Zika virus infection
Interim clinical guidance for Primary Care

Zika virus infection is a **notifiable disease** in Ireland under the Infectious Diseases (Amendment) Regulations 2016 (S.I. No. 276 of 2016). All medical practitioners and laboratories are required to notify it to the Medical Officer of Health.

Information on the process of notifying infectious diseases including the case definition of Zika infection is available at: http://www.hpsc.ie/NotifiableDiseases/.

Background

Zika virus infection is an emerging viral threat that is currently circulating most prominently in the Americas and the Caribbean, with over 30 countries currently affected.

There is strong evidence that infection with Zika virus is the cause of a serious birth condition called microcephaly. Zika virus infection has also been linked with Guillain-Barré syndrome.

Zika virus is primarily spread through the bite of the *Aedes* genus of mosquito that is largely tropical and subtropical in distribution. It has also been recognised that Zika virus disease can be transmitted sexually. Finally, Zika virus disease can be transmitted vertically, from a pregnant woman to her developing foetus

This guidance summarises key advice for those working in Primary Care, since they may be consulted by patients, including pregnant women, who plan on travelling to or are returning from countries with active Zika virus transmission.

The HPSC website also provides the following Zika virus resources:

- Clinical guidelines for health professionals on Zika virus infection and pregnancy
- Laboratory investigation of Zika virus infection
- Frequently asked questions for the general public
- Frequently asked questions for pregnant women and women who are planning a pregnancy
- A list of countries reporting local transmission of confirmed Zika virus infection.

Symptoms

An estimated three out of four people infected with Zika virus do not have symptoms at all. In symptomatic patients, Zika virus generally causes a mild illness that lasts from 2 to 7 days. The incubation period is between 3 and 12 days. Serious complications from Zika virus infection are uncommon. The most common symptoms include:

- Itching/pruritis (very common)
- non-purulent conjunctivitis
- muscle or joint pains (quite common)
- headache (in about half of cases)
- mild fever (in only a minority of cases)
- lower back pain
- retro-orbital pain

Treatment

There is currently no specific treatment for Zika virus infection. Treatment consists of relieving pain, fever and any other symptoms. To prevent dehydration, it is advised to control the fever, rest and drink plenty of water.

Diagnosis

Zika virus infection should be considered in:

- individuals who develop symptoms consistent with Zika virus infection within 10 days of returning from an area with active transmission of virus
- symptomatic individuals who have had unprotected sex with a recently* returned traveller from an area with active transmission of virus
- **pregnant women** with **acute onset** of symptoms **NOT** consistent with Zika virus infection but who are within **10 days of return** from an affected area and **IF** the symptoms are **not explained** by other common infectious causes (e.g. URTI, UTI).

Diagnostic testing for men or non-pregnant women who have **never experienced symptoms** suggestive of Zika virus infection do **not** require laboratory investigation.

Zika virus laboratory investigations

Zika virus has been detected in whole blood (also serum and plasma), urine, cerebrospinal fluid, amniotic fluid, semen and saliva. There is accumulating evidence that Zika virus is present in urine and semen for longer periods than in whole blood or saliva. Table 1 details the recommended Zika virus tests in relation to the time elapsed since symptom onset and the specimen types required. Detailed information on laboratory investigation of Zika virus infection is available on the HPSC website.

* Within 6 months of return from an affected area

Table 1: Recommended Zika virus laboratory tests in relation to time elapsed since symptom onset

Time elapsed since symptom onset	Appropriate tests to order	Specimen type required
0-7 days	• Zika RNA NAT • Zika RNA NAT	• Blood (EDTA tube) • Urine without preservative
8-10 days	• Zika RNA NAT • Zika serology –IgM, IgG	• Urine without preservative • Clotted blood (plain tube or serum separator tube)
10 days-12 weeks	• Zika serology –IgM, IgG	• Clotted blood (plain tube or serum separator tube)
>12 weeks	• Zika serology – IgG	• Clotted blood (plain tube or serum separator tube)

Samples taken seven days post-symptom onset will also be tested for other flaviviruses (e.g. Dengue virus and Yellow Fever virus). Chikungunya serological testing will be performed based upon relevant travel history, as the clinical presentation is similar to that of Zika virus infection.

Pregnant women

Both symptomatic and asymptomatic pregnant women should have a baseline **fetal ultrasound** at 18-20 weeks gestation performed at a Fetal Medicine Unit. Appropriate psychosocial care can also be offered at this stage.

For asymptomatic pregnant women, taking and storing a clotted blood sample locally, without immediate testing is also recommended. This sample can then be tested for Zika virus IgG in the event that there is a later concern about fetal development.

See Appendix 1 for further details on the assessment of pregnant women who have travelled to a Zika affected area. For detailed guidance on Zika virus and pregnancy, please refer to Clinical guideline for health professionals on Zika virus and pregnancy.

Additional testing notes:

- Clinicians should consider other travel-associated infections including dengue and chikungunya virus infections, malaria, common infections and non-infectious diseases in the differential diagnosis.
- Clinicians should consider other causes of rash in the differential diagnosis, as appropriate.
- Laboratory test request forms must clearly indicate the following:
    - whether the patient is pregnant (including the number of weeks gestation)
    - travel history (countries visited and the dates of the outward and return journeys)
    - clinical details (patient's symptoms, date of symptom onset).

If in doubt about the eligibility or requirements for testing the NVRL can be contacted for further advice.

Infection prevention

There is currently no vaccine or drug available to prevent Zika virus infection. The most important thing is to avoid mosquito bites to prevent infection with Zika virus or other infections transmitted by mosquitoes. Prevention of sexual transmission of Zika virus infection is also an important message to get across to patients. For further advice on prevention of sexual transmission see Figure 1.

Travel advice

A General Practitioner may be consulted by patients travelling to, or returning from areas with active Zika virus transmission. In addition, pregnant women may also request supporting documentation to justify deferral or cancellation of travel to affected areas on medical grounds. Current advice relating to the clinical management of travellers to affected areas and advice for women who are pregnant or trying to becoming pregnant can be found on the HPSC's website.

- **Pregnant women are advised to postpone non-essential travel** to a Zika affected area until after delivery.
- **If travel is unavoidable** pregnant travellers or those planning pregnancy must be informed by the healthcare provider of the risks which Zika may present.
- It is strongly recommended that women should **avoid becoming pregnant** while travelling in an area with active Zika virus transmission
- **Pregnant travellers or those planning pregnancy** who travel to affected areas, **should use condoms** during vaginal, anal and oral sex for the **duration of their stay**
- All travellers should follow the advice in the section below on Preventing Potential Sexual Transmission.
- All travellers should ensure **scrupulous mosquito bite avoidance measures**, both during daytime and night time hours but especially **during mid-morning and late afternoon to dusk**, when *Aedes* mosquitoes are most active.
- Repellents containing 50% DEET can be used by pregnant women, but higher concentrations **should not be used**. DEET should be applied after the sunscreen. Sunscreen with a 30 to 50 SPF rating should be applied to compensate for DEET-induced reduction in SPF. The use of DEET is not recommended for infants less than two months of age.

Preventing sexual transmission

Sexual transmission has been reported in several countries. For further advice on prevention of sexual transmission see Figure 1.

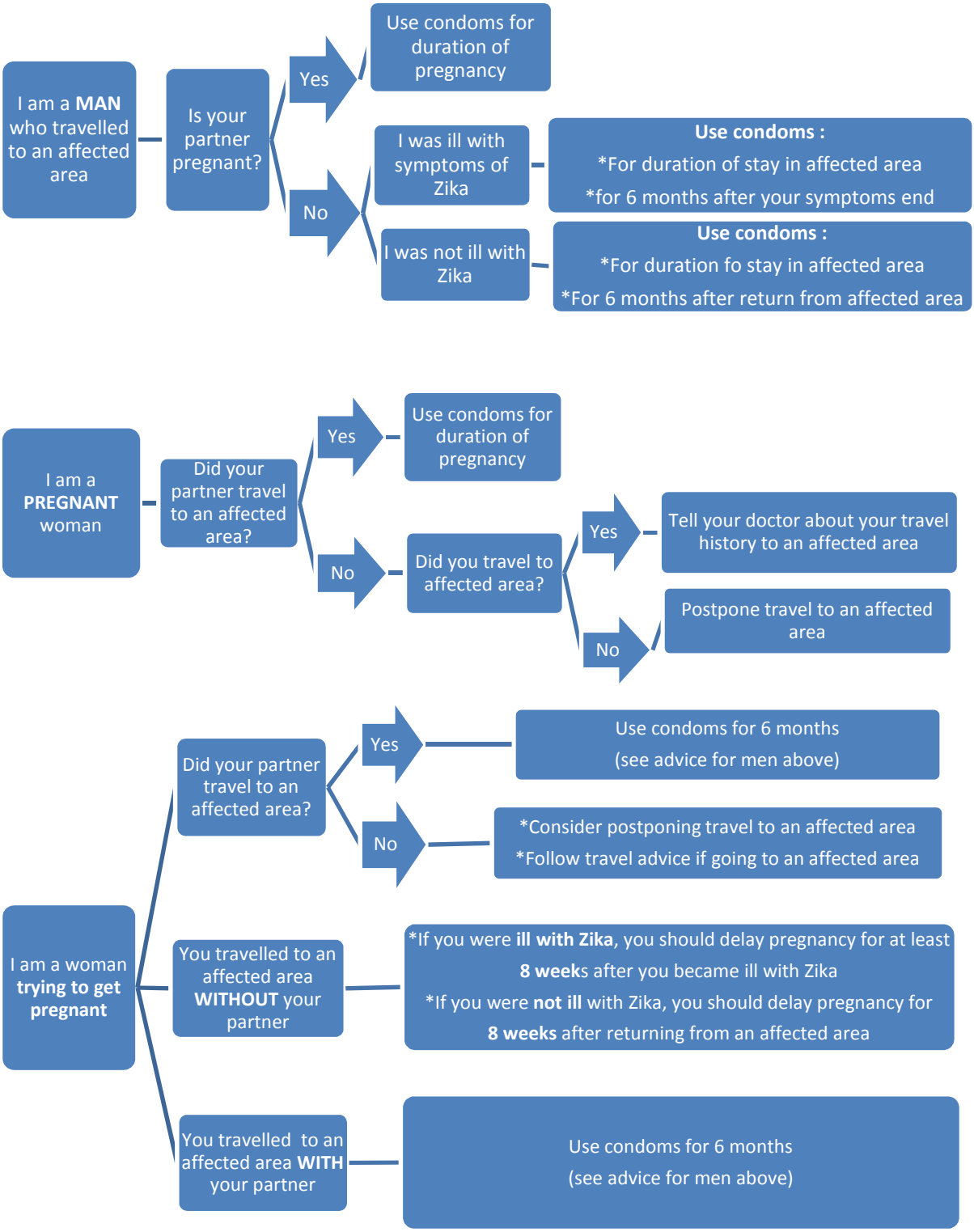
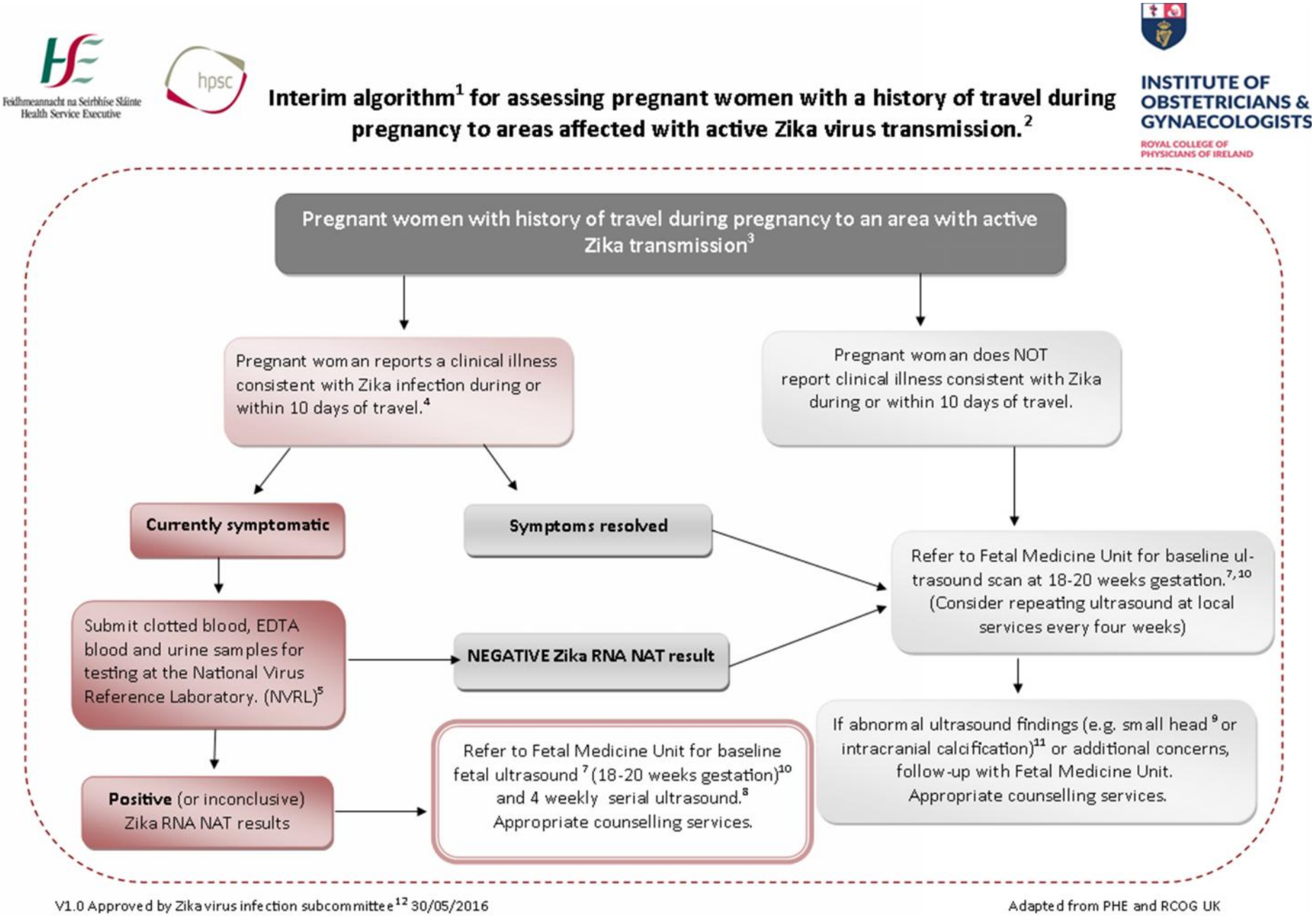


Figure 1: Advice on how individuals can prevent sexual transmission of Zika virus infection

Appendix 1: Algorithm for assessment of a pregnant woman with a history of travel to a Zika affected area



Interim algorithm for assessing pregnant women with a history of travel during pregnancy for areas affected with active Zika virus transmission

ADDITIONAL NOTES

1. Interim guidance will be updated as more information becomes available. Currently this algorithm applies to women in all stages of pregnancy although based on information available from Brazil and experience from other congenital infections (such as CMV, rubella and toxoplasmosis), infection in early pregnancy is likely to be the greatest risk.
2. Laboratory testing is performed by the National Virus Reference Laboratory (NVRL). Zika virus testing will be performed using Zika virus RNA NAT testing or serology.
3. Assessment of pregnant women should be based on a history of travel to countries and territories reporting active ZIKV transmission in the last 9 months. See the most up to date list at www.hpsc.ie. This is in contrast to pre travel advice where countries or overseas territories are classified as having **current active** ZIKV transmission if confirmed autochthonous cases have been reported in the last 3 months.
4. Clinical illness is consistent with Zika virus disease if two or more symptoms (acute onset of fever, maculopapular rash, arthralgia, or conjunctivitis) are present. However, testing can also be considered for pregnant women with acute onset of symptoms within 10 days of travel to an area with Zika virus transmission that are not explained by other common infectious causes (e.g. URTI, UTI).
5. The samples required are a clotted blood (plain tube or serum separator tube) for serology, or EDTA blood and a small volume of urine without preservative for Zika virus RNA testing The sample form must clearly state both the travel history (i.e. which countries visited and the dates of the outward and return journeys) and the clinical details (i. e .the patient's symptoms and the date of illness onset). This is so that the appropriate investigations can be performed and their results correctly interpreted.
6. If an alternative diagnosis is made there is no need for further Zika virus-specific follow up.
7. For women without current symptoms, taking and storing a clotted blood sample locally, without immediate testing, is recommended. In the event that there is a later concern about fetal development, this sample will be available for retrospective testing, including detection of Zika antibodies.
8. This evaluation and follow-up is likely to include repeat fetal ultrasound at four weekly intervals and consideration of fetal MRI. Abnormal fetal findings will prompt appropriate investigation including, for example, submission of booking and current serum samples for toxoplasma, rubella, parvovirus and CMV serology.
9. In this context, 'small fetal head' is defined as: Head Circumference more than 2 Standard Deviations below the mean for gestational age, i.e. below the 25th centile.
10. Time of first scan and subsequent ultrasound has been recommended because fetal ultrasound might not detect microcephaly or intracranial calcifications until the late second or early third trimester of pregnancy.
11. Apart from microcephaly and intracranial calcifications, other brain abnormalities that have been reported in association with Zika virus infection are ventriculomealy, cell migration abnormalities (e.g. lissencephaly, pachygyria), arthyrogryposis (congenital contractures) secondary to central or peripheral nervous system involvement.
12. This interim algorithm for assessing pregnant women with a history of travel during pregnancy for areas affected with active Zika virus transmission has been adapted from the Public Health England and UK Royal College of Obstetrics with due consideration given to the Irish context.