

Provider Toolkit: Counseling and Testing Guidance for Pregnant Women with Possible Zika Virus Exposure



Based on Morbidity and Mortality Weekly Report (MMWR), "Update: Interim Guidance for Health Care Providers Caring for Pregnant Women with Possible Zika Virus Exposure — United States (Including U.S. Territories), July 2017"

Rhode Island Department of Health
Division of Preparedness, Response, Infectious Disease and Emergency Medical Services
Center for Acute Infectious Disease Epidemiology
401-222-2577



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*** To access the documents found in this packet electronically, please visit <http://health.ri.gov/ZikaGuidance> ***



Key Takeaways and Screening Tools for Pregnant Women Exposed to Zika Virus

KEY TAKEAWAYS



Updated Interim Guidance for Pregnant Women with Possible Zika Virus Exposure

CDC updated its interim guidance to incorporate what has been learned over the past year and reduce misinterpretation of Zika test results for pregnant women. CDC's updated interim guidance presents the updated recommendations in two algorithms- one for pregnant women with Zika symptoms and one for pregnant women without Zika symptoms.

Rationale for changes in guidance

- Overall, the number of people with Zika infection in the Americas is declining. Testing people when there is a lower occurrence of disease could lead to a higher proportion of false-positive test results.
- Emerging data show that Zika virus antibodies can persist for months in some pregnant women. Because of this, antibody test results may not be able to tell healthcare providers if Zika virus infection occurred during or before pregnancy, and results may not provide useful information about whether the pregnancy is at risk of Zika infection.



Overview of changes

This updated guidance emphasizes a shared decision-making model for testing and screening pregnant women, one in which patients and providers work together to make decisions about testing and care plans based on patient preferences, clinical judgment, a balanced assessment of risks and expected outcomes, jurisdictional recommendations, and values.

Pregnant women with Zika symptoms

- CDC recommends two different types of Zika tests (one that looks for Zika RNA and one that looks for Zika antibodies) be conducted concurrently. Previously, CDC recommended sequential testing.
- The timeframe for testing for Zika RNA has been extended from the previous recommendation of up to 2 weeks to the new recommendation of up to 12 weeks after symptom onset. However, testing as soon as possible after symptom onset is best.
- Healthcare providers should consider Zika exposure both *before* and *during* pregnancy to appropriately interpret testing for Zika antibodies and counsel patients.

Pregnant women without Zika symptoms but who have ongoing exposure to Zika (live in or frequently travel to an area with risk of Zika)

- Testing for Zika RNA should be offered at the first prenatal care visit, and two additional tests should be offered during subsequent routine prenatal care visits.
- CDC no longer recommends routine testing for Zika antibodies for this group because emerging evidence on persistence of Zika antibodies suggests these test results could make it difficult for healthcare providers to determine whether an infection occurred during the current pregnancy or before conception.

Pregnant women without Zika symptoms who had recent exposure but do not have ongoing exposure to Zika

- Given the increased likelihood of false-positive results because of the decline in Zika in the Americas, Zika testing is no longer routinely recommended for pregnant women without Zika symptoms who were recently exposed to Zika but do not have ongoing exposure. Testing should be considered according to patient preferences and clinical judgment and in line with the state or local area recommendations.
- It is important to check with your state or local area for tailored recommendations. Based on the spread of Zika virus and other considerations (e.g., mosquito season), certain areas might recommend testing of asymptomatic pregnant women either for clinical care or as part of Zika virus surveillance.

Healthcare providers' clinical judgment is imperative. When deciding whether to test, healthcare providers should consider factors such as

- Duration and type of travel
- Use of regular protection measures
- Timing of pregnancy
- How intensely Zika is being spread by mosquitoes in the location of travel

Other recommendations for healthcare providers to consider

- The updated guidance contains more explicit testing recommendations for pregnant women exposed to Zika whose fetus has birth defects potentially associated with Zika detected on ultrasound.
- The updated guidance modifies recommendations for testing placental and fetal tissues.

Implications for care of infants with possible congenital Zika exposure

Throughout the response, testing infants for Zika has been closely linked to their mother's test results. Given these changes and the likelihood that fewer pregnant women without Zika symptoms will be tested, it is critical that pediatricians ask about potential maternal and congenital Zika exposure for every newborn. For infants born to mothers with possible Zika exposure during pregnancy who were not tested for Zika, healthcare providers should perform a comprehensive physical exam, including standardized measurement of head circumference and standard newborn hearing screen, as part of routine pediatric care. Based on level of exposure (noted in box above), the healthcare providers should consider whether further evaluation of the newborn is warranted for possible congenital Zika infection, and if so, a head ultrasound and ophthalmologic assessment should be considered. Based on results of the evaluation, testing of the infant for Zika virus infection could be considered



Zika prevention is key

Healthcare providers play a key role in prevention by encouraging people, especially pregnant women, to follow CDC's Zika prevention recommendations.

- Pregnant woman should not travel to any areas with risk of Zika.
- For pregnant women who must travel or who live in areas with risk of Zika, they should strictly follow steps to prevent mosquito bites and sexual transmission.



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SCREENING PREGNANT WOMEN FOR ZIKA TESTING



To Be Administered by a Nurse or Other Healthcare Provider

Pregnant women should be asked about any possible Zika virus exposure, before and during their pregnancy, at each prenatal visit. Use this tool to evaluate pregnant women for exposure to Zika virus and symptoms of Zika virus disease to determine whether testing is indicated. Visit CDC's map at <http://www.cdc.gov/zika/geo> to determine [areas with risk of Zika](#).



Questions to ask your patient to determine if she needs Zika testing:

- ✓ Have you traveled during pregnancy?
 - Where did you travel?
 - How long did you stay?
- ✓ Have you lived in any area where mosquitoes are spreading Zika during your pregnancy?
- ✓ Has your partner lived in or traveled to any area where mosquitoes are spreading Zika during your pregnancy?
 - When and where did your partner travel?
 - Did your partner have any signs or symptoms of Zika (including fever, rash, headache, joint pain, red eyes, or muscle pain) when he or she were on the trip, or after returning?
 - Did you have sex without a condom with your partner after they returned from the trip?
- ✓ Have you had any symptoms of Zika during your pregnancy?
 - Use the chart on page 2 of this document to discuss Zika symptoms. The most common symptoms of Zika are fever, rash, headache, joint pain, red eyes, and muscle pain.

Use the responses to the questions above to determine if Zika testing is indicated.

Testing is recommended for

- Symptomatic pregnant women possibly exposed to Zika (who lived in or traveled to or have unprotected sex with a partner who lived in or traveled to an area with risk of Zika), and
- Asymptomatic pregnant women who have ongoing exposure (who live in or frequently travel to) to areas with risk of Zika.

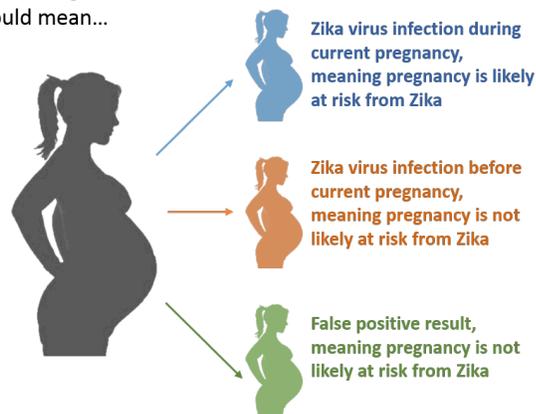
Testing is not routinely recommended for asymptomatic pregnant women with recent possible Zika exposure but without ongoing possible exposure. However, testing may be considered as a shared decision between patients and providers, according to patient preferences and clinical judgement, or if a state or local area recommends it.

Other considerations that might affect interpretation of Zika test results:

- ✓ Did you live in any area where mosquitoes were spreading Zika before you became pregnant?
- ✓ Have you frequently traveled (for example, daily or weekly) to one of these areas before you became pregnant?
- ✓ If you did visit one of these areas before pregnancy, did you protect yourself from mosquito bites?
 - Did you wear long sleeves and pants?
 - Did you use insect repellent through the day and night? Did you follow the instructions on the label?
 - Did you stay somewhere with window and door screens or air conditioning?

If your patient reports exposure to any area with risk of Zika before her current pregnancy, the test that looks for Zika IgM antibodies may be difficult to interpret and may have limited usefulness for clinical decision-making. The patient may choose not to be tested. For more information, visit CDC's website at <http://tinyurl.com/WhenToTest>.

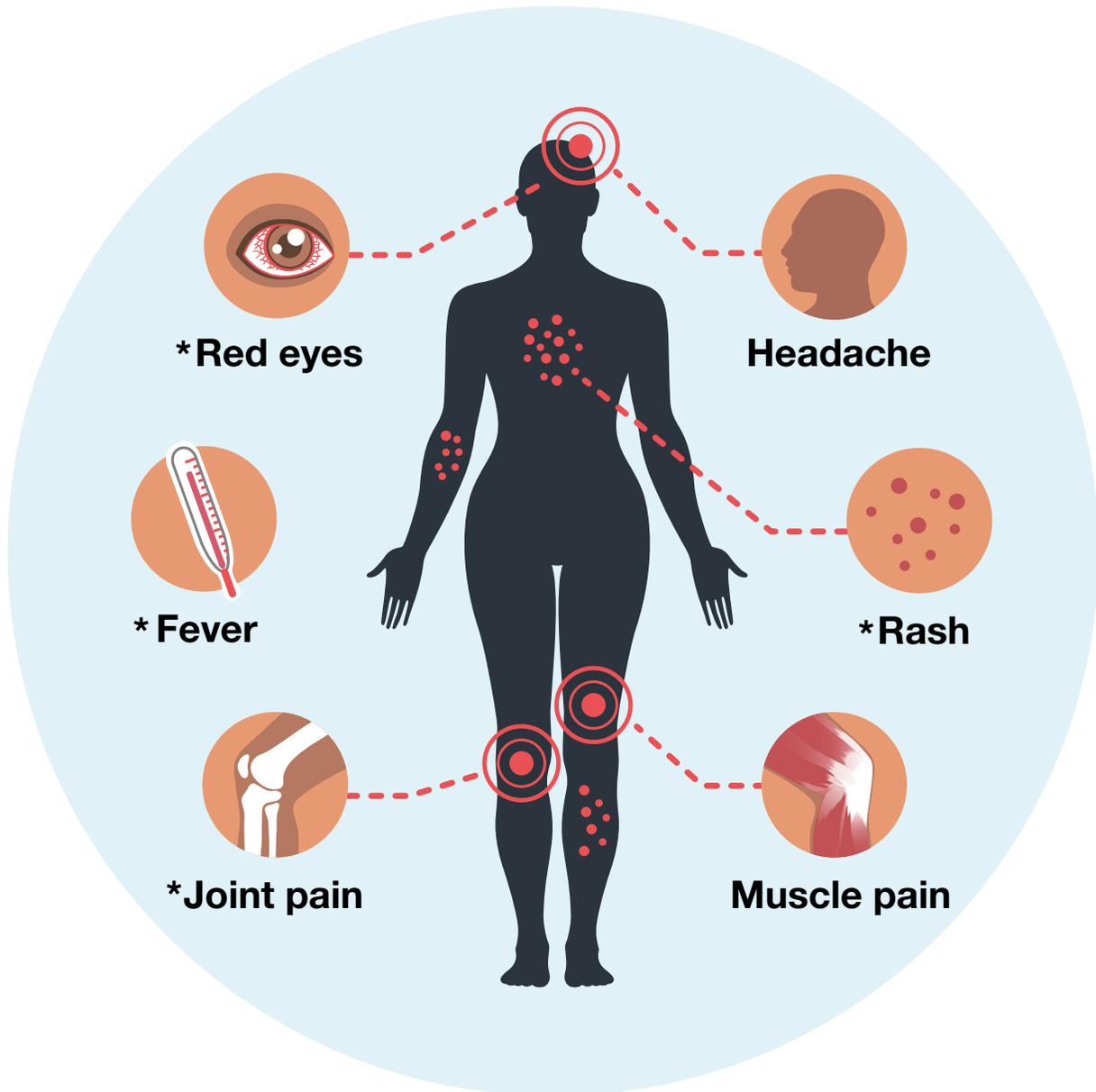
A positive Zika IgM test result could mean...



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Zika Symptoms

The most common symptoms for Zika are fever, rash, headache, joint pain, and muscle pain.

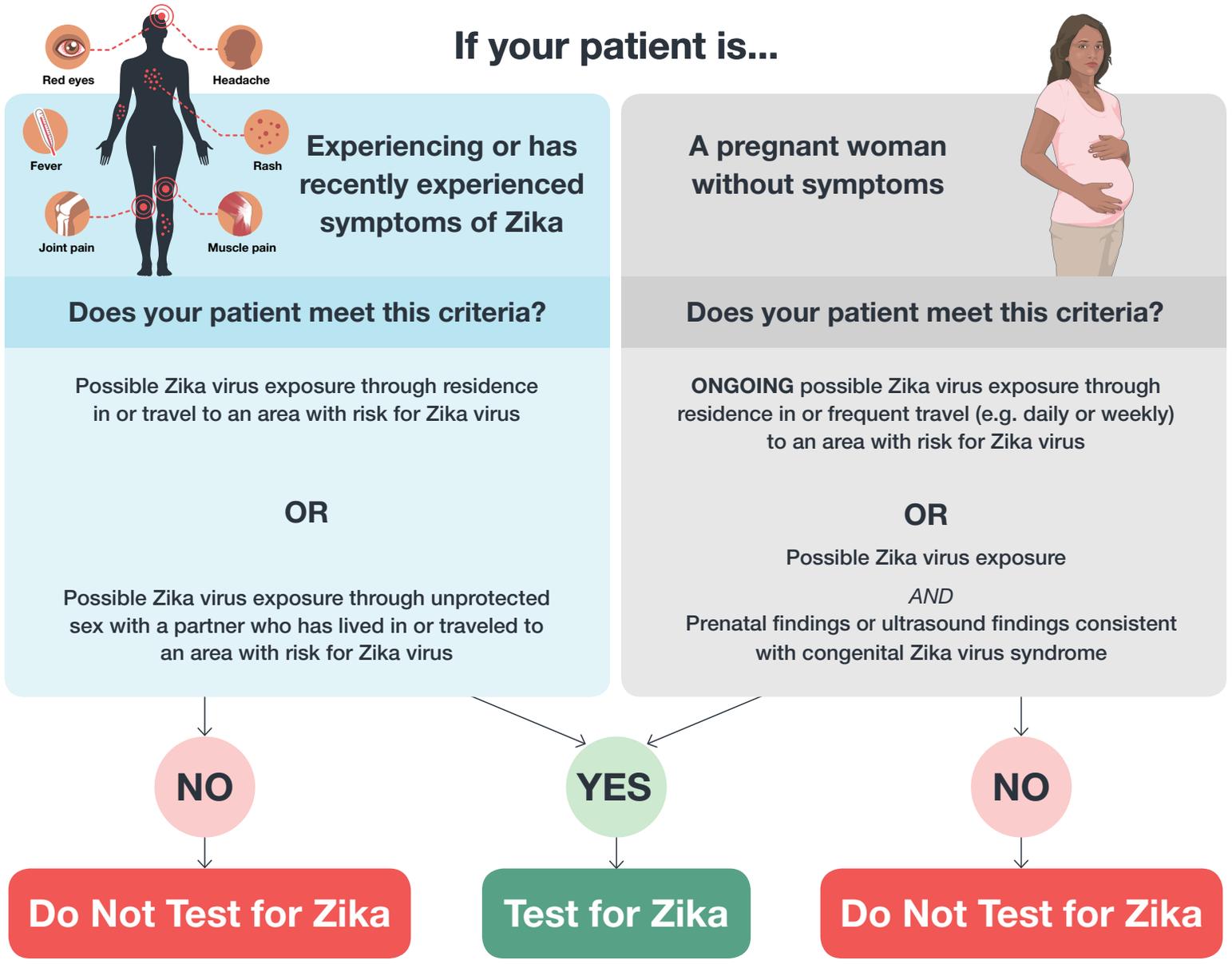


*** In Rhode Island, individuals are considered symptomatic for Zika virus if they have at least one of the following symptoms: fever (measured or reported), rash, joint pain, or red eyes.**

WHEN TO TEST FOR **ZIKA VIRUS**



As a healthcare provider, you decide if a patient should be tested for Zika virus infection. The algorithm below will help you determine whether or not to test your patient for Zika virus infection.



- NOTE:**
- Asymptomatic pregnant women with recent possible Zika virus exposure (i.e. through travel or sexual exposure) who do not have ongoing exposure are not routinely recommended to have Zika virus testing. Testing should be considered using a decision-making model, one in which patients and providers work together to make decisions about testing and care plans based on a balanced assessment of risks and expected outcomes, clinical judgement, patient preferences and values, and the jurisdiction's recommendations.
 - Healthcare providers should review their local and state health jurisdiction guidelines regarding testing of patients with clinically compatible illness without known travel or sexual exposures.
 - For details on which tests to order, visit <https://www.cdc.gov/zika/hc-providers/testing-guidance.html>.

CDC does not recommend Zika virus testing for asymptomatic

- Men
- Children
- Women who are not pregnant





**Pretest Counseling and Testing
Recommendations for Symptomatic
Pregnant Women with Possible
Zika Virus Exposure**

UPDATED INTERIM PREGNANCY GUIDANCE: SYMPTOMATIC PREGNANT WOMEN WITH POSSIBLE ZIKA VIRUS EXPOSURE

Testing Recommendations and Interpretation of Results for Healthcare Providers

ASK PREGNANT WOMEN ABOUT

Travel to or residence in any areas with risk for Zika virus transmission before and during the current pregnancy^{1,2} • Possible sexual exposure before and during the current pregnancy³ • A diagnosis of laboratory-confirmed Zika virus infection before current pregnancy³ • Symptoms of Zika virus disease during current pregnancy (e.g., fever, rash, conjunctivitis, arthralgia) If no symptoms reported, refer to asymptomatic algorithm.

Before testing, discuss testing limitations and potential risks for misinterpretations of test results.

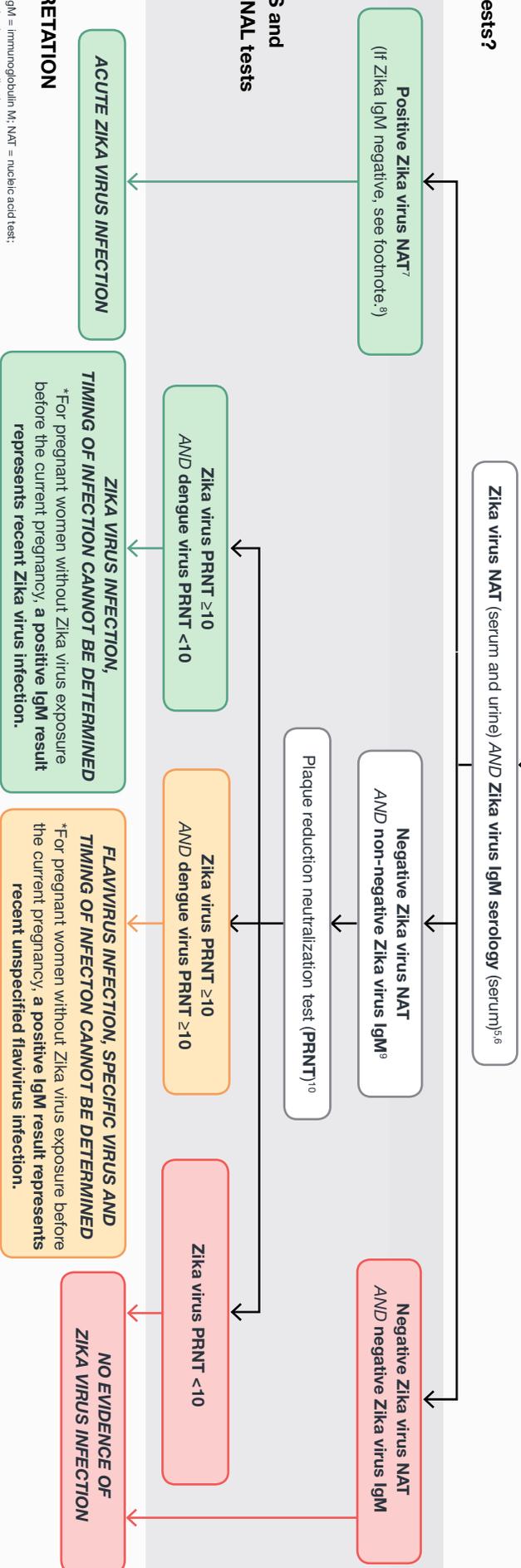
WHOM to test?

Pregnant women reporting possible exposure during current pregnancy and symptoms of Zika virus disease⁴

WHEN to test?

Test as soon as possible; through 12 weeks after symptom onset

WHICH tests?



RESULTS and ADDITIONAL tests

INTERPRETATION

Abbreviations: IgM = immunoglobulin M; NAT = nucleic acid test; PRNT = plaque reduction neutralization test

- Ask about type and duration of Zika virus exposure before and during the current pregnancy. Exposure before the current pregnancy might limit interpretation of Zika virus IgM antibody results; pretest counseling can help inform testing decisions. Some patients may choose not to receive Zika virus IgM testing.
- Possible Zika virus exposure includes travel to or residence in an area with risk for Zika virus transmission (<https://wwwnc.cdc.gov/travel/page/zika-travel-information>) during pregnancy or the periconceptional period (8 weeks before conception [6 weeks before the last menstrual period], or sex without a condom during pregnancy, or the periconceptional period, with a partner who traveled to, or resides in an area with risk for Zika virus transmission).

Zika virus testing is not routinely recommended for pregnant women with a previous diagnosis of laboratory-confirmed Zika virus infection by either NAT or serology (positive equivocal Zika virus or dengue virus IgM and Zika virus PRNT ≥ 10 and dengue virus PRNT < 10 results).

- This algorithm also applies to pregnant women with possible Zika virus exposure who have a fetus with prenatal ultrasound findings consistent with congenital Zika syndrome.
- The duration of detectable Zika virus in pregnant women following infection is not known. Preliminary data suggest NAT may remain positive for several weeks after symptom onset. In some pregnant women, Zika virus IgM antibodies are most likely to be detected within 12 weeks after infection however IgM antibodies

**ZIKA VIRUS INFECTION,
TIMING OF INFECTION CANNOT BE DETERMINED**
*For pregnant women without Zika virus exposure before the current pregnancy, a positive IgM result represents recent Zika virus infection.

**FLAVIVIRUS INFECTION, SPECIFIC VIRUS AND
TIMING OF INFECTION CANNOT BE DETERMINED**
*For pregnant women without Zika virus exposure before the current pregnancy, a positive IgM result represents recent unspecified flavivirus infection.

**NO EVIDENCE OF
ZIKA VIRUS INFECTION**

might be detected for months after infection, limiting the ability to determine whether infection occurred before or during the current pregnancy.

6 Dengue virus IgM antibody testing is recommended for symptomatic pregnant women. For laboratory interpretation in the presence of dengue virus IgM results, refer to <https://www.cdc.gov/dpdx/cdcclinical/labreport.html>

7 Despite the high specificity of NAT, false positive NAT results have been reported. If both serum and urine specimens are NAT-positive, regardless of IgM antibody results, results should be interpreted as evidence of acute Zika virus infection. If either serum or urine specimen is NAT positive in conjunction with a positive Zika virus IgM test (Table 1), results should be interpreted as evidence of acute Zika virus infection.

8 If NAT is only positive on serum or urine and IgM antibody testing is negative, repeat testing on the original NAT positive specimen. If repeat NAT is positive, results should be interpreted as evidence of acute Zika virus infection. If repeat NAT testing is negative, results are indeterminate and healthcare providers should repeat Zika virus IgM antibody testing on a serum specimen collected ≥ 2 weeks after symptom onset. If subsequent IgM antibody test is positive, interpret as evidence of acute Zika virus infection but if negative, interpret as no evidence of Zika virus infection.

9 Non-negative results include positive, equivocal, presumptive positive, or possible positive. These are examples of assay interpretations that might accompany test results; non-negative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/medicaldevices/safety/urgent/situations/cdm161496.htm#zika>, under the "Labeling" for the specific assay.

10 Currently, PRNT confirmation is not routinely recommended for individuals living in Puerto Rico. For laboratory interpretation in the absence of PRNT testing, refer to Table 1.

Note: For the purposes of this guidance, recent possible Zika virus exposure or Zika virus/flavivirus infection is defined as a possible exposure or infection during the current pregnancy or periconceptional period.



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TABLE 1. Interpretation of results¹ of nucleic acid and antibody^{2,3} testing for suspected Zika virus infection – United States (including US territories), 2017

Zika NAT (serum) ¹	Zika NAT (urine) ⁴	Zika virus IgM ⁵	Zika virus PNT	Dengue virus PNT	Interpretation and recommendations
Positive	Positive	Any result	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Positive	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Negative	Not indicated	Not indicated	Suggests acute Zika virus infection <i>Repeat testing on original urine specimen</i> <ul style="list-style-type: none"> • If repeat NAT result is positive, interpret as evidence of acute Zika virus infection • If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date – If repeat IgM antibody result is positive,⁶ interpret as evidence of acute Zika virus infection – If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection
Positive	Negative or not performed	Positive	Not indicated	Not indicated	Acute Zika virus infection
Positive	Negative or not performed	Negative	Not indicated	Not indicated	Suggests acute Zika virus infection <i>Repeat testing on original serum specimen</i> <ul style="list-style-type: none"> • If repeat NAT result is positive, interpret as evidence of acute Zika virus infection • If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥2 weeks after symptom onset or possible exposure or specimen collection date – If repeat IgM antibody result is positive,⁶ interpret as evidence of acute Zika virus infection – If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection
Negative	Negative or not performed	Any non-negative result ⁷	≥10	<10	Zika virus infection; timing of infection cannot be determined. <ul style="list-style-type: none"> • For persons without prior Zika virus exposure, a positive IgM result represents recent Zika virus infection
Negative	Negative or not performed	Any non-negative result ⁷	≥10	≥10	Flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined <ul style="list-style-type: none"> • For persons without prior Zika virus exposure, a positive IgM result represents recent unspecified flavivirus infection
Negative	Negative or not performed	Any non-negative result ⁷	<10	Any result	No evidence of Zika virus infection
For areas where PNT is not recommended⁸					
Negative	Negative or not performed	Positive for Zika virus AND negative for dengue virus	Not performed because PNT is not recommended	Not performed because PNT is not recommended	Presumptive Zika virus infection; timing of infection cannot be determined⁸
Negative	Negative or not performed	Positive for Zika virus AND positive for dengue virus	Not performed because PNT is not recommended	Not performed because PNT is not recommended	Presumptive flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined⁸
Negative	Negative or not performed	Equivocal (either or both assays)	Not performed because PNT is not recommended	Not performed because PNT is not recommended	Insufficient information for interpretation <ul style="list-style-type: none"> • Consider repeat testing
Negative	Negative or not performed	Negative on both assays	Not performed because PNT is not recommended	Not performed because PNT is not recommended	No laboratory evidence of Zika virus infection

Abbreviations: IgM = immunoglobulin M; NAT = nucleic acid test; PNT = plaque reduction neutralization test.

1 Final interpretations of results of Zika virus tests should be performed after all testing is complete.

2 Serology test results that indicate flavivirus infection should be interpreted in the context of circulating flaviviruses.

3 Currently, PNT confirmation is not routinely recommended for persons living in Puerto Rico.

4 Serum must be submitted for all persons tested for Zika virus infection; a urine specimen for Zika virus NAT testing should always be submitted concurrently with a serum specimen.

5 Dengue virus IgM antibody testing is recommended for symptomatic pregnant women, as well as for asymptomatic pregnant women residing in areas where PNT confirmation is not recommended. For laboratory interpretation in the presence of dengue virus IgM results, refer to <https://www.cdc.gov/dengue/clinical/lab/aboratory.html>.

6 Positive results include "positive," "presumptive Zika virus positive," or "possible Zika virus positive." These are examples of assay interpretations that might accompany test results; positive serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/medical-devices/safety/emergent-situations/ucm161498.htm#zika> under the "Labeling" for the specific assay.

7 Non-negative results include "positive," "equivocal," "presumptive positive," or "possible positive." These are examples of assay interpretations that might accompany test results; nonnegative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/medical-devices/safety/emergent-situations/ucm161498.htm#zika> under the "Labeling" for the specific assay.

8 Zika virus IgM positive result is reported as "presumptive positive or flavivirus infection" to denote the need to perform confirmatory PNT tests against Zika virus, dengue virus, and other flaviviruses to which the person might have been exposed to resolve potential false-positive results that might have been caused by cross-reactivity or nonspecific reactivity. In addition, ambiguous test results (e.g., inconclusive, equivocal, and indeterminate) that are not resolved by retesting also should have PNT tests performed to rule out a false-positive result. However, PNT confirmation is currently not routinely recommended for persons living in Puerto Rico.

PRETEST COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS

FOR PREGNANT WOMEN WITH SYMPTOMS OF ZIKA



This guide describes recommendations for conducting pretesting counseling for symptomatic pregnant women with possible recent exposure (they or their sex partner live in or recently traveled to an area [with risk of Zika](#)). Symptoms of Zika include red eyes, fever, joint pain, rash, muscle pain, and headache. CDC recommends testing for pregnant women with symptoms of Zika. This material includes sample scripts to guide discussions with your patients about the complexity of Zika testing and the testing process with patients. Because a lot of content is outlined for discussion, make additional information available to support messaging and ensure that patients understand what they are being told.

Pregnant women coming in for Zika testing may feel worried or anxious. Support them by providing them with clear and easy-to-understand information and expressing empathy by acknowledging their concerns and feelings during pretesting counseling.

Recommendation

Sample Script

Provide the patient with information on why you will be testing them for Zika and a brief overview of what to expect

Use one of the two following sentences to begin the discussion:

1. You may be at risk for having Zika since you or your sex partner recently traveled to *(replace “recently traveled to” with “live in” as appropriate)* an area with risk of Zika within the past 12 weeks and you have had *(replace “have had” with “during your pregnancy you previously had” as appropriate)* symptoms of Zika.
OR/AND
2. You may be at risk of having Zika because you recently had sex without a condom with a person who traveled to *(replace “traveled to” with “lives in” as appropriate)* an area with risk of Zika within the past 12 weeks and you have had *(replace “have had” with “during your pregnancy you previously developed” as appropriate)* symptoms of Zika.

Since you were exposed to Zika and are experiencing symptoms *(replace “are experiencing” with “during your pregnancy you previously experienced” as appropriate)*, I think it is best to move forward with testing you for Zika. Before we begin, I would like to tell you what to expect throughout this process.

Patients should be informed that a combination of Zika tests will be required before a final result is determined

You will need a combination of tests to determine whether or not you have Zika. Finding out if you have Zika can require up to three different kinds of tests because the result of one test may require more testing to find out if you recently had a Zika infection. The tests we use to detect Zika can detect other similar viruses often found in the same areas with risk of Zika. Sometimes even after several tests, we may not know which type of virus you were infected with. Each test result is important, because it may help me decide how best to care for you during pregnancy.

I want to be sure we take all of the necessary steps to make sure your results are accurate. Each test can take different amounts of time to receive results, which I know can be frustrating. As your healthcare provider I am here to answer any questions you may have.

- Reassure the patient that this method of testing is normal
- Consider providing the fact sheet [What You Should Know About Zika Virus Testing for Pregnant Women with Symptoms of Zika](#).

Let the patient know that you will be

I am going to start the testing process by ordering two tests:

ordering two tests; one to look for Zika RNA and one to look for Zika antibodies. Define these terms as they may be unfamiliar

- The first test looks for pieces of Zika virus, known as RNA. RNA can be found in blood and urine.
- The second test looks for Zika antibodies, which are proteins that your body makes to fight off a Zika infection.

Zika test results can be difficult to interpret. If you've had exposure to Zika virus or another similar virus before this pregnancy, it's possible that you've been infected before, and this could affect today's test results.

Recommendation

Sample Script

Patients should be informed that it can be challenging to understand test results and that previous exposure to Zika could affect their test results

Scientists have learned that Zika antibodies can stay in the body for several months after infection. Antibodies show evidence that your body fought off a recent Zika infection. It is possible that you may have already developed antibodies against Zika virus if you've lived in or frequently traveled to an area with risk of Zika before becoming pregnant. Because of this, it is possible that your Zika antibody test results may not tell me if you were infected in the past or if you were infected more recently during your current pregnancy. This means if you test positive, we may not know if you are currently infected or not.

Inform the patient of what the possible results of the Zika RNA and antibody tests may be

Ask the patient if she has any questions before you move forward with providing information on the testing process.

- If your Zika RNA test comes back with a positive result, regardless of your test result for Zika antibodies, it means that you have recently been infected with Zika.
- If your Zika RNA test comes back negative and your antibody test is positive, we will need to do one more round of testing to figure out whether or not you actually have or recently had Zika. It may mean that you had Zika but the virus is no longer in your body or it could mean that you had an infection with another similar virus.
- If your Zika RNA test and your antibody test are both negative, it means there is no evidence that you have Zika or another similar virus and I will continue evaluating you to find out what may be causing your symptoms.

Ask the patient if they have any questions before you move forward with providing information on step two of testing.

If the patient requires further testing after the Zika RNA and Zika antibody test, inform the patient and provide them with information on what to possibly expect next.

If you test negative for Zika RNA and your antibody test is positive, I will need to order a third test to confirm whether the antibodies are for Zika or a similar virus. This test takes the longest to receive results because I have to send the results to a specialized lab and then work with the state or local health department to interpret the results.

Ask the patient if they have any questions on what to expect during each step of the testing process.

Inform patients of what each test result could mean for their pregnancy.

Now we'll go over what each test result could mean for your pregnancy.

If Zika test results are positive

If you test positive for Zika, I will need to watch your pregnancy more closely. I may do more ultrasounds or other tests to check for your fetus's growth and development.

If Zika test results are not clearly positive or negative

Sometimes test results will not come back as a clear negative or positive. If this happens, I'd rather be more cautious and still do more ultrasounds and other tests to closely monitor your pregnancy.

If Zika test results are negative.

If your test results are negative, I will do an ultrasound to check the growth and development of your fetus and check for any signs of Zika virus infection. If I see any signs of Zika during the ultrasound, then I may order additional tests. If there are no signs of Zika, we will continue with routine prenatal care.



**Counseling and Testing
Recommendations for
Asymptomatic Pregnant Women
with Possible Zika Virus Exposure**

UPDATED INTERIM PREGNANCY GUIDANCE: ASYMPTOMATIC PREGNANT WOMEN WITH POSSIBLE ZIKA VIRUS EXPOSURE

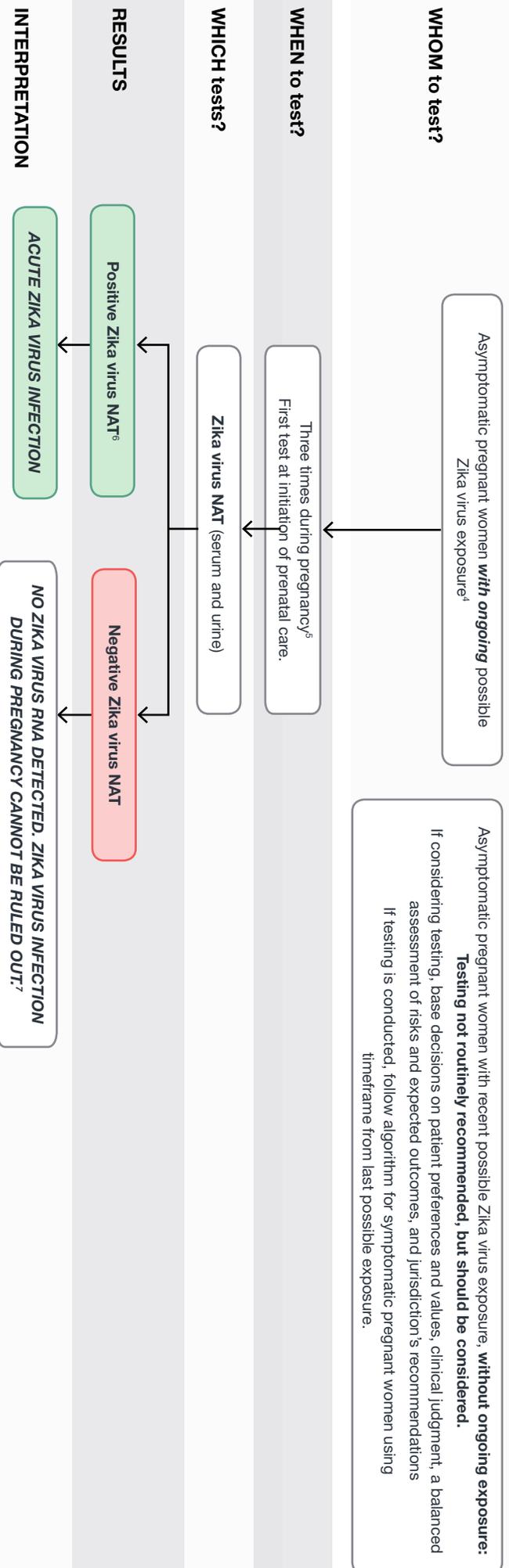


Testing Recommendations and Interpretation of Results for Healthcare Providers

ASK PREGNANT WOMEN ABOUT

Travel to or residence in any areas with risk for Zika virus transmission before and during the current pregnancy^{1,2}
Possible sexual exposure before and during the current pregnancy • A diagnosis of laboratory-confirmed Zika virus infection before current pregnancy³ • Symptoms of Zika virus disease during current pregnancy (e.g., fever, rash, conjunctivitis, arthralgia) • If symptoms are reported, refer to symptomatic algorithm.

Before testing, discuss testing limitations and potential risks of misinterpretations for test results.



Abbreviations: IgM = immunoglobulin M; NAT = nucleic acid test; PRNT = plaque reduction neutralization test

- 1 Ask about type and duration of Zika virus exposure before and during the current pregnancy. Exposure prior to the current pregnancy may limit interpretation of Zika IgM antibody results; pretest counseling can help inform testing decisions.
- 2 Possible Zika virus exposure includes travel to or residence in an area with risk for Zika virus transmission (<https://wwwnc.cdc.gov/travel/page/zika-travel-information>) during pregnancy or the periconceptional period (8 weeks before conception [6 weeks before the last menstrual period], or sex without a condom during pregnancy or the periconceptional period, with a partner who traveled to, or resides in an area with risk for Zika virus transmission).
- 3 Zika virus testing is not routinely recommended for pregnant women with a previous diagnosis of laboratory-confirmed Zika virus infection by either NAT or serology (positive/equivocal Zika virus or dengue virus IgM and Zika virus PRNT ≥ 10 and dengue virus PRNT < 10 results).
- 4 Persons with ongoing possible exposure include those who reside in or frequently travel (e.g., daily or weekly) to an area with risk for Zika virus transmission.
- 5 The interval for Zika virus NAT testing during pregnancy is unknown. Preliminary data suggest that NAT might remain positive for several weeks after infection in some pregnant women. For women without a prior laboratory-confirmed diagnosis of Zika virus, NAT testing should be offered at the initiation of prenatal care, and if Zika virus RNA is not detected on clinical specimens, two additional tests should be offered during the course of the pregnancy coinciding with prenatal visits. The proportion of fetuses and infants with Zika virus-associated birth defects is highest among women with first and early, second trimester infections; therefore, conducting all NAT testing during the first and second trimesters might be considered

to help identify infections early in pregnancy. However, adverse outcomes have been associated with infection diagnosed in the third trimester; therefore, testing every trimester might be considered.

- 6 Despite the high specificity of NAT, false positive NAT results have been reported. **If both serum and urine specimens are NAT positive, interpretation should be acute Zika virus infection.** If NAT is only positive on serum or urine, testing should be repeated on the original NAT-positive specimen. **If repeat NAT is positive, results should be interpreted as evidence of acute Zika virus infection.** If repeat NAT testing is negative, results are indeterminate and healthcare providers should perform IgM antibody testing on a specimen collected ≥ 2 weeks after the initial specimen collection. For laboratory interpretation, see [Table 1](#).
 - 7 A negative Zika virus NAT result does not exclude infection during pregnancy because it represents a single point in time. Zika virus RNA levels decline over time, and the duration of the presence of Zika virus RNA in serum and urine following infection vary among pregnant women. Despite Zika virus IgM test limitations (e.g., cross-reactivity with other flaviviruses and prolonged detection for months, presenting challenges in determining the timing of infection), which should be discussed as part of pretest counseling, patients may still choose to receive Zika virus IgM testing.
- Note:** For the purposes of this guidance, recent possible Zika virus exposure or Zika virus/flavivirus infection is defined as a possible exposure or infection during the current pregnancy or periconceptional period.



U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

TABLE 1. Interpretation of results¹ of nucleic acid and antibody^{2,3} testing for suspected Zika virus infection – United States (including US territories), 2017

Zika NAT (serum) ¹	Zika NAT (urine) ⁴	Zika virus IgM ⁵	Zika virus PNT	Dengue virus PNT	Interpretation and recommendations
Positive	Positive	Any result	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Positive	Not indicated	Not indicated	Acute Zika virus infection
Negative	Positive	Negative	Not indicated	Not indicated	Suggests acute Zika virus infection <i>Repeat testing on original urine specimen</i> <ul style="list-style-type: none"> If repeat NAT result is positive, interpret as evidence of acute Zika virus infection If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥ 2 weeks after symptom onset or possible exposure or specimen collection date If repeat IgM antibody result is positive,⁶ interpret as evidence of acute Zika virus infection If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection
Positive	Negative or not performed	Positive	Not indicated	Not indicated	Acute Zika virus infection
Positive	Negative or not performed	Negative	Not indicated	Not indicated	Suggests acute Zika virus infection <i>Repeat testing on original serum specimen</i> <ul style="list-style-type: none"> If repeat NAT result is positive, interpret as evidence of acute Zika virus infection If repeat NAT result is negative, repeat Zika virus IgM antibody testing on a serum specimen collected ≥ 2 weeks after symptom onset or possible exposure or specimen collection date If repeat IgM antibody result is positive,⁶ interpret as evidence of acute Zika virus infection If repeat IgM antibody result is not positive, interpret as no evidence of Zika virus infection
Negative	Negative or not performed	Any non-negative result ⁷	≥ 10	< 10	Zika virus infection; timing of infection cannot be determined. <ul style="list-style-type: none"> For persons without prior Zika virus exposure, a positive IgM result represents recent Zika virus infection
Negative	Negative or not performed	Any non-negative result ⁷	≥ 10	≥ 10	Flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined <ul style="list-style-type: none"> For persons without prior Zika virus exposure, a positive IgM result represents recent unspecified flavivirus infection
Negative	Negative or not performed	Any non-negative result ⁷	< 10	Any result	No evidence of Zika virus infection
For areas where PNT is not recommended⁸					
Negative	Negative or not performed	Positive for Zika virus AND negative for dengue virus	Not performed because PNT is not recommended	Not performed because PNT is not recommended	Presumptive Zika virus infection; timing of infection cannot be determined⁸
Negative	Negative or not performed	Positive for Zika virus AND positive for dengue virus	Not performed because PNT is not recommended	Not performed because PNT is not recommended	Presumptive flavivirus infection; specific virus cannot be identified; timing of infection cannot be determined⁸
Negative	Negative or not performed	Equivocal (either or both assays)	Not performed because PNT is not recommended	Not performed because PNT is not recommended	Insufficient information for interpretation <ul style="list-style-type: none"> Consider repeat testing
Negative	Negative or not performed	Negative on both assays	Not performed because PNT is not recommended	Not performed because PNT is not recommended	No laboratory evidence of Zika virus infection

Abbreviations: IgM = immunoglobulin M; NAT = nucleic acid test; PNT = plaque reduction neutralization test.

1 Final interpretations of results of Zika virus tests should be performed after all testing is complete.

2 Serology test results that indicate flavivirus infection should be interpreted in the context of circulating flaviviruses.

3 Currently, PNT confirmation is not routinely recommended for persons living in Puerto Rico.

4 Serum must be submitted for all persons tested for Zika virus infection; a urine specimen for Zika virus NAT testing should always be submitted concurrently with a serum specimen.

5 Dengue virus IgM antibody testing is recommended for symptomatic pregnant women, as well as for asymptomatic pregnant women residing in areas where PNT confirmation is not recommended. For laboratory interpretation in the presence of dengue virus IgM results, refer to <https://www.cdc.gov/dengue/diagnostic/Laboratory.html>.

6 Positive results include "positive," "presumptive Zika virus positive," or "possible Zika virus positive." These are examples of assay interpretations that might accompany test results; positive serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/medical-devices/safety/emergencysituations/ucm161496.htm#zika> under the "Labeling" for the specific assay.

7 Non-negative results include "positive," "equivocal," "presumptive positive," or "possible positive." These are examples of assay interpretations that might accompany test results; nonnegative serology terminology varies by assay. For explanation of a specific interpretation, refer to the instructions for use for the specific assay performed. Information on each assay can be found at <https://www.fda.gov/medical-devices/safety/emergencysituations/ucm161496.htm#zika> under "Labeling" for the specific assay.

8 Zika virus IgM positive result is reported as "presumptive positive or flavivirus infection" to denote the need to perform confirmatory PNT tests against Zika virus, dengue virus, and other flaviviruses to which the person might have been exposed to resolve potential false-positive results that might have been caused by cross-reactivity or nonspecific reactivity. In addition, ambiguous test results (e.g., inconclusive, equivocal, and indeterminate) that are not resolved by retesting also should have PNT tests performed to rule out a false-positive result. However, PNT confirmation is currently not routinely recommended for persons living in Puerto Rico.

COUNSELING CONVERSATION GUIDE FOR HEALTHCARE PROVIDERS FOR ASYMPTOMATIC PREGNANT WOMEN WHO WERE RECENTLY EXPOSED TO ZIKA BUT DO NOT HAVE ONGOING EXPOSURE



This guide provides talking points for discussing why testing is not routinely recommended for asymptomatic pregnant women who were recently exposed to Zika (meaning they or their sex partner recently traveled to [an area with risk of Zika \(Visit <http://www.cdc.gov/zika/geo>\)](http://www.cdc.gov/zika/geo) but do not have ongoing exposure. However, testing can be considered on a case-by-case basis depending on patient preferences, your clinical judgement, or if your state or local jurisdiction recommends it. This material includes sample scripts to guide discussions with your patients about why Zika testing is not recommended for asymptomatic pregnant women who do not have ongoing exposure. To increase patient understanding, it may be helpful to make additional information available to support messaging.

Pregnant women who may have been exposed to Zika may feel worried or anxious. Support them by providing them with clear and easy-to-understand information and expressing empathy by acknowledging their concerns and feelings during discussions.

Recommendation

Sample Script

Discuss with the patient why Zika testing is no longer routinely recommended for asymptomatic pregnant women without ongoing exposure

Thank you for coming in to discuss your concerns about possibly being exposed to Zika virus. Possible exposure means that you or your sex partner recently traveled to [an area with risk of Zika](#).

As you may know, the Centers for Disease Control and Prevention (CDC) issues up-to-date recommendations for pregnant women possibly affected by Zika as more continues to be learned about the virus. Currently, routine Zika testing is not recommended for pregnant women if they don't have ongoing exposure and do not have symptoms. The most common symptoms of Zika virus disease are fever, rash, headache, joint pain, red eyes, and muscle pain.

Overall, the number of people with reported Zika infection in the Americas is decreasing. Testing people without symptoms when there is a smaller number of new cases occurring could increase the chances of test results being positive when they may actually be negative. This means the test might tell you that you have Zika when you actually don't.

False test results are a concern. They may cause stress and anxiety and lead to me performing more tests and procedures than are necessary. Testing is typically recommended when it can provide us with valuable information for us to make informed decisions about care during your pregnancy. When more positive results will be false, we should only consider testing after discussing the possibility of false results and what this might mean for you.

What questions do you have?

- *Consider providing the fact sheet [What You Should Know about Zika Virus Testing for pregnant women without symptoms who were recently exposed to an area with risk of Zika but do not have ongoing exposure](#). Visit http://www.cdc.gov/zika/pdfs/living_in.pdf*
- *If the patient still requests to be tested, refer to [What You Should Know About Zika Virus Testing for Pregnant Women with Symptoms of Zika to guide them through the steps of the testing process](#). Visit <http://www.cdc.gov/zika/pdfs/testing-symptomatic-pregnant.pdf>*





Rhode Island Department of Health Zika Virus Testing Tables

Zika Virus Testing Table 1: Symptomatic

To report individuals with Zika virus exposure and obtain preauthorization for testing, call the RI Department of Health at 401-222-2577.

	Day 1-13 After Symptom Onset (The Day of Illness Onset is Day 1)	2-12 Weeks After Symptom Onset	>12 Weeks After Symptom Onset
A Exposed† Symptomatic* Pregnant Female	Submit serum and urine to RISHL for concurrent PCR** and IgM testing as soon as possible. <ul style="list-style-type: none"> If both serum and urine PCR tests are negative and IgM is positive, equivocal or indeterminate, RISHL will send serum to MADPH for PRNT. 		Zika virus IgM testing may be considered. Discuss on a case-by-case basis.
B Exposed† Symptomatic* Male with a Pregnant Partner	Submit serum and urine to RISHL for testing. <ul style="list-style-type: none"> If both serum and urine PCR** tests are negative, RISHL will perform serum IgM. If IgM is positive, equivocal or indeterminate, RISHL will send serum to MADPH for PRNT. 	Submit serum to RISHL for IgM. <ul style="list-style-type: none"> If IgM positive, equivocal or indeterminate, RISHL will send serum to MADPH for PRNT. 	Testing is not recommended. Evaluate pregnant partner (see Zika Virus Testing Table 2, row A).
C Exposed† Suspect Case of Guillain-Barré Syndrome	Submit serum, urine and CSF (if available) to RISHL for testing. <ul style="list-style-type: none"> If serum, urine, and CSF PCR** tests are negative, RISHL will perform serum and CSF IgM. If IgM is positive, equivocal or indeterminate, RISHL will send serum to MADPH for PRNT. 	Submit serum and CSF (if available) to RISHL for IgM. <ul style="list-style-type: none"> If IgM positive, equivocal or indeterminate, RISHL will send serum to MADPH for PRNT. 	Discuss on a case-by-case basis.
D Exposed† Suspect Case of Acute Disseminated Encephalomyelitis (ADEM)	Submit serum and urine to Reference Lab for testing. <ul style="list-style-type: none"> If both serum and urine PCR** tests are negative, serum IgM testing should be performed. If IgM is positive, equivocal or indeterminate, send serum for PRNT. 	Submit serum to Reference Lab for IgM. <ul style="list-style-type: none"> If IgM positive, equivocal or indeterminate, send serum for PRNT. 	Testing is not recommended
All Other Exposed† Symptomatic* Individuals	Specimens on these individuals should no longer be submitted to the RISHL.		

RISHL= Rhode Island State Health Laboratory

MADPH= Massachusetts Department of Public Health

† Possible exposure to Zika virus includes travel to or residence in an area with active Zika virus transmission, or sex without a barrier method with a partner who traveled to, or lives in an area with active Zika virus transmission.

* Only one of the four symptoms consistent with Zika virus infection (acute onset of fever [measured or reported], maculopapular rash, arthralgia, conjunctivitis) need to be present for the individual to be considered symptomatic.

** Urine, CSF, and amniotic fluid specimens must be accompanied by a serum specimen collected on the same day.

Rhode Island Department of Health

Division of Preparedness, Response, Infectious Disease and Emergency Medical Services

Center for Acute Infectious Disease Epidemiology

Zika Virus Testing Table 2: Asymptomatic

To report individuals with Zika virus exposure and obtain preauthorization for testing, call the RI Department of Health at 401-222-2577.

A Asymptomatic Pregnant Female with limited risk of exposure defined as travel to and/or former residence in an area with active Zika virus transmission or unprotected sex with a partner who lives in or traveled to area with transmission.	Testing is not routinely recommended, but should be considered using a shared decision-making model. If considering testing, base decisions on patient preferences and values, clinical judgement, and a balanced assessment of risks and expected outcomes. Potential exposure risk factors to consider include any past symptomatology, type and length of possible exposure, Zika virus transmission trends at location of possible exposure, and use of prevention measures (e.g. insect repellent, appropriate clothing, and condom use). If testing is conducted, follow guidance below.	
	Up to 12 Weeks After Last Exposure	> 12 Weeks After Last Exposure
B Asymptomatic Pregnant Female with ongoing risk of exposure defined as residence in or frequent travel to an area with active Zika virus transmission.	A pregnant woman should be tested three times during her pregnancy. Submit serum and urine to RISHL for PCR** testing. IgM testing is no longer routinely recommended. For a pregnant woman who has received a diagnosis of laboratory confirmed Zika virus infection any time before or during the current pregnancy, additional Zika virus testing is not recommended.	
	Do not test Asymptomatic Male, but refer pregnant partner to provider for evaluation/testing. The pregnant female would be considered exposed if they have had unprotected sex. Refer to line A above (Asymptomatic Pregnant Female with Limited Risk of Exposure) for guidance.	
C Asymptomatic Male who has Traveled to a Country with Zika Virus Transmission and has a Pregnant Partner who has Not Traveled	Preconception Testing is not routinely recommended.	
	Preconception Testing is not routinely recommended.	
D Asymptomatic Non-Pregnant Female Seeking Preconception Testing	Preconception Testing is not routinely recommended.	
	Preconception Testing is not routinely recommended.	

RISHL= Rhode Island State Health Laboratory

MADPH= Massachusetts Department of Public Health

† Possible exposure to Zika virus includes travel to or residence in an area with active Zika virus transmission, or sex without a barrier method with a partner who traveled to, or lives in an area with active Zika virus transmission.

** Urine, CSF, and amniotic fluid specimens must be accompanied by a serum specimen collected on the same day.