners, both of which are encouraged to be included in plans. If your jurisdiction or healthcare entity has a Zika Response Plan that you would like included in ASPR TRACIE, please send the plan to askasprtracie@hhs.gov for consideration.

National and International Plans

- Zika: CDC Interim Response Plan (Updated June 12, 2017)
- WHO: Zika Strategic Response Plan (Updated August 13, 2018)

State and Locally-Developed Plans and Resources (Updated July 7, 2016)

- Alabama
  - A Guide for Public Health Environmentalists, Municipalities, and County Commissions. (Updated October 7, 2016)
- California
  - Operational Checklist for Local Health Departments, Local Vector Control Agencies, and California Department of Public Health in the Event of Local Dengue, Chikungunya, or Zika Transmission. (Updated August 13, 2018)
- Florida
  - Sample Clinical Protocol for Suspected Zika Virus Infection. (Updated August 5, 2016)
- Kentucky
  - Louisville Zika Response Plan. (Updated July 7, 2016)
- Louisiana
  - City of New Orleans Zika Virus Plan (Updated July 7, 2016)
- Maryland
  - Zika Public Service Announcements (Updated October 7, 2016)
- Pennsylvania
  - Zika Virus Response Plan (Updated July 7, 2016)
- Texas
  - Regional Response Teams: Zika Response. (Updated July 7, 2016)
  - Texas Integrated Vector Management Capacity. (Updated July 7, 2016)
  - Zika Communications Toolkit. (Updated October 7, 2016)
  - Zika in Texas Website. (Updated September 29, 2017)
  - Zika Virus Preparedness and Response Plan. (Updated January 27, 2017)
- Virginia
  - Zika Virus Disease Response Annex (Updated July 7, 2016)

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Appendix A: ASPR Resources

ASPR.HHS.gov serves as the key one-stop website for all federal public health and medical information sources and assets. The site is searchable for multiple resources. https://aspr.hhs.gov/Pages/Home.aspx

The Technical Resources, Assistance Center, and Information Exchange (TRACIE) is a healthcare emergency information gateway that provides timely access to resources and promising practices, identifies and remedies knowledge gaps, and connects users with responses to a range of requests for technical assistance. https://asprtracie.hhs.gov/

Appendix B: Full References with Annotations

Adams, L., Bello-Pagan, M., Lozier, M., et al. (2016) Update: Ongoing Zika Virus Transmission – Puerto Rico. Morbidity and Mortality Weekly Report. 65(30): 774-779.

This report provides an update on the continued transmission of Zika virus disease in Puerto Rico including a review of the epidemiology of the outbreak and the public health response.

Adams Waldorf, K., Nelson, B., Stencel-Baerenwald, J., et al. (2018). Congenital Zika Virus Infection as a Silent Pathology with Loss of Neurogenic Output in the Fetal Brain. Nature Medicine. 24(3): 368-374.

The authors describe the findings of studies on Zika virus infection in a non-human primate model. They recommend long-term follow-up of children exposed to Zika virus disease in utero for neurocognitive deficits even if the child had a normal head size at birth.

American Medical Association. (2016). Zika Virus Resource Center.

This webpage provides a compilation of resources related to Zika virus disease.

Bhatnagar, J., Rabeneck, D., Martines, R., et al. (2016). Zika Virus RNA Replication and Persistence in Brain and Placental Tissue. Emerging Infectious Diseases. 23(3).

This study examined placental tissues from 44 women and brain tissues from 8 deceased infants who had microcephaly. All samples were from patients suspected to be infected with Zika, and testing detected Zika virus in all infant tissues and nearly three-quarters of the placental tissues of women with adverse pregnancy or birth outcomes. Zika virus RNA was found in placentas and fetal brains more than seven months after pregnant women contracted Zika. Additionally, Zika RNA levels were 1,000 times higher in the brain than the placenta tissues.

Bingham, A., Cone, M., Mock, V., et al. (2016). Comparison of Test Results for Zika Virus RNA in Urine, Serum, and Saliva Specimens from Persons with Travel-Associated Zika Virus Disease – Florida, 2016. Morbidity and Mortality Weekly Report. 65(18).

The Florida Department of Health Bureau of Public Health Laboratories conducted testing on samples from 913 persons who met the state criteria for testing. Results for urine and serum samples showed that approximately twice as many urine specimens tested positive for Zika virus than serum specimens, suggesting that urine might be a more useful specimen for identifying acute Zika virus infection.

Bogoch, I., Brady, O., Kraemer, M., et al. (2016). Anticipating the International Spread of Zika Virus from Brazil. The Lancet. 387:335-336.

Through evaluation of travel patterns from current countries with Zika virus disease spread and mosquito habitation patterns, the authors have predicted possible Zika virus

disease spread throughout the Americas, including the U.S. The authors also included a predictive map.

Boulet, S., D'Angelo, D., et al. (2016) Contraceptive Use Among Non-pregnant and Postpartum Women at Risk for Unintended Pregnancy, and Female High School Students, in the Context of Zika Preparedness. Morbidity and Mortality Weekly Report. 65(30): 780-787.

This study is a review of surveys and studies that aims to provide State-based estimates of contraception use among nonpregnant and postpartum women at risk for unintended pregnancies and sexually active female high school students. This data can be used to target campaigns for effective use of contraception.

Braga, J., Bressan, C., Dalvi, A., et al. (2017). Accuracy of Zika Virus Disease Case Definition During Simultaneous Dengue and Chikungunya Epidemics. PLOS One. 12(6):e0179725.

The authors developed and tested the accuracy of a clinical case definition model to distinguish Zika virus infection when dengue and chikungunya viruses are co-circulating. They found that presence of rash with pruritus or conjunctival hyperemia was the best case definition and that the sensitivity and specificity of their case definition were better than existing case definitions.

Brasil, P., Pereira, J., Moreira, E., et al. (2016). Zika Virus Infection in Pregnant Women in Rio de Janeiro. The New England Journal of Medicine. 375: 2321-2334.

This follow-up study looked at 207 enrolled pregnant women expected to give birth by July 31, 2016. Among the 125 women who tested positive for Zika via PCR with confirmed pregnancy outcomes, 46.4 percent had adverse pregnancy outcomes compared to 11.5 percent in the non-Zika positive cohort. The adverse outcomes occurred in 55 percent of women infected during the first trimester, 52 percent in the second trimester, and 29 percent in the third trimester.

Brasil, Patricia, et al. (2016). Zika Virus Infection in Pregnant Women in Rio de Janeiro – Preliminary Report. The New England Journal of Medicine.

Researchers in Rio de Janeiro enrolled 88 pregnant women in a prospective study, where they were tested for Zika virus and then followed throughout their pregnancies. Seventy-two of the 88 women enrolled tested positive for Zika virus infection. The authors concluded that "despite mild clinical symptoms, Zika virus infection during pregnancy appears to be associated with grave outcomes, including fetal death, placental insufficiency, fetal growth restriction, and CNS injury."

Center for Infectious Disease Research and Policy. (2021). Zika Resource Page.

This webpage offers a compilation of resources on Zika virus disease including governmental publications, academic publications, research pieces, and popular media mentions.

Centers for Disease Control and Prevention. (2016). Executive Orders and Emergency Declarations for the West Nile Virus: Applying Lessons from Past Outbreaks to Zika.

This document provides an overview of Executive Orders and Emergency Declarations issued by states and territories in the past (specific to West Nile Virus), and how those authorities may be used to support prevention, response, and recovery actions for Zika virus.

Centers for Disease Control and Prevention. (2016). Possible Zika Virus Infection Among Pregnant Women – United States and Territories, May 2016. Morbidity and Mortality Weekly Report. 65(20).

This article discusses the establishment of a comprehensive surveillance system to monitor pregnant women with Zika virus in the United States.

Centers for Disease Control and Prevention. (2021). Zika Virus.

This website provides the Centers for Disease Control and Prevention resources related to Zika Virus disease including current transmission and spread information, current clinical recommendations, and prevention and mitigation information.

Cragan, J., Mai, C., Petersen, E., et al. (2017). Baseline Prevalence of Birth Defects Associated with Congenital Zika Virus Infection – Massachusetts, North Carolina, and Atlanta, Georgia, 2013-2014. Morbidity and Mortality Weekly Report. 66(8):219-222.

The authors retrospectively applied the CDC case definition for birth defects potentially associated with Zika virus infection to data from birth defect surveillance programs in three jurisdictions for the 2013-2014 time period, before Zika was introduced in the Americas. This data was used as a baseline for comparison to data on infants and fetuses of women with laboratory evidence of possible Zika infection reported to the U.S. Zika Pregnancy Registry (USZPR) during the first 9 months of 2016. The comparison found that the prevalence of infants and fetuses with birth defects was 20 times higher and the prevalence of brain abnormality or microcephaly was 33 times higher for those in the USZPR than in the three surveillance programs pre-Zika.

Cuevas, E., Tong, V., Rozo, N., et al. (2016). Preliminary Report of Microcephaly Potentially Associated with Zika Virus Infection During Pregnancy – Columbia, January-November 2016. Morbidity and Mortality Weekly Report. 65(49): 1409-1413.

This preliminary report examined cases of congenital microcephaly in Colombia identified between January 31 and November 12, 2016. The study found a fourfold increase in microcephaly prevalence compared to the same study period in 2015. The peak number of cases occurred approximately 24 weeks after the peak of the country's Zika virus disease outbreak, suggesting infection with Zika virus disease is most risky in the first trimester and early second trimester of pregnancy. The authors note several limitations to the study, including that a majority of cases did not have laboratory-confirmed Zika infection, the passive surveillance system used in Colombia is less complete than an active one, birth defects may be underreported among pregnancy losses and may not be detected until several months after birth, and prevalence ratios may be unstable when examining rare outcomes.

Da Silva, A., Ganz, J., Sousa, P., et al. (2016). Early Growth and Neurologic Outcomes of Infants with Probable Congenital Zika Virus Syndrome. Emerging Infectious Diseases. 22(11).

This article describes findings from a study of 48 infants up to eight months of age with probable congenital Zika virus syndrome. The study found that additional neurological symptoms emerged with age and that head circumference measurements fell further from the mean, suggesting that affected infants may continue to fall further behind non-affected children.

Eppes, C., Rac, M., Dunn, J., et al. (2017). Testing for Zika Virus Infection in Pregnancy: Key Concepts to Deal with an Emerging Epidemic. American Journal of Obstetrics and Gynecology. 216(3):209-225.

This expert review discusses screening and diagnostic considerations, epidemiological data on the risk of congenital Zika virus disease by trimester of exposure, and using alternative neurosonographic approaches to detect malformations other than microcephaly.

Goodman, A, Dziuban, E., Powell, K., et al. (2016). Characteristics of Children Aged <18 Years with Zika Virus Disease Acquired Postnatally – U.S. States, January 2015-July 2016. Morbidity and Mortality Weekly Report. 65(39): 1082-1085.

This MMWR early release examined 158 cases of confirmed or probable Zika virus disease in children under 18 reported to the CDC by 30 states. All cases were acquired postnatally and most had mild symptoms, with 2 hospitalizations and no deaths reported. Nearly half of the cases were aged 15-17, which the authors attributed to healthcare-seeking or testing bias (five cases were pregnant) or a greater likelihood of exposure through travel.

Graham, K., Fox, D., Talati, A., et al. (2017). Prevalence and Clinical Attributes of Congenital Microcephaly – New York, 2013-2015. Morbidity and Mortality Weekly Report. 66(5):125-129.

The authors used reports requested from birth hospitals and a statewide administrative discharge database to identify infants born with severe congenital microcephaly between 2013 and 2015, before Zika virus infections were identified in New York. This baseline prevalence estimate can be used to approximate the risk of severe congenital microcephaly attributable to Zika virus infection.

Honein, M., Dawson, A., Petersen, E., et al. (2016). Birth Defects Among Fetuses and Infants of US Women with Evidence of Possible Zika Virus Infection During Pregnancy. Journal of the American Medical Association. 317(1):59-68.

Using preliminary data from the U.S. Zika Pregnancy Registry, this study found that six percent of completed pregnancies following Zika virus infection resulted in potentially Zika-related birth defects. This included 11 percent of women infected with Zika during the first trimester having fetuses or infants with birth defects. The four percent of completed pregnancies with findings of microcephaly was substantially higher than the

background prevalence of 0.07 percent.

Honein, M., Woodworth, K., and Gregory, C. (2020). Neurodevelopmental Abnormalities Associated with In Utero Zika Virus Infection in Infants and Children – The Unfolding Story. JAMA Pediatrics. 174(3): 237-238.

The authors review the current state of knowledge about potential neurodevelopmental abnormalities in children who had congenital Zika virus exposure but without Zika virus-associated birth defects. They stress the importance of follow-up developmental screenings to detect any potential issues and refer children to appropriate services.

Krauer, F., Riesen, M., Reveiz, L., et al. (2017). Zika Virus Infection as a Cause of Congenital Brain Abnormalities and Guillain-Barré Syndrome: Systematic Review. PLOS Medicine.

The authors describe the development of a causality framework for Zika virus and congenital brain abnormalities and Guillain-Barré Syndrome (GBS), a systematic review of literature on the topic through Mary 30, 2016, and the convening of a multidisciplinary expert panel to assess research findings of causality. The review found sufficient evidence to conclude that Zika virus causes congenital abnormalities and triggers GBS.

Krittanawong, C., Zhang, H., and Sun, T. (2016). Cardiovascular Complications After Zika Virus Infection. International Journal of Cardiology. 221:859.

This correspondence notes short- and long-term cardiovascular complications are associated with other flaviviruses, the virus family in which Zika is included. The authors encourage additional research to determine whether similar effects may be associated with Zika, particularly because complications may be underdiagnosed in those with mild or asymptomatic Zika virus infection.

Lee, B., Alfaro-Murillo, J., Parpia, A., et al. (2017). The Potential Economic Burden of Zika in the Continental United States. PLOS Neglected Tropical Diseases.

The authors modeled the potential economic burden in direct medical costs, Medicaid costs, productivity losses, and total costs to society at different attack rates in six states considered to be at greatest risk of Zika emergence. Costs ranted from $183.4 million at an attack rate of 0.01% to $1.2 billion at an attack rate of 1%.

Li, G., Poulsen, M., Fenyvuesvolgyi, C, et al. (2016). Characterization of Cytopathic Factors Through Genome-wide Analysis of the Zika Viral Proteins in Fission Yeast. Proceedings of the National Academy of Sciences of the United States of America. 114(3): E376-E385.

This study identifies seven Zika virus proteins that had cytopathic effects in a fission yeast cell system. These effects included inhibition of growth/proliferation, cell hypertrophy, cell cycle dysregulation, and cell death.

Lima, A., Lovin, D., Hickner, P., et al. (2015). Evidence for an Overwintering Population of Aedes Aegypti in Capitol Hill Neighborhood, Washington, DC. The American Journal of Tropical Medicine and Hygiene. 94(1):231-5.

This article describes a research study demonstrating that *Aedes aegypti* mosquitoes were present in samples taken in Capitol Hill, Washington, DC throughout 2011-2014. These mosquitoes were not previously thought to travel further north than the average 10 degree Celsius isotherm.

Lucey, D. (2016). Will Zika Virus and Microcephaly Epidemics Emerge After Ebola in West Africa? The Need for Prospective Studies Now. Health Security. 14(2).

The author discusses the emerging cases of Zika virus in Cape Verde, West Africa, and the need to begin surveillance and mosquito control to prevent more transmission. The author also discusses the timeline of the epidemic, beginning in October 2015 and predicting an increase in cases of microcephaly in May/June 2016, from mothers infected with Zika virus who have not been properly screened and evaluated.

Lucey, D. and Gostin, L. (2016). The Emerging Zika Pandemic: Enhancing Preparedness. Journal of the American Medical Association. 315(9):865-866.

The authors discuss the current outbreak of Zika virus disease and why it is a concern for the U.S. public health and healthcare systems. They also describe steps that should be taken now to prevent and mitigate spread and steps that should be taken to prepare. The article also includes an outline for a Zika virus disease research agenda.

Marston, H., Lurie, N., Borio, L., and Fauci, A. (2016). Considerations for Developing a Zika Virus Vaccine. The New England Journal of Medicine. 375:1209-1212.

This articles presents the perspective of federal officials on three potential strategies for investigators to consider when conducting clinical trials on Zika vaccine candidates. The strategies are following the traditional 3 phase vaccine development approach, conducting human challenge studies after phase 2 studies, and relying on the FDA's Animal Rule. The officials advise selecting a pathway based on disease incidence and its effect on the generation of reliable safety and efficacy data as well as active engagement with affected communities in trial design and execution.

Mead, P., Duggal, N., Hook, S., et al. (2018). Zika Virus Shedding in Semen of Symptomatic Infected Men. The New England Journal of Medicine. 389: 1377-1385.

The authors conducted a prospective study of the frequency and duration of Zika virus shedding in men with symptomatic Zika virus infection. They found that while Zika RNA was often present and persisted for an extended time period, shedding of infectious Zika virus was less common and only occurred in the initial weeks following illness onset.

Mlakar, J., Korva, M., Tul, N., et al. (2016). Zika Virus Associated with Microcephaly. New England Journal of Medicine. 374(10): 951-958.

This article discusses a case report of an expectant mother infected with Zika during the end of her first trimester while in Brazil. Serial ultrasounds at 14 and 20 weeks showed normal fetal growth and anatomy. An ultrasound performed at 29 weeks confirmed

intrauterine growth retardation and fetal anomalies. Medical termination of the pregnancy occurred at 32 weeks of gestation. Fetal autopsy findings detail the severe brain injury and placental damage associated with the infection. Genome sequence identity was also performed.

Moore, C., Staples, J., Dobyns, W., et al. (2017). Characterizing the Pattern of Anomalies in Congenital Zika Syndrome for Pediatric Clinicians. JAMA Pediatrics. 171(3): 288-295.

This review of public reports of birth defects associated with intrauterine Zika virus infection through September 2016 identified five features that are unique to congenital Zika virus infection or rarely seen in other congenital infections. The features are severe microcephaly with partially-collapsed skull, thin cerebral cortices with subcortical calcifications, macular scarring and focal pigmentary retinal mottling, congenital contractures, and marked early hypertonia and symptoms of extrapyramidal involvement.

Mulkey, S., Arroyave-Wessel, M., Peyton, C., et al. (2020). Neurodevelopmental Abnormalities in Children with In Utero Zika Virus Exposure Without Congenital Zika Syndrome. The Journal of the American Medical Association Pediatrics. 174(3): 269-276.

The authors of this cohort study investigate infants exposed to Zika virus (ZIKV) in utero with no clinical sign of Congenital Zika Syndrome (CZS). A longitudinal study of infant neurodevelopment includes infants born to women who met the Centers for Disease Control and Prevention criteria for probable Zika virus infection and laboratory confirmed tests during their pregnancies. The focus is to evaluate the early neurodevelopmental outcomes of infants with normocephaly who were exposed to the virus and had normal neuroimaging findings at birth and whether they are at risk as they age for neurodevelopmental delays.

Muniz, L., Maciel, R., Ramos, D., et al. (2022). Audiological Follow-up of Children with Congenital Zika Syndrome. Heliyon. 8:e08720.

The authors of this prospective observational study describe the frequency of hearing loss in children with congenital Zika syndrome (CZS). They hypothesized CZS may contribute to functional disabilities due to continued viral activity in neural tissue following birth. The study showed that sensorineural hearing loss is a clinical feature of CZS and present at birth with no delayed onset or progressive decline in hearing.

Pan American Health Organization. (2016). Epidemiological Update: Neurological Syndrome, Congenital Anomalies, and Zika Virus Infection.

This document is one in a series of epidemiological updates provided by the Pan American Health Organization. It highlights the specific issues related to the correlation between Zika virus disease outbreaks and the increase in neurological syndromes, including Guillain-Barre syndrome and congenital anomalies, specifically microcephaly. The document details recommendations for management, increased surveillance, and other public health recommendations.

Pan American Health Organization. (2016). Zika Virus Infection.

This website provides an outline of the disease and its progression, specifically in the Americas. It provides information for the general public and health professionals on disease spread, identification, treatment, and prevention.

Rasmussen, S., Jamieson, D., Honein, M., and Petersen, L. (2016). Zika Virus and Birth Defects – Reviewing the Evidence for Causality. The New England Journal of Medicine. 374:1981-1987.

The authors evaluated available data to determine causality of Zika infection and birth defects, most notably microcephaly. This evidence included Zika virus infection during specific times in pregnancy, a specific rare phenotype involving microcephaly, and data that support biologic plausibility. The researchers concluded that the evidence supports a causal relationship between Zika virus infection and birth defects.

Reagan-Steiner, S., Simeone, R., Simon, E., et al. (2017). Evaluation of Placental and Fetal Tissue Specimens for Zika Virus Infection – 50 States and District of Columbia, January-December, 2016. Morbidity and Mortality Weekly Report. 66(24): 636-643.

The authors describe that placental tissue RT-PCR testing confirmed maternal Zika virus infection for 10% of live births to mothers with possible exposure who tested positive for an unspecified flavivirus infection or tested negative for Zika infection when serum collection occurred more than 12 weeks after exposure. The study demonstrates the value of placental testing when maternal testing is not definitive or testing is not performed during the recommended time.

Reefhuis, J. Gilboa, S., Johansson, M., et al. (2016). Projecting Month of Birth for At-Risk Infants after Zika Virus Disease Outbreaks. Emerging Infectious Diseases. 22(5).

This article looked at Zika virus occurrence and surges of microcephaly births to determine if projections could be made. Researchers developed a modifiable spreadsheet tool that public health officials can use to plan for delivery of infants from mothers infected with Zika virus.

Reynolds, M., Jones, A., Petersen, E., et al. (2017). 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. Morbidity and Mortality Weekly Report. 66(13): 366-373.

The authors analyzed completed pregnancies with laboratory evidence of possible Zika virus infection reported to the US Zika Pregnancy Registry from January 15-December 27, 2016. Zika virus-associated birth defects were reported in 5% of fetuses/infants from completed pregnancies with laboratory evidence of possible recent Zika virus infection and 15% with confirmed Zika virus infection in the first trimester. Only 28% of infants born after CDC updated guidance recommending routine postnatal neuroimaging and testing for infants born to women with laboratory evidence of Zika virus infection during pregnancy received postnatal neuroimaging.

Rosa, R., Abbo, L., Kapur, G., et al. (2017). Development and Implementation of a Zika Virus Disease Response Protocol at a Large Academic Medical Center. Disaster Medicine and Public Health Preparedness. 11(2): 256-258.

The authors describe the process used to develop a Zika response protocol at a large academic medical center.

Roth, N., Reynolds, M., Lewis, E., et al. (2022). Zika-Associated Birth Defects Reported in Pregnancies with Laboratory Evidence of Confirmed or Possible Zika Virus Infection-U.S. Zika Pregnancy and Infant Registry, December 1, 2015-March 31, 2018. Morbidity and Mortality Weekly Report. 71(3): 73-79.

The authors provide an updated report on previous data collected in the U.S. Zika Pregnancy and Infant Registry (USZPIR) regarding the frequency of Zika associated brain and eye defects from laboratory confirmation or known Zika virus infection. The report includes data from December 2020 with follow-up on cases from infancy to 5 years of age. The aggregate exposed the potential of associated abnormalities and aligns with continuing USZPIR surveillance in understanding the effects of Zika and future outbreaks.

Ruckert, C., Weger-Lucarelli, J., Garcia-Luna, S., et al. (2017). Impact of Simultaneous Exposure to Arboviruses on Infection and Transmission by Aedes Aegypti Mosquitoes. Nature Communications.

The authors exposed Aedes aegypti mosquitoes to Zika, dengue, and chikungunya viruses individually and as double and triple co-infections. They found that the mosquitoes could be infected with and transmit all combinations of the viruses simultaneously and that infection, dissemination, and transmission rates were only mildly affected by coinfection.

Shapiro-Mendoza, C., Rice, M., Galang, R., et al. (2017). Pregnancy Outcomes After Maternal Zika Virus Infection During Pregnancy – U.S. Territories, January 1, 2016-April 25, 2017. Morbidity and Mortality Weekly Report. 66(23): 615-621.

This study of 2,549 completed pregnancies reported by U.S. territories confirmed findings from other recent studies that Zika virus infection during any trimester of pregnancy may result in Zika-related birth defects. The authors emphasize the importance of follow-up of women with laboratory evidence of Zika infection and adherence to newborn testing recommendations to facilitate timely and appropriate clinical interventions and follow-up for Zika-affected infants.

Sharp, T., Fischer, M., Munoz-Jordan, J., et al. (2019). Dengue and Zika Virus Diagnostic Testing for Patients with a Clinically Compatible Illness and Risk for Infection with Both Viruses. Morbidity and Mortality Weekly Report. 68(1): 1-10.

The authors summarize current guidance on dengue and Zika virus diagnostic testing.

Tang, H., Hammack, C., Ogden, S., et al. (2016). Zika Virus Infects Human Cortical Neural Progenitors and Attenuates Their Growth. Cell Stem Cell. 18(5): 1–4.

Researchers working with Zika virus and human neural cells demonstrated that Zika virus does infect the neural cells and affects their ability to replicate and survive.

The Network for Public Health Law. (2016). Emergency Legal Preparedness Concerning Zika Virus.

This primer, presented in a PowerPoint format, outlines public health concerns from Zika Virus disease and discusses potential legal issues in the U.S. and abroad.

Ticona, J., Nery, N., Doss-Gollin, S., et al. (2021). Heterogeneous Development of Children With Congenital Zika Syndrome-Associated Microcephaly. PLoS ONE. 16(9):e0256444.

The authors of this study followed 42 children, 2 years of age and older with Congenital Zika Syndrome (CZS) related to microcephaly. A correlation was observed between heterogenous neurodevelopment and neurological capabilities which indicate cognitive and motor development outcomes to children exposed to Zika virus in utero. The children experienced major neurodevelopmental delays to include spasticity.

Vasquez, A., Sapiano, M., Basavaraju, S., et al. (2016.) Survey of Blood Collection Centers and Implementation of Guidance for Prevention of Transfusion-Transmitted Zika Virus Infection – Puerto Rico, 2016. Morbidity and Mortality Weekly Report. 65(14): 375–378.

The authors have gathered information on blood collection operations in Puerto Rico to assess the impact the Zika-related restriction on blood collection is having and what would be needed to replace the affected products.

World Health Organization. (2016). Zika App. Android. iOS.

Healthcare providers and others can download this app to access the latest World Health Organization information Zika virus disease.

World Health Organization. (2016). Zika Virus and Complications: Questions and Answers.

This webpage provides responses to commonly asked questions about Zika virus and mosquito protection and surveillance, sexual transmission, travel, neurological syndromes, pregnancy, and government response.

World Health Organization. (2016). WHO Announces a Public Health Emergency of International Concern.

This page includes the official statement from the World Health Organization Director-General declaring Zika virus disease a Public Health Emergency of International Concern. The declaration was made on February 1, 2016, after a meeting of the International Health Regulations (2005) Emergency Committee.

World Health Organization. (2016). Zika Virus.

This World Health Organization website provides an outline of Zika and an overview of its progression around the world. Links to information on signs and symptoms, transmission, diagnosis, treatment, and prevention along with Situation Reports are included on the page.