National Women & Infants Health Programme

National Clinical Practice Guideline

Varicella in pregnancy

INSTITUTE OF OBSTETRICIANS & GYNAECOLOGISTS

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

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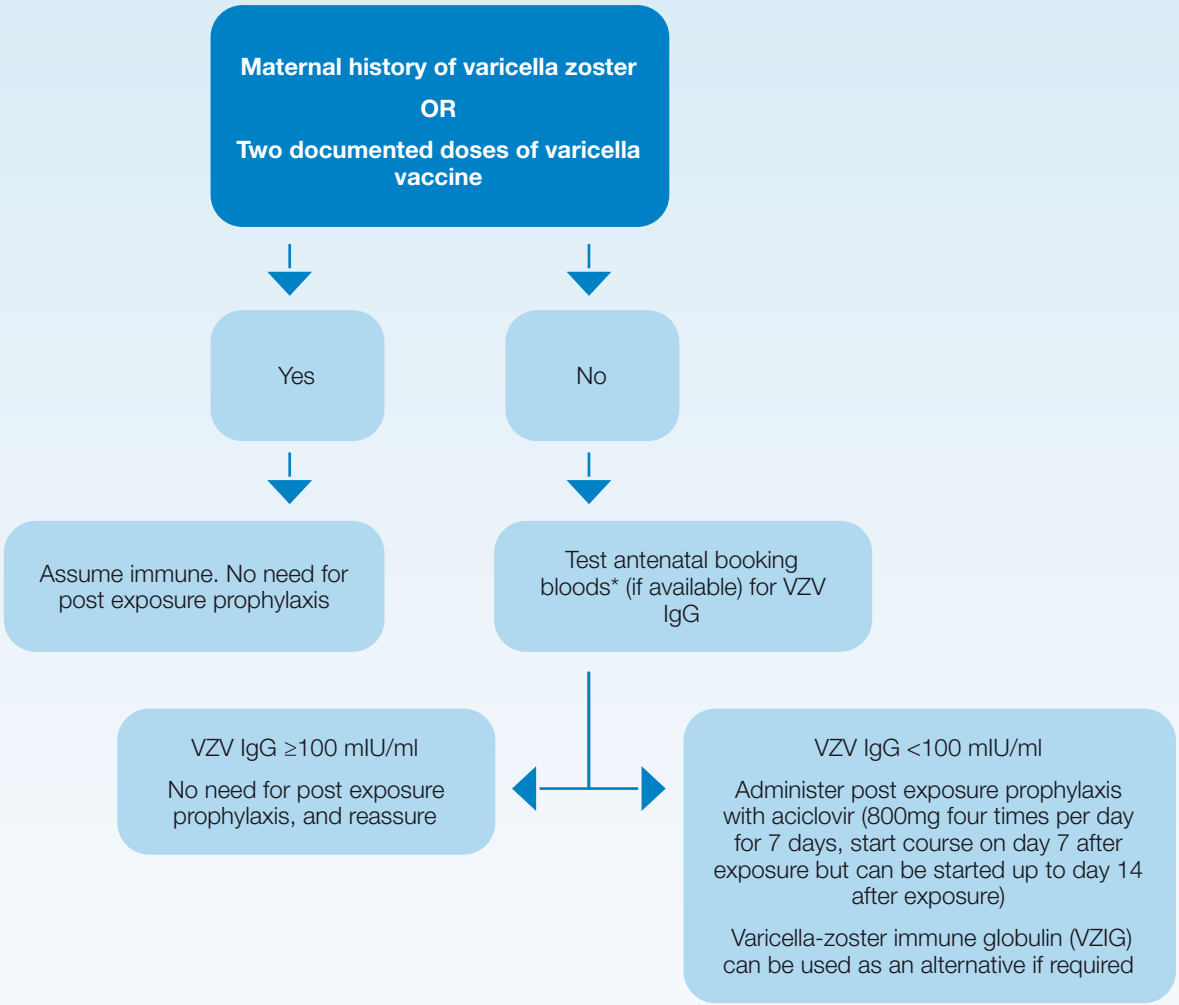
Algorithms

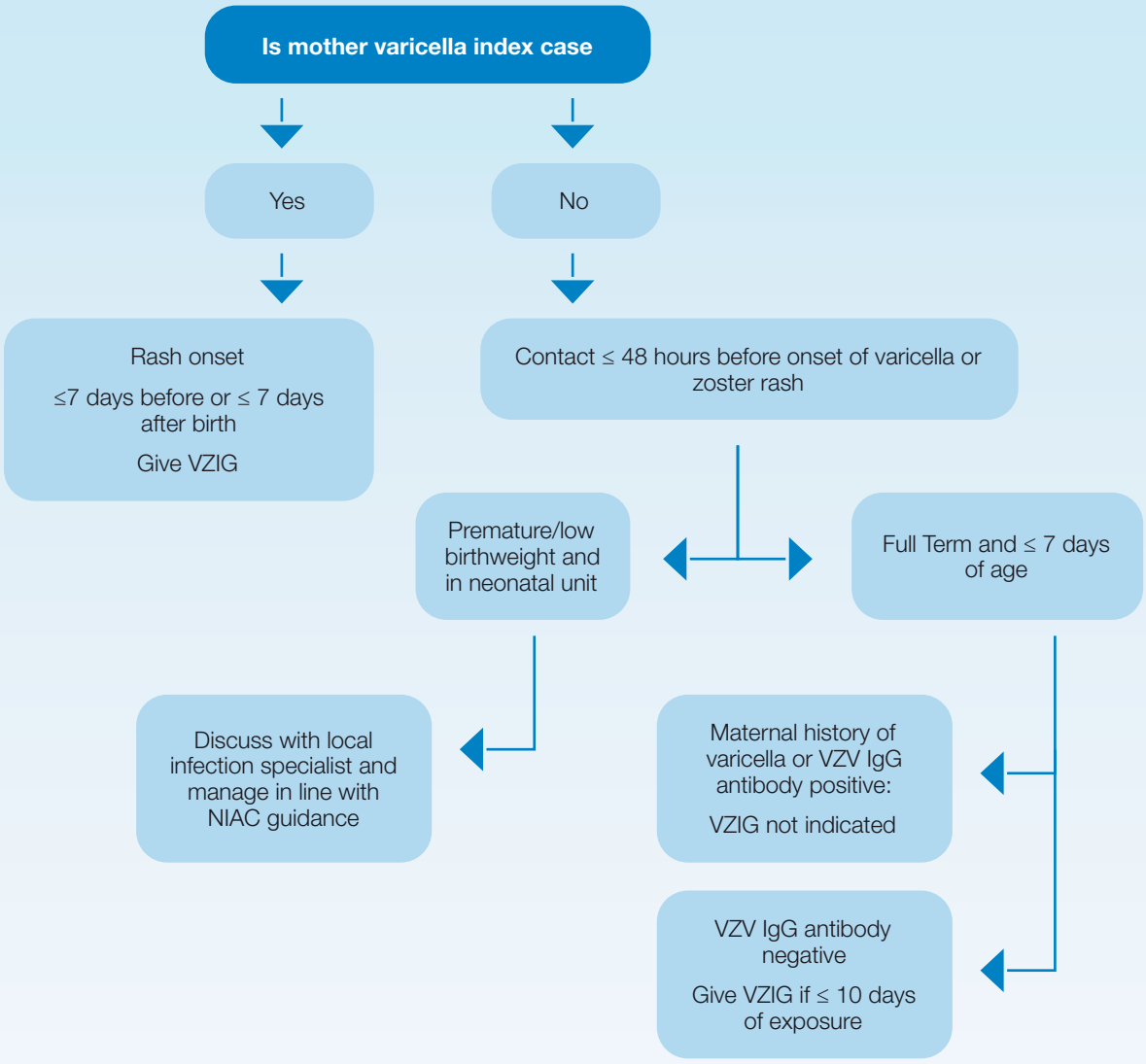
Algorithm 1: Post exposure prophylaxis for pregnant women exposed to Varicella-zoster virus (VZV)[1]



* A repeat serum sample should be taken for VZV IgG in cases of repeated exposure to varicella in the same pregnancy if the booking bloods or most recent serology demonstrate non-immunity, unless the woman has received VZIG or blood products in the last 3 months.

1 https://www.rcpi.ie/Healthcare-Leadership/NIAC/Immunisation-Guidelines-for-Ireland

Algorithm 2: Use of Varicella-zoster immune globulin (VZIG) in neonates exposed to Varicella-zoster virus (VZV) [2]



2 https://www.rcpi.ie/Healthcare-Leadership/NIAC/Immunisation-Guidelines-for-Ireland

Key Recommendations

Antenatal Care and varicella prevention

1. We suggest that women planning to conceive and/or engaging with fertility services, should have their varicella status assessed as part of pre-conception counselling either by history or laboratory testing. *Best practice*
2. We strongly recommend that women should have their immunity to varicella discussed and documented at their booking visit. Their immunity can be confirmed by either reliable history of varicella, two varicella vaccines or by a laboratory test (varicella IgG) following exposure in line with National Immunisation Advisory Committee (NIAC) guidance. Laboratories may choose to only send varicella IgG if a woman is exposed, rather than on all women with an uncertain varicella history. *Best practice*
3. We recommend that if there is any uncertainty around the history of varicella or shingles infection, that immunity should be confirmed by laboratory testing, at either booking or if exposure occurs. *Best practice*
4. We strongly recommend that women who are non-immune to varicella should be offered varicella vaccine in the postnatal period in line with NIAC guidance. *Grade 1B*
5. We strongly recommend that varicella vaccination should not be given during pregnancy in line with NIAC guidance. *Grade 1B*
6. We suggest that women with underlying medical conditions, or who are on immunosuppressive drug treatments which would put them at higher risk of severe varicella infection, should have this documented at the time of booking also. *Best practice*
7. We strongly recommend that pregnant women, who have no known immunity to varicella, should avoid children who are ill with varicella where possible. *Best practice*

Post-exposure prophylaxis for the non-immune pregnant woman exposed to varicella

8. If a pregnant woman contacts a healthcare provider following a potential varicella exposure, we strongly recommend that an assessment is done of her immunity and the nature of the exposure, in line with NIAC guidance. *Best practice*
9. We strongly recommend that if the history of immunity is uncertain, that a varicella IgG test is performed either after exposure or at the time of booking. *Grade 1C*
10. If non-immune, or if immunity tests are pending, we recommend that the woman should be isolated with contact and respiratory precautions, if attending a healthcare facility during her potentially infectious period. This is from day 8-21 post-exposure if they receive aciclovir or no prophylaxis and from day 8-28 post exposure if they receive Varicella-zoster immune globulin (VZIG). *Best practice*
11. If the varicella exposure is deemed significant, and the woman is non-immune, we strongly recommend that post exposure prophylaxis should be given in line with NIAC guidance. This should be oral aciclovir as first line option, with VZIG as an alternative. *Grade 1B*

12. We recommend that any pregnant woman exposed to varicella, should be encouraged to contact their healthcare provider if a rash or fever develops in the next 3-4 weeks. *Best practice*
13. We suggest that if a woman has additional medical conditions or is on immunosuppressive medications, then this should be taken into account when deciding on post exposure prophylaxis. A woman with prior history of varicella or shingles, may require post exposure prophylaxis if she is on significant immunosuppression. If unsure, consult NIAC guidance (Chapter 3) and liaise with the medical specialty team. *Best practice*

Management of a pregnant woman or recently post-partum (<6 weeks post-birth) woman with suspected or confirmed acute primary varicella infection

14. We strongly recommend that all suspected or confirmed cases of varicella are isolated in a single room with ensuite facilities under airborne precautions if they require admission to hospital. *Grade 1C*
15. We strongly recommend that staff caring for the woman should be immune to varicella (natural immunity or vaccination or confirmed by laboratory testing as part of an occupational health assessment) to prevent hospital outbreaks, in line with NIAC guidance. *Grade 1C*
16. We strongly recommend that women with disseminated varicella should avoid contact with other vulnerable people (i.e. immunocompromised due to biologics, chemotherapy or other varicella non-immune pregnant women) until all the lesions are completely crusted. In case of shingles outbreak the lesions should be kept covered where possible. *Grade 1C*
17. We recommend that if a pregnant woman presents with acute varicella, aciclovir should be given as soon as possible, and ideally within the first 24 hours of the rash appearing. The benefit of aciclovir after 24 hours of the rash should be judged on a case-by-case basis. *Grade 1B*
18. We strongly recommend that IV aciclovir (10mg/kg every 8 hours) is given to pregnant women at all gestations if they have severe varicella with organ dysfunction (i.e. hepatitis, pneumonitis, encephalitis). Renal function should be monitored carefully, especially if receiving other nephrotoxic drugs, as aciclovir dosage adjustment may be required. *Grade 1C*
19. We strongly recommend that there is no role for VZIG once the rash has started to develop. *Best practice*
20. We suggest that, in addition to the management of acute varicella, pregnant women should be managed in line with the national sepsis guidelines, and be monitored for possible secondary bacterial infection especially with Group A Streptococcus. *Best practice*
21. Women with sepsis (i.e. organ dysfunction and suspected infection) should have their care escalated through established pathways to HDU or ICU level, and be managed in line with national sepsis pathways. *Best practice*
22. We suggest that any pregnant woman with symptoms or signs of meningoencephalitis be discussed with the local adult general medical service. *Best practice*
23. We recommend that women are advised to monitor for rash or symptoms for 8-21 days post exposure if given aciclovir or no prophylaxis, and 8-28 days if given VZIG. *Best practice*
24. The care and follow up of women with acute primary varicella should be individualised, with senior Obstetricians involved in the care. *Best practice*
25. We suggest that routine referral to a Fetal Medicine Specialist is not required for women without symptoms of varicella post exposure, unless there are particular concerns about fetal growth or anomalies. *Best practice*

Management of the pregnant woman whose fetus is exposed to varicella in utero

26. We recommend that women who develop primary varicella infection in pregnancy should be referred to a Fetal Medicine Specialist from 16-20 weeks gestation, and at least 5 weeks after the infection. Consultation with a Neonatologist is recommended if fetal anomalies are diagnosed on antenatal ultrasound. *Best practice*

27. We suggest that women who develop primary varicella infection during pregnancy should be counselled about the risks versus benefits of amniocentesis to detect varicella DNA by polymerase chain reaction (PCR). Amniocentesis should not be performed before the skin lesions have completely healed, and at least five weeks after infection to minimise risk of a false negative result. *Best practice*

28. If the mother develops primary varicella infection in the last four weeks before giving birth, she should be counselled that there is an increased risk of the baby developing severe disseminated varicella which would warrant antiviral treatment as soon as possible. *Best practice*

29. We suggest that clinicians should consider avoiding elective birth as clinically appropriate, until the infectious period has passed. *Best practice*

30. We recommend that care is taken around placement of epidural/spinal anaesthesia in line to avoid vesicles, and this should be done in consultation with senior anaesthetists. The suitability for epidural or spinal anaesthesia will depend on the presence or absence of skin lesions at the site of insertion, suspicion of viraemia and when treatment was commenced. *Best practice*

31. Mode of delivery should be considered on an individualised basis. Where there is evidence of fetal compromise or maternal respiratory failure delivery by emergency caesarean section is recommended. *Best practice*

32. We strongly recommend that all babies born to mothers with acute primary varicella infection during pregnancy or birth, should be referred to the neonatology team at the time of birth. *Best practice*

Management of the neonate exposed to varicella in utero, at time of birth or within first week of life

33. Babies whose mothers develop varicella in pregnancy at any gestation up to 7 days before birth:

    a. We suggest that all babies with in utero exposure to maternal varicella more than 7 days before birth, should have a neonatal assessment at birth and pre-discharge, and their mother be encouraged to attend the routine developmental checks to ensure that they achieve their developmental milestones. *Best practice*

    b. The risk of severe varicella infection following exposure of preterm infants, i.e. <28 weeks or <1kg birth weight, to varicella should be discussed with senior Neonatologists (Consultant or Specialist Registrar), and Infection Specialists (Microbiology and/or Infectious Diseases) *Best practice*

34. Babies whose mothers develop varicella either within 7 days before birth or 7 days after birth:

    a. We strongly recommend the use of post-exposure VZIG prophylaxis in line with NIAC guidance *Grade 1B*

35. When the index case is not the mother, then NIAC guidelines should be followed when considering prophylaxis for the neonate. *Best practice*

36. If a varicella exposed baby develops any rash or febrile illness in the neonatal period, we suggest that caregivers should contact the local GP or return to the local paediatric unit rather than the local maternity unit. They should be isolated in a single room to minimise risk of spread pending further investigation. *Best practice*

Management of the neonate with suspected or confirmed varicella in the first month of life

37. We recommend that the neonate should, at a minimum, be referred to the local secondary level paediatric centre for assessment and treatment, if they believe that the neonate has acute varicella infection. *Best practice*

38. We strongly recommend that empirical IV aciclovir should be started in an unwell neonate with a disseminated vesicular rash, pending confirmation of the aetiology (i.e. HSV, VZV or enterovirus). *Grade 1C*

39. We strongly recommend that babies with disseminated vesicular rash should be isolated in single rooms with airborne and contact precautions, and their placement discussed with local infection control teams to prevent secondary cases in neonatal and paediatric units. *Grade 1C*

40. If varicella is confirmed, we strongly recommend that IV aciclovir should be continued in preterm infants (<28 weeks gestation or 1kg birthweight) irrespective of maternal immunity, those with respiratory compromise or those with severe end organ damage (encephalitis, hepatitis). These cases should be discussed with local Infection Specialists. *Best practice*

Varicella and breastfeeding

41. We recommend that women with varicella should be supported and encouraged to breastfeed if they wish. *Best practice*

42. Vesicles on the breast should be covered to minimise risk of transmission. If vesicles are present close to the nipple, we suggest that women are advised to express from that side until the vesicles have crusted over. In this instance, the expressed breast milk may be fed to the baby who is receiving treatment with VZIG and/or aciclovir. If the baby is not on VZIG or anti-viral therapy, this expressed milk should be discarded. *Best practice*

43. We recommend that clinicians advise mothers that aciclovir is not contra-indicated in breastfeeding. Aciclovir is present in breast milk after systemic administration but is not expected to cause any adverse effects in breastfed infants. *Best practice*

Reactivation of varicella zoster in pregnancy (i.e. localised shingles)

44. We suggest that Fetal Medicine assessment is not required, in the case of secondary infection/ herpes zoster infection, as shingles is not associated with fetal varicella syndrome. *Best practice*

45. We suggest that the placement of women with shingles, if admitted to hospital, is discussed with local infection control teams. In the cases of disseminated shingles, vesicles in an exposed site (e.g. ophthalmic shingles) or infection in an immunocompromised woman, infection control precautions are the same as acute primary varicella infection – isolation in a single room with ensuite facilities, under airborne precautions. *Best practice*

46. We suggest that oral aciclovir can be considered in certain women with shingles, but this should be done on a case-by-case basis. Aciclovir may be warranted particularly if the rash has spread to multiple dermatomes, involves non-truncal areas (i.e. near the eye) or the woman is immunocompromised. *Grade 2B*

Chapter 1: **Initiation**

The National Clinical Effectiveness Committee (NCEC) and Health Information and Quality Authority (HIQA) define clinical guidelines as systematically developed statements, based on a thorough evaluation of the evidence, to assist practitioner and patient decisions about appropriate healthcare for specific clinical circumstances, across the entire clinical spectrum.[3]

1.1 Purpose

The purpose of this Guideline is to provide a comprehensive evidence-based guidance for the management of varicella in pregnancy, and the management of the exposed or symptomatic neonate in the first week of life.

1.2 Scope

Target Users

The Guideline is a resource or all clinicians working in primary, secondary and tertiary care who clinically work with pregnant women, post-partum women up to 6 weeks after birth or their babies in the first week of life.

Target Population

The target population is pregnant women who are either exposed to or develop varicella, as well as their babies in the first week of life who are exposed to or develop varicella. This document is not for management of the infant beyond the first week of life.

1.3 Objective

To provide evidence based recommendations for the care of women with varicella as well as promoting a standardised approach nationally across all maternity units.

1.4 Guideline development process

The Guideline Developers agreed to undertake this work under the direction of the Guideline Programme Team (GPT). An Expert Advisory Group (EAG) was commissioned by the GPT. Their role was to critically review the Guideline prior to submission to the National Women and Infants Health Programme (NWIHP) for final approval.

In this document we have harmonised advice in line with guidance from the National Immunisation Advisory Committee (NIAC), who are the group charged with preparing the national guidance on vaccination. This alignment of guidance is important to ensure consistent approach to management and prevention of varicella.

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3 National Clinical Effectiveness Committee (NCEC) and Health Information and Quality Authority (HIQA) (2015) National quality assurance criteria for clinical guidelines. Version 2. Dublin: NCEC and HIQA. https://www.hiqa.ie/sites/default/files/2017-01/National-Quality-Assurance-Criteria.pdf

See Appendix 1 for EAG membership and Appendix 2 for Guideline Programme Process. The Guideline Developer Group consisted of:

- Prof Richard Drew, Consultant Microbiologist
- Dr Rachel Barry, Microbiology Specialist Registrar
- Dr Elaine Houlihan, Microbiology Specialist Registrar
- Ms Úna Cahill, Assistant Director of Midwifery
- Dr Mahmoud Farhan, Consultant Neonatologist
- Prof Patrick Gavin, Consultant in Paediatric Infectious Diseases
- Dr Minna Geisler, Consultant Obstetrician and Gynaecologist
- Dr Susan Knowles, Consultant Microbiologist
- Dr Judi Lynch, Consultant Microbiologist
- M. Mary Lynch, Clinical Midwifery Manager 3
- Dr Gillian Ryan, Consultant Obstetrician and Gynaecologist.

1.5 Stakeholder involvement

The Guideline Development Group was made up of representatives from obstetrics, midwifery, neonatology, paediatric infectious diseases, and clinical microbiology, each of whom have experience of managing varicella in pregnancy and/or the newborn period.

The Expert Advisory Group has representatives from Patient Advocacy Ireland and the Irish Neonatal Health Alliance. Also included in the membership are professionals from the areas of neonatology, obstetrics and midwifery.

1.6 Disclosure of interests

Guideline developers and reviewers bring a range of experiences and perspectives to the work of the national Guideline Programme. It is likely that both Guideline developers and stakeholders/reviewers will have a variety of interests, arising from different contexts and activities done in a professional or personal capacity. These can include employment and other sources of income, speaking engagements, publications and research, and membership of professional or voluntary organisations. The involvement of individuals with relevant content expertise is essential for enhancing the value of Guideline recommendations, but these individuals may also have interests that can lead to conflicts of interest, as may peer reviewers, patient representatives and researchers.

All interests should be declared if, in the view of a reasonable person, they are relevant, or could be perceived to be relevant, to the work of the clinical practice Guideline in question.[4] Declaring an interest does not mean there is a conflict of interest.

4 NICE (2019) Policy on declaring and managing interests for NICE advisory committees https://www.nice.org.uk/Media/Default/About/Who-we-are/Policies-and-procedures/declaration-of-interests-policy.pdf

It is important that interests are openly declared so they can be appropriately managed. Conflicts of interest can bias recommendations and ultimately be harmful to women and the health system. Disclosures of interests and appropriate management of conflicts of interest, when identified, are therefore essential to producing high-quality, credible health guidelines.[5]

The Guidelines International Network (GIN), a global network of Guideline developers that aims to promote best practices in the development of high-quality guidelines, developed a set of 9 principles to provide guidance on how financial and non-financial conflicts of interest should be both disclosed and managed. It is recommended that Guideline developers follow the GIN principles.[6]

For this National Clinical Practice Guideline, all Guideline developers are asked to complete a conflict of interest declaration form. The response to declared interests will be managed by the Guideline programme team, in accordance with GIN principles. Conflicts of interest may be reported in the published Guideline and declarations of interest can be made available.

1.7 Disclaimer

These guidelines have been prepared to promote and facilitate standardisation and consistency of good clinical practice, using a multidisciplinary approach. Information in this Guideline is current at the time of publication.

The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the Clinician in light of clinical data presented by the woman and the diagnostic and treatment options available.

Clinical material offered in this Guideline does not replace or remove clinical judgment or the professional care and duty necessary for each specific woman.

Clinical care carried out in accordance with this Guideline should be provided within the context of locally available resources and expertise.

This Guideline does not address all elements of standard practice and assumes that individual clinicians are responsible for:

- Discussing care with women in an environment that is appropriate and which enables respectful confidential discussion. This includes the use of interpreter services where necessary
- Advising women of their choices and ensure informed consent is obtained
- Provide care with professional scope of practice, meeting all legislative requirements and maintaining standards of professional conduct
- Applying standard precautions and additional precautions, as necessary, when delivering care
- Documenting all care in accordance with local and mandatory requirements.

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5 Traversy G, Barnieh L, Akl EA, Allan GM, Brouwers M, Ganache I, Grundy Q, Guyatt GH, Kelsall D, Leng G, Moore A, Persaud N, Schünemann HJ, Straus S, Thombs BD, Rodin R, Tonelli M. CMAJ. 2021, 193(2):E49-E54. DOI: 10.1503/cmaj.200651 https://www.cmaj.ca/content/193/2/E49

6 Annals of Internal Medicine, Schünemann HJ, Al-Ansary, LA, Forland F, et al. Guidelines International Network: Principles for disclosure of interests and management of conflicts in guidelines, 163(7), 548-53. Copyright © 2015 American College of Physicians. https://www.acpjournals.org/doi/10.7326/m14-1885

1.8 Use of language

Within this guidance we use the terms 'woman' and 'women's health'. However, it is important to acknowledge that people who do not identify as cis-gender women are excluded from this descriptor, including people who identify as transgender, gender diverse and gender non-binary[7]. We also appreciate that there are risks to desexing language when describing female reproduction[8 9]. Services and delivery of care must be appropriate, inclusive and sensitive to the needs of people whose gender identity does not align with the sex they were assigned at birth. This includes training and education regarding diverse pathways to pregnancy and the use of practices which affirm the sexual and gender identities of all people using Obstetrics and Gynaecology services.

Language use is key to effectively communicate options, recommendations, and respectfully accept a woman's fully informed decision[10]. With this in mind, the use of birth is preferable to the term delivery in all circumstances and is used consistently where possible throughout the guidelines. It is acknowledged that in some circumstances (e.g., in the case of a medically indicated intervention or surgery) and in some contexts, substituting with the term delivery is considered appropriate and this term may be used instead.

7 Moseson H, Zazanis N, Goldberg E, et al. The Imperative for Transgender and Gender Nonbinary Inclusion. Obstet Gynecol. 2020;135(5):1059-1068. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7170432/

8 Brotto LA, Galea LAM. Gender inclusivity in women's health research. BJOG: An International Journal of Obstetrics & Gynaecology. https://obgyn.onlinelibrary.wiley.com/doi/full/10.1111/1471-0528.17231

9 Gribble KD, Bewley S, Bartick MC, et al. Effective Communication About Pregnancy, Birth, Lactation, Breastfeeding and Newborn Care: The Importance of Sexed Language. *Frontiers in Global Women's Health*. 2022;3. Accessed June 9, 2022. https://www.frontiersin.org/article/10.3389/fgwh.2022.818856

10 https://blogs.bmj.com/bmj/2018/02/08/humanising-birth-does-the-language-we-use-matter/

Chapter 2: **Clinical Practice Guideline**

Background

Varicella-zoster virus (VZV) is a DNA virus of the herpes family that is highly contagious and transmitted by respiratory droplets and by direct personal contact with vesicle fluid or indirectly via fomites (e.g. skin cells, hair, clothing and bedding).[1] Primary VZV infection (chickenpox) is characterised by low-grade fever, malaise and a pruritic rash that develops into crops of maculopapules, which become vesicular and crust over before healing.[2] The incubation period is between one to three weeks and the disease is infectious 48 hours before the rash appears and continues to be infectious until the vesicles crust over. The vesicles will usually have crusted over within five days.

Chickenpox is a common childhood disease that usually causes a mild infection. Over 90% of the antenatal population in the UK and Ireland are seropositive for VZV IgG antibody.[3, 4] For this reason, although contact with chickenpox is common in pregnancy, especially in women with young children, primary VZV infection in pregnancy is uncommon; it is estimated to complicate three in every 1000 pregnancies.[5]

Following primary infection, VZV remains dormant in sensory nerve root ganglia but can reactivate to cause herpes zoster (HZ) (shingles) a vesicular erythematous rash in a dermatomal distribution.[6] The risk of acquiring infection from an immunocompetent individual with herpes zoster in non-exposed sites (e.g. thoracolumbar) is remote. However, disseminated zoster or exposed zoster (e.g. ophthalmic) in any individual or localised zoster in an immunosuppressed patient should be considered to be infectious. Immunocompromised patients can develop disseminated zoster, with associated complications of encephalitis or pneumonia. [7-10]

Recommendations relevant to this Guideline can also be found in:

- Department of Health 2021: Sepsis Management for adults (including maternity)[11]
- HSE Clinical Programme in Obstetrics and Gynaecology. Medication Guidelines for Obstetrics and Gynaecology volume 1[12] and 2.[13]
- National Immunisation Advisory Committee guidelines, Chapter 23 Varicella.[14]

11 Department of Health (2021). Title (NCEC National Clinical Guideline No. 26 2021). Available at: http://health.gov.ie/national-patient-safety-office/ncec/

12 https://www.hse.ie/eng/services/publications/clinical-strategy-and-programmes/antimicrobial-prescribing-guidelines.pdf

13 https://www.hse.ie/eng/services/publications/clinical-strategy-and-programmes/antimicrobial-safety-in-pregnancy-and-lactation.pdf

14 https://www.rcpi.ie/Healthcare-Leadership/NIAC/Immunisation-Guidelines-for-Ireland

The evidence to support the recommendations in this Guideline is largely derived from journals and textbooks, as well as from research exploring clinicians' knowledge and decision-making in the area of varicella in pregnancy and the postnatal period.

To inform the development of this Guideline, existing policies and recently published international documents on varicella were also reviewed. The international varicella guidelines reviewed were from UK, Switzerland, South Australia, USA, Australia, Canada as well as guidelines in the Irish health service from the NIAC.

Section 1: Antenatal Care and varicella prevention

Introduction

It is important to try and reduce the risk of varicella infection for all pregnant women, given the risk of severe infection to themselves, the fetus and to the newborn baby. Pre-conception counselling for women trying to conceive and/or attending fertility services should include testing for varicella immunity and if required offering the varicella vaccine.

Clinical Question 2.1: **How can the risk of a woman developing acute varicella infection during pregnancy be minimised?**

Evidence Statement

Varicella may cause severe disease in susceptible pregnant women, fetal death or congenital varicella syndrome, characterised by limb hypoplasia, cutaneous scarring, ocular and CNS anomalies. In a cohort study of 1373 women with varicella during the first 36 weeks of pregnancy, nine cases developed congenital varicella syndrome and all had the infection in the first 20 weeks of pregnancy.[11] Increased morbidity and mortality has been reported in pregnant women who develop varicella, with pneumonia occurring in approximately 10-20% of cases.[12-15] Varicella vaccine is 92% (95% CI 88-95%) effective in preventing severe disease after two doses.[16]

Clinical Practice

- Women who are considering trying to conceive, or engaging with fertility services, should have their varicella immune status assessed, and if necessary be offered the varicella vaccine.
- Varicella vaccine is a live vaccine and should not be given knowingly to pregnant women.
- Women attending for their antenatal booking visit, should be asked about their history of varicella infection or vaccination. Routine serological testing is not recommended as it uses laboratory resources to do testing, which may not be required.
- Individual hospitals may recommend VZV IgG testing for women who are unsure of their history of varicella infection or only do so following reported exposure. The decision should be made at a local level after discussion between the obstetric team and the Laboratory Director.
- Women susceptible to varicella, should be advised to take precautions during pregnancy and where possible avoid contact with people infected with varicella. If they are exposed, they should be advised to contact their healthcare provider for review.

- Women who are non-immune to varicella should be offered varicella vaccination in the postnatal period as part of routine postnatal care. If not given at the same time as the MMR vaccine, the MMR and varicella vaccines should be separated by at least four weeks. The risk of breakthrough varicella is increased if the varicella vaccine is given less than four weeks following MMR vaccine (NIAC guidance).

Recommendations

1. **We suggest that women planning to conceive and/or engaging with fertility services, should have their varicella status assessed as part of pre-conception counselling either by history or laboratory testing.**
2. **We strongly recommend that women should have their immunity to varicella discussed and documented at the booking visit. Their immunity can be confirmed by either reliable history of varicella, two varicella vaccines or by a laboratory test (varicella IgG) following exposure in line with National Immunisation Advisory Committee (NIAC) guidance. Laboratories may choose to only send varicella IgG if a woman is exposed, rather than on all women with an uncertain varicella history.**
3. **We recommend that if there is any uncertainty around the history of varicella or shingles infection, that immunity should be confirmed by laboratory testing at either booking or if exposure occurs.**
4. **We strongly recommend that women who are non-immune to varicella should be offered varicella vaccine in the postnatal period in line with NIAC guidance.**
5. **We strongly recommend that varicella vaccination should not be given during pregnancy in line with NIAC guidance.**
6. **We suggest that women with underlying medical conditions or who are on immunosuppressive drug treatments which would put them at higher risk of severe varicella infection, should have this documented at the time of booking also.**
7. **We strongly recommend that pregnant women, who have no known immunity to varicella, should avoid children who are ill with varicella where possible.**

Section 2: Post-exposure prophylaxis for the non-immune pregnant woman exposed to varicella

Introduction

Pregnant women who are non-immune to varicella should be advised to avoid contact with people with varicella. This may not always be possible and inadvertent exposures may occur. Chickenpox is infectious 48-hours before the rash appears. During antenatal care, non-immune women should be advised to contact their healthcare provider if they have a significant exposure to varicella (General Practitioner, Midwife or Obstetrician). Significant contact with a varicella or disseminated zoster case would be contact in the same room for an hour or more, face to face contact within 1m (i.e. conversation) for usually less than five minutes while the index person is infectious (from 48 hours before rash onset until all lesions have crusted over). For full definitions see the varicella chapter in the NIAC guidelines.

Clinical Question 2.2: **How should a pregnant woman be managed, if she reports an exposure to varicella?**

Evidence Statement

An Italian cohort study was performed over 20 years, and reported on 215 pregnant women exposed to varicella.[17] The risk of maternal varicella was statistically significantly lower in women who received VZIG (42%, n=21 of 50), than in those that did not receive the VZIG prophylaxis (72%, n=13 of 18). There is sufficient evidence that immunoprophylaxis with oral aciclovir is as effective as VZIG. A recent study from the UK found no statistically significant difference in the incidence of maternal varicella in exposed women who received aciclovir (30%, 8/26) and women who received VZIG (36%, 53/145) post-exposure prophylaxis[18]. In this cohort of 186 women, 145 (78%) received VZIG, 26/186 (14%) received oral aciclovir and 15/186 (8%) received no prophylaxis. The incidence of varicella was 36% (n=53/145) in the VZIG group, while it was 30% (n=8/26) in the aciclovir group, and this was found not to be a statistically significant difference. Consequently, it is important to discuss with the exposed pregnant woman that VZIG cannot completely prevent congenital varicella but it is a risk reduction strategy. VZIG should be given as soon after exposure as possible and preferably < 96 hours, but can be given up to 10-days after exposure.

South Australian and Australasian Society for Infectious Diseases guidelines, recommend oral aciclovir or valaciclovir post-exposure prophylaxis be considered if varicella exposure occurs >96 hours previously in women in the second half of pregnancy, or if the woman has an underlying lung disorder, is immunocompromised or is a smoker. Reassuring data around aciclovir use in pregnancy comes from a Danish registry that has shown no statistical difference in the incidence of major birth defects between aciclovir exposed and non-exposed babies.[19]

Clinical Practice

- If a woman is exposed to varicella in pregnancy an assessment of her immunity should be performed along with a detailed history on the nature of the exposure, in line with NIAC guidance.
- If the history of immunity is uncertain, laboratory confirmation of immunity should be done if an exposure occurs. Some centres may choose to test all women without a definite history at the time of booking.
- If non-immune or if result of immunity testing is pending, the woman should isolate from day 8-21 post-exposure if they do not receive VZIG and from day 8-28 post exposure if they receive VZIG.
- If the contact is deemed significant, and the woman is non-immune, post exposure prophylaxis should be given in line with NIAC guidance. Significant contact with a varicella or disseminated zoster case would be contact in the same room for an hour or more, face to face contact within 1m (i.e. conversation) for usually less than five minutes while the index person is infectious (from 48 hours before rash onset until all lesions have crusted over). For full definitions see the varicella chapter in the NIAC guidelines. Oral aciclovir should be considered as the first-line option, with VZIG available if aciclovir use is not possible (i.e. renal impairment, allergy). This advice to use aciclovir should apply at all gestations (see NIAC guidance for full details). The use of aciclovir is cheaper than VZIG, and also is easier to administer without requiring hospital attendance.
- Any woman exposed to varicella, should be encouraged to contact their healthcare provider if a rash or fever develops within 4 weeks post exposure.

- A woman with prior history of varicella or shingles, may require post exposure prophylaxis if she is on significant immunosuppression. This group would include adults and children with no history of varicella and/or a negative immune status, receiving immunosuppressive therapy including steroids, cytostatic agents, radiotherapy, recent stem cell transplantation or who have congenital or acquired immunodeficiency disorders and are not receiving replacement therapy with immunoglobulin. If unsure, consult NIAC guidance (Chapter 3) and liaise with the medical specialty team.

Recommendations

8. **If a pregnant woman contacts a healthcare provider following a potential varicella exposure, we strongly recommend that an assessment is done of her immunity and the nature of the exposure, in line with NIAC guidance.**
9. **We strongly recommend that if the history of immunity is uncertain, that a varicella IgG test is performed either after exposure or at the time of booking.**
10. **If non-immune, or if immunity tests are pending we recommend that the woman should be isolated with contact and respiratory precautions, if attending a healthcare facility, during her potentially infectious period. This is from day 8-21 post-exposure if they receive aciclovir or no prophylaxis and from day 8-28 post exposure if they receive Varicella-zoster immune globulin (VZIG).**
11. **If the varicella exposure is deemed significant, and the woman is non-immune, we strongly recommend that post exposure prophylaxis should be given in line with NIAC guidance. This should be oral aciclovir as first line option, with VZIG as an alternative.**
12. **We recommend that any pregnant woman exposed to varicella, should be encouraged to contact their healthcare provider if a rash or fever develops in the next 3-4 weeks.**
13. **We suggest that if a woman has additional medical conditions or is on immuno-suppressive medications, then this should be taken in to account when deciding on post exposure prophylaxis. A woman with prior history of varicella or shingles, may require post exposure prophylaxis if she is on significant immunosuppression. If unsure, consult NIAC guidance (Chapter 3) and liaise with the medical specialty team.**

Section 3: Management of a pregnant woman or recently post-partum (<6 weeks post-birth) woman with suspected or confirmed acute primary varicella infection

Introduction

Pregnant women are at a higher risk of associated morbidity from acute disseminated varicella, as it can lead to hepatotoxicity and respiratory failure. It is important that women with severe varicella are identified early, and their care escalated in line with national sepsis guidelines.

Clinical Question 2.3: **How should a pregnant woman or recently postpartum woman (<6 weeks post-birth) be managed at time of initial presentation with suspected or confirmed acute varicella infection?**

Evidence Statement

Oral aciclovir has been shown to be effective in reducing severe disease if given with the first 24 hours of the rash developing in adults and children[20-22]. The safety of aciclovir in lactation and pregnancy is discussed in the HSE medications in Obstetrics and Gynaecology document[15] which was produced by the HSE clinical programme in Obstetrics and Gynaecology. Based on a review of the evidence presented in the HSE document, therapeutic doses of aciclovir are unlikely to pose a substantial teratogenic risk. A large Danish nationwide cohort study of 1804 pregnancies exposed to aciclovir, valaciclovir or famciclovir in the first trimester, showed that the major defect birth rate was equivalent between the exposed and non-exposed groups (2.2% Vs 2.4%, 95% CI 0.65-1.22).[19] This was a large population based historical cohort study of live infants in Denmark, where the authors were able to match maternal antiviral use and birth defect diagnoses to determine teratogenic risk of the three antivirals (aciclovir, famciclovir and valaciclovir). Intravenous aciclovir has been shown to reduce the morbidity from varicella pneumonia, however the intravenous use of aciclovir has been associated with nephrotoxicity in pregnant women[23-26].

Clinical Practice

- Women who are suspected or confirmed to have varicella should be isolated in a single room with ensuite facilities under airborne precautions.
- Staff caring for the woman should be immune to varicella (natural immunity or vaccination or confirmed by laboratory testing) to prevent hospital outbreaks, in line with NIAC guidance.
- Women with disseminated varicella should avoid contact with other vulnerable people until all the lesions are completely crusted. In case of shingles outbreak the lesions should be kept covered where possible.
- If a pregnant woman presents with acute varicella, oral aciclovir should be given as soon as possible, and ideally within the first 24 hours of the rash appearing. The benefit of oral aciclovir after 24 hours of the rash should be judged on a case-by-case basis.
- IV aciclovir is given to pregnant women at all gestations if they have severe complications from varicella such as meningoencephalitis, pneumonitis or other end organ damage such as hepatitis. Renal function should be monitored carefully, especially if receiving other nephrotoxic drugs. The intravenous dose of aciclovir should be as for immunocompromised hosts when treating varicella in pregnancy (10mg/kg every 8 hours).
- Women with sepsis (i.e. organ dysfunction and suspected infection) should have their care escalated through established pathways to HDU or ICU level, and be managed in line with national sepsis pathways.

15 Medication Guidelines For Obstetrics and Gynaecology (First Edition). Volume 2. Antimicrobial safety In Pregnancy and Lactation. HSE Clinical Programme in Obstetrics and Gynaecology. November 2016.

- For aciclovir dosing use:
  - Oral: Herpes zoster or primary varicella if treatment required (800mg given 5 times a day for 7 days)
  - Intravenous infusion: 10mg/kg every 8 hours. Usually 5 days for cutaneous varicella, but given 10-14 days or possibly longer in encephalitis and end organ complicated cases (i.e. hepatitis, pneumonitis). Use with caution in renal impairment and seek specialist advice in complicated cases from local infection services (Microbiology/Infectious Diseases).

Recommendations

14. We strongly recommend that all suspected or confirmed cases of varicella are isolated in a single room with ensuite facilities under airborne precautions if they require admission to hospital.
15. We strongly recommend that Staff caring for the woman should be immune to varicella (natural immunity or vaccination or confirmed by laboratory testing as part of an occupational health assessment) to prevent hospital outbreaks, in line with NIAC guidance.
16. We strongly recommend that women with disseminated varicella should avoid contact with other vulnerable people (i.e. immunocompromised due to biologics, chemotherapy or other varicella non-immune pregnant women) until all the lesions are completely crusted. In case of shingles outbreak the lesions should be kept covered where possible.
17. We recommend that if a pregnant woman presents with acute varicella, aciclovir should be given as soon as possible, and ideally within the first 24 hours of the rash appearing. The benefit of aciclovir after 24 hours of the rash should be judged on a case-by-case basis.
18. We strongly recommend that IV aciclovir (10mg/kg every 8 hours) is given to pregnant women at all gestations if they have severe varicella with organ dysfunction (i.e. hepatitis, pneumonitis, encephalitis). Renal function should be monitored carefully, especially if receiving other nephrotoxic drugs, as aciclovir dosage adjustment may be required.
19. We strongly recommend that there is no role for VZIG once the rash has started to develop.
20. We suggest that, in addition to the management of acute varicella, pregnant women should be managed in line with the national sepsis guidelines, and be monitored for possible secondary bacterial infection especially with Group A Streptococcus.
21. Women with sepsis (i.e. organ dysfunction and suspected infection) should have their care escalated through established pathways to HDU or ICU level, and be managed in line with national sepsis pathways.
22. We suggest that any pregnant woman with symptoms or signs of meningoencephalitis be discussed with the local adult general medical service.

Section 4: Management of the pregnant woman whose fetus is exposed to varicella in utero

Introduction

The risk of congenital varicella syndrome is low, however women diagnosed with chickenpox in pregnancy, or with fetal growth anomalies after confirmed varicella exposure, should be referred to a Fetal Medicine Specialist.

Clinical Question 2.4: **How should an asymptomatic pregnant woman, with confirmed varicella exposure, be managed in terms of fetal assessment?**

Evidence Statement

There does not appear to be an increased risk of spontaneous miscarriage if varicella occurs in the first trimester, however the risk of fetal varicella syndrome increases if infection occurs later in pregnancy.[27] Incidence of congenital varicella syndrome is 0.5%-1% with maternal varicella in the first trimester, and up to 2% between 13-20 weeks, and is very rare thereafter.[28]

Clinical Practice

- Asymptomatic pregnant women should be advised to monitor for a rash or other symptoms post exposure, for a period of 8-21 days post exposure if given acyclovir or no prophylaxis and 8-28 days post exposure if given VZIG.
- Referral for routine Fetal Medicine Specialist review is not required for women without symptoms of varicella post exposure.

Recommendations

23. **We recommend that women are advised to monitor for rash or symptoms for 8-21 days post exposure if given aciclovir or no prophylaxis and 8-28 days if given VZIG.**
24. **The care and follow up of women with acute primary varicella should be individualised, with senior Obstetricians involved in the care.**
25. **We suggest that routine referral to a Fetal Medicine Specialist is not required for women without symptoms of varicella post exposure, unless there are particular concerns about fetal growth or anomalies.**

Clinical Question 2.5: **How should a pregnant woman, with confirmed varicella infection be managed in terms of fetal assessment and subsequent birth?**

Evidence Statement

Women who develop varicella in pregnancy should be referred to a Fetal Medicine Specialist for a detailed anatomical ultrasound assessment. The RCOG, South Australia and Australasian Society for Infectious Diseases recommend that the referral should be after 16-20 weeks, and at least five weeks after the infection.[29-31]

Congenital varicella syndrome secondary to maternal chickenpox infection in pregnancy is associated with neonatal cutaneous scarring, limb hypoplasia, ocular and CNS abnormalities. Incidence of congenital varicella syndrome is 0.5%-1% with maternal varicella in the first trimester, and up to 2% between 13-20 weeks, and is very rare thereafter.[28]

A more recent study describes a risk of up to 2% in the first 20 weeks.[32] Amniocentesis shouldn't be performed while there are active lesions, in case of the risk of introducing infection. The role of amniocentesis and VZV PCR on amniotic fluid is of limited use due to poor sensitivity, and also given the low risk of congenital varicella syndrome[33]. Fetal MRI may be of benefit in certain cases, as an adjunct to ultrasonography, if available.[34, 35]

The mode and timing of delivery will need to be individualised, taking in to account the risk for the mother and the baby. Delivery may need to be expedited for non-varicella reasons such as chorioamnionitis or fetal growth restriction. The decision to perform an emergency C-section in a woman with acute varicella should be discussed with senior obstetricians (i.e. Consultant or Specialist Registrar), and anaesthetics should be contacted early to consider mode of anaesthesia.

Clinical Practice

- Women who develop primary varicella infection in pregnancy should be referred to a fetal medicine specialist from 16-20 weeks gestation, and at least 5 weeks after the infection. Consultation with neonatologist is advised if fetal anomalies are diagnosed on antenatal ultrasound or MRI.
- Women who develop varicella during pregnancy should be counselled about the risks versus benefits of amniocentesis to detect varicella DNA by polymerase chain reaction (PCR). Amniocentesis should not be performed before the skin lesions have completely healed, and at least five weeks after infection to minimise risk of false negative.
- Care should be taken around placement of epidural/spinal lines to avoid vesicles, and this should be done in consultation with senior anaesthetists.
- Mode of delivery should be considered on an individualised basis. Where there is evidence of fetal compromise or maternal respiratory failure expedited delivery is recommended.
- All babies born to mothers with chickenpox infection during pregnancy or birth, should be referred to neonatology at the time of birth.
- Clinicians should consider to avoid elective delivery, as clinically appropriate, until infectious period has passed. As alluded to above the disease is infectious 48 hours before the rash appears and continues to be infectious until the vesicles crust over. The vesicles will usually have crusted over within 5 days.

Recommendations

26. We recommend that women who develop primary varicella infection in pregnancy should be referred to a Fetal Medicine Specialist from 16-20 weeks gestation, and at least 5 weeks after the infection. Consultation with a Neonatologist is recommended if fetal anomalies are diagnosed on antenatal ultrasound.
27. We suggest that women who develop primary varicella infection during pregnancy should be counselled about the risks versus benefits of amniocentesis to detect varicella DNA by polymerase chain reaction (PCR). Amniocentesis should not be performed before the skin lesions have completely healed, and at least five weeks after infection to minimise risk of a false negative result.
28. If the woman develops primary varicella infection in the last four weeks before giving birth, she should be counselled that there is an increased risk of the baby developing severe disseminated varicella which would warrant antiviral treatment as soon as possible.
29. We suggest that the clinicians should consider avoiding elective birth as clinically appropriate, until infectious period has passed.
30. We recommend that care is taken around placement of epidural/spinal anaesthesia in line to avoid vesicles, and this should be done in consultation with senior anaesthetists. The suitability for epidural or spinal anaesthesia will depend on the presence or absence of skin lesions at the site of insertion, suspicion of viraemia and when treatment was commenced.
31. Mode of delivery should be considered on an individualised basis. Where there is evidence of fetal compromise or maternal respiratory failure delivery by emergency caesarean section is recommended.
32. We strongly recommend that all babies born to mothers with acute primary varicella infection during pregnancy or birth, should be referred to neonatology at the time of birth.

Section 5: Management of the neonate exposed to varicella in utero, at time of birth or within first week of life

Introduction

Neonates born to varicella susceptible mothers with chickenpox within one week before and one week after birth, are at an increased risk of neonatal infection. Risk is highest with maternal infection from five days before to two days after birth, with a mortality rate of 30%. Post exposure prophylaxis should be administered in line with NIAC guidance.

Clinical Question 2.6: **How should the asymptomatic neonate be managed if they are exposed to varicella in utero, around the time of the birth or within the first seven days after the birth?**

Evidence Statement

Management of neonatal varicella exposure depends on the presence of maternal VZV antibodies and the timing of exposure, as well as host factors such as prematurity and requirement for specialist/ICU level care. Risk stratification and requirement for post exposure prophylaxis should be done in line with NIAC guidelines. Post exposure prophylaxis is generally not indicated for full-term infants exposed more than seven days after birth or for those whose mother develops shingles before or after birth, as these infants will have protective antibodies which wane over the first few months of life.[36]

Congenital varicella syndrome as a result of maternal primary chickenpox infection is associated with neonatal complications such as skeletal, ophthalmic and cardiovascular abnormalities and limb hypoplasia. The incidence of fetal varicella syndrome amongst pooled data from nine cohort studies was 0.91% in the first 20 weeks (n=1423). The risk appeared to be lower in the first trimester (0.55%).[28] More recent studies describe a risk of up to 2% in the first 20 weeks.[32] If a baby is exposed to varicella around the time of the birth, the neonatal infection will usually occur between the 5th and 10th day of life, and these neonates should be administered immediate post exposure prophylaxis as per NIAC and referred to specialist healthcare facilities. However, neonatal infections presenting after the first 10-12 days of life are usually postnatally acquired and typically milder.

The greatest risk of VZV to the neonate is five days before to two days after the birth, which on rare occasions can manifest in severe disseminated neonatal varicella (purpura fulminans) and death, with mortality rates reported around 30%.[37] Infants exposed during this timeframe should be administered immediate post exposure prophylaxis as per NIAC and referred to specialist neonatal healthcare units.

Clinical Practice

- All infants with confirmed in utero exposure to primary varicella infection in the antenatal period more than 7 days before birth, should have a neonatal assessment at birth and again prior to discharge. Their mother should also be advised of the importance of attending routine developmental checks.
- VZIG should be given to varicella exposed neonates at increased risk of severe infection: neonates whose mothers develop chickenpox within 5 days before or 2 days after birth; neonates <7days old born to non-immune mothers; and preterm infants in neonatal units. The use of post-exposure prophylaxis should be offered in line with NIAC guidance for exposed neonates.
- If the varicella exposed baby develops any rash or febrile illness in the neonatal period, caregivers should be aware to contact their GP or return to their local paediatric unit, rather than the local maternity hospital/unit. They should be isolated in a single room to minimise risk of spread.

Recommendations

33. Babies whose mothers develop varicella in pregnancy at any gestation up to 7 days before birth:
    a. We suggest that all babies with in utero exposure to maternal varicella more than 7 days before birth, should have a neonatal assessment at birth and pre-discharge, and their mother be encouraged to attend the routine developmental checks to ensure that they achieve their developmental milestones.
    b. The risk of severe varicella infection following exposure of preterm infants, <28 weeks or <1kg birth weight, to maternal varicella should be discussed with senior Neonatologists (Consultant or Specialist Registrar), and Infection Specialists (Microbiology and/or Infectious Diseases)
34. Babies whose mothers develop varicella either within 7 days before birth or 7 days after birth:
    a. We strongly recommend the use of post-exposure VZIG prophylaxis in line with NIAC guidance
35. When the index case is not the mother, then NIAC guidelines should be followed when considering prophylaxis for the neonate.
36. If a varicella exposed baby develops any rash or febrile illness in the neonatal period, we suggest that caregivers should contact the local GP or return to the local paediatric unit rather than the local maternity unit. They should be isolated in a single room to minimise risk of spread pending further investigation.

Section 6: Management of the neonate with suspected or confirmed varicella in the first month of life

Clinical Question 2.7: **How should a neonate with suspected or confirmed varicella be managed?**

Evidence Statement

Management of a neonate with suspected or confirmed varicella infection should be led by secondary level specialist paediatric care. Treatment with IV aciclovir should be considered. VZIG is not indicated once the varicella rash has developed. Alternative aetiologies for a disseminated vesicular rash in a neonate should be interrogated, and should include investigations for herpes simplex virus (HSV) and enterovirus.[38-40]

Clinical Practice

- Any infant with suspected neonatal varicella infection should be assessed in a secondary level paediatric centre.
- HSV and enterovirus infection should also be considered in the differential diagnosis in the setting of a disseminated vesicular rash. A sample of vesicular fluid can be sent for PCR for HSV, VZV and enterovirus to confirm the underlying aetiology.
- Any infant with a disseminated vesicular rash should be isolated in a single room with airborne and contact precautions, and their placement discussed with local infection control team to prevent secondary cases in neonatal and paediatric units.
- Empirical IV aciclovir should be started in an unwell neonate with disseminated vesicular rash, pending confirmation of the aetiology (i.e. HSV, VZV or enterovirus)
- If varicella infection is confirmed, IV aciclovir should be continued in preterm infants (<28 weeks gestation or 1Kg birthweight) irrespective of maternal immunity, and in those with respiratory compromise or those with severe end organ damage (encephalitis, hepatitis). These cases should be discussed with local infection specialists.
- Babies outside of these groups should have their duration of IV and/or oral aciclovir discussed with local infection specialists and paediatricians.

Recommendations

37. **We recommend that the neonate should at a minimum be referred to the local secondary level paediatric centre for assessment and treatment, if they believe that the neonate has acute varicella infection.**
38. **We strongly recommend that empirical IV aciclovir should be started in an unwell neonate with a disseminated vesicular rash, pending confirmation of the aetiology (i.e. HSV, VZV or enterovirus).**
39. **We strongly recommend that babies with disseminated vesicular rash should be isolated in single rooms with airborne and contact precautions, and their placement discussed with local infection control teams to prevent secondary cases in neonatal and paediatric units.**
40. **If varicella is confirmed, we strongly recommend that IV aciclovir should be continued in preterm infants (<28 weeks gestation or 1kg birthweight) irrespective of maternal immunity, those with respiratory compromise or those with severe end organ damage (encephalitis, hepatitis). These cases should be discussed with local Infection Specialists.**

Section 7: Varicella and breastfeeding

Introduction

It is important to ensure that women with acute varicella around the time of the birth, are still able to bond with their baby and breastfeed if they wish.

Clinical Question 2.8: **How should a postpartum mother with acute varicella infection be advised regarding the risk of varicella transmission and breastfeeding?**

Evidence Statement

The RCOG states that it is safe for the woman with pre-, intra- or post-natal chickenpox to breastfeed and that breastfeeding should be encouraged. Vesicles on the breast should be covered to minimise risk of transmission. If vesicles are present close to the nipple, women are advised to express from that side until the vesicles have crusted over (and thus non-infectious). In this instance, the expressed breast milk may be fed to the baby who is receiving treatment with VZIG and/or aciclovir, however if the baby is not on VZIG or anti-viral therapy, this expressed milk should be discarded.[41, 42] Aciclovir is present in breastmilk after systemic administration; it is not known to be harmful but manufacturer advises caution [British National Formulary].

Recommendations

41. **We recommend that women with varicella should be supported and encouraged to breastfeed if they wish.**
42. **Vesicles on the breast should be covered to minimise risk of transmission. If vesicles are present close to the nipple, we suggest that women are advised to express from that side until the vesicles have crusted over. In this instance, the expressed breast milk may be fed to the baby who is receiving treatment with VZIG and/or aciclovir. If the baby is not on VZIG or anti-viral therapy, this expressed milk should be discarded.**
43. **We recommend that clinicians advise mothers that aciclovir is not contra-indicated in breastfeeding. Aciclovir is present in breast milk after systemic administration but is not expected to cause any adverse effects in breastfed infants.**

A mother with chickenpox or zoter does not need to be isolated from her own baby.[43] Women hospitalised with varicella infection should be nursed in isolation from other babies, other potentially susceptible pregnant women and non-immune staff.

Clinical Practice

- Women should be informed that acute varicella infection is not a contraindication to breastfeeding and they should be supported to do so if they wish to breastfeed.
- Vesicles on the breast should be covered to minimise risk of transmission. If vesicles are present close to the nipple, women should be advised to express from that breast until the vesicles have crusted over.

- The expressed breast milk may be fed to an infant receiving treatment with VZIG and/or aciclovir. This is because they are receiving prophylaxis with the VZIG and/or aciclovir and so the risk of severe disease is lower.
- If the baby is not receiving VZIG or anti-viral therapy, this expressed milk should be discarded.
- Aciclovir is not contra-indicated in breastfeeding. Women should be advised that while aciclovir is present in breastmilk after systemic administration it is not expected to cause any adverse effects in breastfed infants.

Section 8: Reactivation of varicella zoster in pregnancy (i.e. localised shingles)

Introduction

Following primary infection, i.e. in the varicella immune woman, VZV remains dormant in sensory nerve root ganglia and may reactivate as a localised shingles rash. Any woman with a disseminated vesicular rash should be managed as acute primary varicella irrespective of any prior reported varicella infection or immunity testing. The section below refers only to women with localised varicella reactions with the clinical diagnosis of shingles. Shingles presents as a vesicular erythematous skin rash in a dermatomal distribution and is always unilateral. Patients with shingles can transmit infection to non-immune individuals by direct contact with the vesicular fluid. The risk of acquiring infection from an immunocompetent person with shingles in non-exposed sites (e.g. thoracolumbar) is remote but can occur. In cases of disseminated shingles, vesicles in an exposed area of the body (e.g. ophthalmic shingles) or in an immunocompromised individual, risk of viral shedding is greater and transmission can also occur by the respiratory tract. Shingles is infectious to non-immune individuals until all the lesions have crusted over completely.

Clinical Question 2.9: **How should a pregnant woman or post-partum (<6 weeks from birth) woman with localised shingles rash be managed?**

Evidence Statement

Shingles in pregnancy is typically mild – there is generally no danger to the pregnancy and there is no risk of transmission to the baby.[42] General complications of shingles infection, not specific to pregnancy, include post-herpetic neuralgia, ophthalmic zoster infection, Ramsay Hunt Syndrome and meningitis.[44] Administration of antivirals is most effective if started within 72 hours of rash onset.[45] Decision to treat shingles in pregnancy with aciclovir should be on a case-by-case basis, and should be considered in immunocompromised women, individuals with severe pain, cases with a non-truncal rash or in disseminated infection.[44, 45] Providing adequate analgesia is also important to improve the overall care of the woman.[44]

Clinical Practice

- Women should be advised that shingles in pregnancy is typically mild and there is no increased risk of transmission to the baby**.**
- They should be reassured that shingles is not associated with fetal varicella syndrome and referral to a fetal medicine specialist is not indicated.
- Any woman with active shingles admitted to hospital should be discussed with local infection control teams to avoid exposing other women to the risk of acquiring varicella.
- In the cases of disseminated shingles, vesicles in an exposed non-truncal site (e.g. ophthalmic shingles) or infection in an immunocompromised woman, infection control precautions are the same as acute primary varicella infection – isolation in a single room with ensuite facilities, under airborne precautions.
- Oral aciclovir can be considered in certain women with shingles, but this should be done on a case-by-case basis. It should be used for cases where there is disseminated rash, non-truncal spread or if there are lesions near the eyes.

Recommendations

44. **We suggest that Fetal Medicine assessment is not required, in the case of secondary infection/herpes zoster infection, as shingles is not associated with fetal varicella syndrome.**
45. **We suggest that the placement of women with shingles, if admitted to hospital, is discussed with local infection control teams. In the cases of disseminated shingles, vesicles in an exposed site (e.g. ophthalmic shingles) or infection in an immunocompromised patient, infection control precautions are the same as acute primary varicella infection – isolation in a single room with ensuite facilities, under airborne precautions.**
46. **We suggest that oral aciclovir can be considered in certain women with shingles, but this should be done on a case-by-case basis. Aciclovir may particularly be warranted if there is a multi-dermatomal spread of the rash, involves non-truncal areas (i.e. near eye) or the woman is immunocompromised.**

Chapter 3: Development Of Clinical Practice Guideline

3.1 Literature search strategy

A comprehensive literature review was undertaken which included national and international publications. A search was done of the electronic database PUBMED (2013-September 2022) and the Cochrane Library were undertaken. This was done from 2013, as the previous RCPI varicella guidelines had done a search prior to 2013. The main keywords used were "varicella" and "pregnancy". There were no restrictions placed on the searches. The results yielded were reviewed, along with existing international guidelines from United Kingdom, Switzerland, Canada and United States of America.

Search: **varicella pregnancy** Filters: **from 2013-2022**

(("herpesvirus 3, human"[MeSH Terms] OR "human herpesvirus 3"[All Fields] OR "varicella"[All Fields] OR "chickenpox"[MeSH Terms] OR "chickenpox"[All Fields] OR "varicellae"[All Fields]) AND ("pregnancy"[MeSH Terms] OR "pregnancy"[All Fields] OR "pregnancies"[All Fields] OR "pregnancy s"[All Fields])) AND (2013:2022[pdat])

Translations

varicella: "herpesvirus 3, human"[MeSH Terms] OR "human herpesvirus 3"[All Fields] OR "varicella"[All Fields] OR "chickenpox"[MeSH Terms] OR "chickenpox"[All Fields] OR "varicellae"[All Fields]

pregnancy: "pregnancy"[MeSH Terms] OR "pregnancy"[All Fields] OR "pregnancies"[All Fields] OR "pregnancy's"[All Fields]

This search yielded 242 documents, which were then reviewed for relevance and to remove reviews or commentary pieces. Twenty-five papers were then reviewed in more depth and sixteen were included for the purposes of writing this manuscript.

3.2 Appraisal of evidence

Following a comprehensive literature review the quality, validity and relevance of the evidence gathered were critically appraised by the Guideline developers under the following headings:

- Study design
- Relevance of primary and secondary outcomes
- Consistency of results across studies
- Magnitude of benefit versus magnitude of harm
- Applicability to practice context

A number of evidence-based recommendations for management of varicella were agreed upon. They have been adapted to reflect care in the Irish healthcare setting.

3.3 AGREE II process

While being developed, the Guideline was assessed using the AGREE II checklist (Appendix 3) as recommended the Department of Health in the 'How to Develop a National Clinical Guideline: a manual for Guideline developers', 2019[16].

The purpose of AGREE II is to provide a framework to:

1. Assess the quality of guidelines;
2. Provide a methodological strategy for the development of guidelines; and
3. Inform what information and how information ought to be reported in guidelines

3.4 Literature review

Details of supportive evidence based literature for this Guideline are reported in chapter two.

- The electronic search of the literature was done by Prof. Richard Drew on 28th September 2022, and the final documents were selected.
- The evidence reviewed comes from both national and international studies and has been adapted to fit the Irish context
- Literature was used when the evidence was relevant, strong and applicable to the Irish setting and omitted when this was not the case.

3.5 Grades of recommendation

GRADE offers a transparent and structured process for developing and presenting evidence summaries and for carrying out the steps involved in developing recommendations.[17] While we acknowledge that for this particular work an extensive GRADE approach is not possible, we have used the suggested language set out in the GRADE table when making recommendations.[18] (Appendix 4)

3.6 Future research

An important outcome of the Guideline development process is in highlighting gaps in the evidence base.

The questions of relevance to this Guideline include;

- Comparison of aciclovir to VZIG for post-exposure prophylaxis
- Pregnancy and neonatal outcomes in women who develop primary varicella in pregnancy

16 Department of Health (2019). How to develop a National Clinical Guideline: a manual for guideline developers. Available at: https://www.gov.ie/en/collection/cd41ac-clinical-effectiveness-resources-and-learning/

17 Guyatt, Gordon, et al. "GRADE Guidelines: 1. Introduction – GRADE Evidence Profiles and Summary of Findings Tables." *Journal of Clinical Epidemiology*, vol. 64, no. 4, 2011, pp. 383-94, https://doi.org/10.1016/j.jclinepi.2010.04.026.

18 SMFM adopts GRADE (Grading of Recommendations Assessment, Development, and Evaluation) for clinical guidelines. Society for Maternal-Fetal Medicine (SMFM), Chauhan SP, Blackwell SC. Am J Obstet Gynecol. 2013 Sep;209(3):163-5. doi: 10.1016/j.ajog.2013.07.012. PMID: 23978245 https://pubmed.ncbi.nlm.nih.gov/23978245/

Chapter 4: Governance and Approval

4.1 Formal governance arrangements

This Guideline was written by the Guideline Developers under the direction of the Guideline Programme Team. An Expert Advisory Group was formed to review the Guideline prior to submission for final approval with the National Women and Infants Health Programme. The roles and responsibilities of the members of each group and their process were clearly outlined and agreed.

4.2 Guideline development standards

This Guideline was developed by the Guideline Developer Group (GDG) within the overall template of the HSE National Framework[19] for developing Policies, Procedures, Protocols and Guidelines (2016) (Appendix 5) and under supervision of the Guideline Programme Team (GPT).

A review was conducted by a group of experts, specialists and advocates (the EAG) prior to approval by the Clinical Advisory Group (CAG) of the National Women and Infants Health Programme (NWIHP) with final sign off for publication by CAG Co-Chairs, the Clinical Director of NWIHP and the Chair of the IOG. See Appendix 6 for list of CAG members.

4.3 Copyright/Permission sought

Permission was obtained from the National Infection Advisory Committee (NIAC) for the use two flowcharts from the current NIAC Immunisation Guidelines, Chapter 23 Varicella-Zoster, updated October 2022.

19 Health Service Executive (2016). National Framework for developing Policies, Procedures, Protocols and Guidelines (PPPGs). Available from: https://www.hse.ie/eng/about/who/qid/nationalframeworkdevelopingpolicies/

Chapter 5: **Communication and Dissemination**

A communication and dissemination plan for this Guideline has been developed by the GPT and endorsed by NWIHP.

Effective ongoing clear communication is essential in explaining why the Guideline is necessary and securing continued buy-in. It provides an opportunity to instil motivation within staff, helps overcome resistance to change and gives an opportunity for feedback[20].

The Clinical Guideline will be circulated and disseminated through the Guideline Programme Team as well as through the professional networks who participated in developing and reviewing the document.

Senior management within the maternity units are responsible for the appropriate dissemination of new and updated guidelines. Local hospital groups including Guideline committees are also instrumental in the circulation of new and updated guidelines and promoting their use in the relevant clinical settings.

The HSE will make this Guideline available to all employees through standard networks as well as storing it in the online PPPG repository. Electronic versions available on the NWIHP https://www.hse.ie/eng/about/who/acute-hospitals-division/woman-infants/clinical-guidelines/ and RCPI https://www.rcpi.ie/faculties/obstetricians-and-gynaecologists/national-clinical-guidelines-in-obstetrics-and-gynaecology/ websites and other communication means can be used to maximise distribution. The NWIHP website will also provide a training webinar introducing each Guideline and where relevant a downloadable version of the recommended algorithm will be available.

20 Department of Health (2018). NCEC Implementation Guide and Toolkit. Available at: https://health.gov.ie/national-patient-safety-office/ncec/

Chapter 6: **Implementation**

6.1 Implementation plan

Implementation was considered at the beginning, and throughout the Guideline development process. The local multidisciplinary clinical team, senior executive and clinical management in each maternity and gynaecology unit are ultimately responsible for the appropriate structured adoption and implementation of the Guidelines within their area of responsibility. They must ensure that all relevant personnel under their supervision have read and understood the Guideline and monitor both its effectiveness and adoption.

Within each site, local multidisciplinary teams are responsible for the clinical implementation of Guideline recommendations, and ensuring that their local clinical practices and processes reflect and are aligned with the Guideline recommendations

In the case of this Guideline the following have been put in place to help facilitate the implementation of this Guideline.

- Quick Summary Document (QSD) for clinical staff (includes key recommendations, auditable standards, algorithms and recommended reading)
- Clinical Guideline mobile application
- Plain language summary.

6.2 Education plans required to implement the Guideline

It is acknowledged that this Guideline should be complemented by ongoing education, training and assessment where required.

6.3 Barriers and facilitators

To ensure successful implementation of guidelines, it is first necessary to look at potential barriers and facilitators. Taking these into account when developing the implementation plan should improve levels of support from relevant users. (DOH 2018, 2019)

Barriers may be categorised as internal (specific to the Guideline itself) or external (specific to the clinical environment).

Facilitators for the introduction of this guideline would be Directors of Midwifery, Obstetricians and Laboratory services.

The Guideline Development Group has aimed to address any internal barriers during the development of this Guideline.

Potential external barriers include:

- Organisational factors (e.g. lack of isolation rooms, limited laboratory resources for VZV IgG screening)
- Individual factors (e.g. knowledge, skills, training)
- Woman's perceptions

In the case of this Guideline it will be necessary to examine possible barriers and consider implementation strategies to address them. By example, this may include discussion with relevant management groups with regards budgetary impact or providing training to the relevant staff.

6.4 Resources necessary to implement recommendations

The implementation of this Guideline should be undertaken as part of the quality improvement of each hospital. Hospitals should review existing service provision against this Guideline, identifying necessary resources required to implement the recommendations in this Guideline.

Chapter 7: Audit and Evaluation

7.1 Introduction to audit

It is important that both implementation of the Guideline and its influence on outcomes are audited to ensure that this Guideline positively impacts on patient care. Institutions and health professionals are encouraged to develop and undertake regular audits of Guideline implementation. Personnel tasked with the job of conducting the audit should be identified on receipt of the most recent version of the Guideline.

7.2 Auditable standards

Audit using the key recommendations as indicators should be undertaken to identify where improvements are required and to enable changes as necessary. Audit should also be undertaken to provide evidence of continuous quality improvement initiatives.

Auditable standards for this Guideline include:

1. Number of women in one year receiving VZIG as post-exposure prophylaxis
2. Number of women whose babies develop congenital varicella syndrome per year
3. Proportion of antenatal booked women who have VZV IgG test sent per 1000 booking serology tests
4. Incidence of acute varicella infection in women who took aciclovir as prophylaxis in one year
5. Number of women treated with VZIG

7.3 Evaluation

Evaluation is defined as a formal process to determine the extent to which the planned or desired outcomes of an intervention are achieved[21]. Implementation of this Guideline will be audited periodically at national level, with standards for this set by the NWIHP. Evaluation of the auditable standards should also be undertaken locally by senior hospital clinical management to support implementation.

21 Health Information Quality Authority (2012). National Standards for Safer Better Healthcare [Internet]. Available from: https://www.hiqa.ie/reports-and-publications/standard/national-standards-safer-better-healthcare

Chapter 8: Revision Plan

8.1 Procedure for the update of the Guideline

It may be a requirement to amend, update or revise this Guideline as new evidence emerges. This Guideline will be reviewed at national level every three years, or earlier if circumstances require it, and updated accordingly.[22]

The Guideline Development Group will be asked to review the literature and recent evidence to determine if changes are to be made to the existing Guideline. If the Guideline Development Group are unavailable, the GPT along with the NWIHP senior management team will select a suitable expert to replace them.

If there are no amendments required to the Guideline following the revision date, the detail on the revision tracking box must still be updated which will be a new version number and date.

The recommendations set out in this Guideline remain valid until a review has been completed.

8.2 Method for amending the Guideline

As new evidence become available it is inevitable that Guideline recommendations will fall behind current evidence based clinical practice. It is essential that clinical guidelines are reviewed and updated with new evidence as it becomes available.

In order to request a review of this Guideline one of the following criteria must be met:

a. 3 years since the Guideline was published

b. 3 years since last review was conducted

c. Update required as a result of new evidence

Correspondence requesting a review of the Guideline should be submitted to the National Women and Infants Health Programme. Any such requests should be dealt with in a timely manner.

22 Health Service Executive (2016). National Framework for developing Policies, Procedures, Protocols and Guidelines (PPPGs). Available from: https://www.hse.ie/eng/about/who/qid/nationalframeworkdevelopingpolicies/

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Supporting Evidence

GRADE: http://www.gradeworkinggroup.org/

AGREE: http://www.agreetrust.org/agree-ii/

HSE: https://www.hse.ie/eng/about/who/qid/use-of-improvement-methods/nationalframeworkdevelopingpolicies/

Glossary
(For The Purpose Of This Guideline)

AGREE Appraisal of Guidelines for Research and Evaluation

ACOG American College of Obstetricians and Gynaecologists

CAG Clinical Advisory Group

EAG Expert Advisory Group

FAU Fetal Assesment Unit

FIGO International Federation of Gynaecology and Obstetrics

GPT Guideline Programme Team

GRADE Grading of Recommendations, Assessments, Developments and Evaluations

HDU High dependency unit

HIQA Health Information and Quality Authority

HSE Health Service Executive

HSV herpes simplex virus

HZ Herpes zoster

ICU Intensive care unit

IOG Institute of Obstetricians and Gynaecologists

MMR measles, mumps and rubella vaccine

NIAC National Immunisation Advisory Committee

NICE The National Institute for Health and Care Excellence

NCEC National Clinical Effectiveness Committee

NWIHP National Women and Infants Health Programme

PCR Polymerase chain reaction

PPPG Policy, Procedures, Protocols and Guidelines

RCOG Royal College of Obstetricians and Gynaecologists

RCPI Royal College of Physicians of Ireland

VZIG Varicella-zoster immune globulin

VZV Varicella-zoster virus

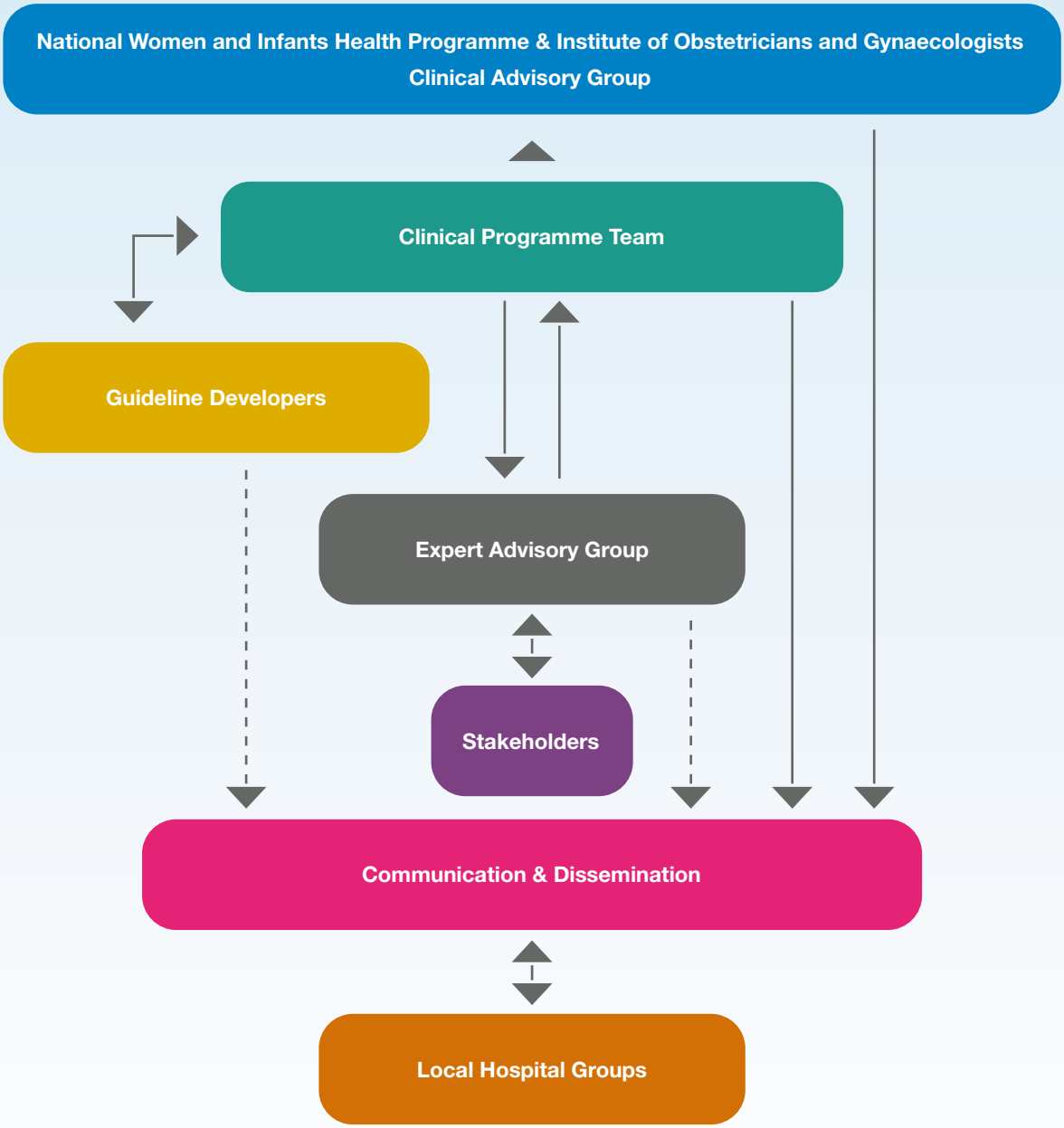
Appendix 1:
Expert Advisory Group Members 2021-

Attendee	Profession	Location (2021)
Dr Fergus McCarthy	Consultant Obstetrician, Gynaecologist, Senior Lecturer and Maternal-Fetal Medicine Sub-specialist	Cork University Maternity Hospital, University College Cork
Dr Mairead Butler	Consultant Obstetrician and Gynaecologist	University Hospital Waterford
Prof Declan Keane	Professor of Obstetrics and Gynaecology	National Maternity Hospital Dublin, Royal College of Surgeons in Ireland
Dr Katherine Astbury	Consultant Obstetrician and Gynaecologist Gynaecology Oncology Sub-specialist	University Hospital Galway
Dr Sarah Petch	Specialist Registrar, Obstetrics and Gynaecology	National Maternity Hospital Dublin
Dr Orla Donohoe	Specialist Registrar, Obstetrics and Gynaecology	Sligo University Hospital
Prof John Murphy	Consultant Neonatologist and Clinical Lead for the National Clinical Programme for Paediatrics and Neonatology	National Women and Infants Health Programme
Ms Siobhan Canny	Group Director of Midwifery	Saolta University Health Care Group
Ms Fiona Hanrahan	Director of Midwifery and Nursing	Rotunda Hospital Dublin
Ms Margaret Quigley	National Lead for Midwifery	Office of Nursing and Midwifery Services Director
Prof Valerie Smith	Professor of Midwifery	School of Nursing and Midwifery, Trinity College Dublin
Ms Triona Cowman	Director of the Centre for Midwifery Education	Centre for Midwifery Education, Coombe Women & Infants University Hospital
Ms Janet Murphy	Advanced Midwifery Practitioner	University Hospital Waterford

Attendee	Profession	Location (2021)
Dr Ciara McCarthy	General Practitioner and ICGP Women's Health Lead	Irish College of General Practitioners
Mr Fergal O' Shaughnessy *And* Dr Brian Cleary *(Shared nomination)*	Senior Pharmacist, Honorary Lecturer *And* Chief Pharmacist, Honorary Clinical Associate Professor and Medications Lead, Maternal & Newborn Clinical Management System	Rotunda Hospital Dublin Royal College of Surgeons in Ireland
Ms Marie Finn	Medical Social Work Counsellor	Saolta University Health Care Group
Ms Marie Culliton	Lab Manager/Chief Medical Scientist	National Maternity Hospital Dublin
Ms Marita Hennessy	Post-Doctoral Researcher	Pregnancy Loss Research Group, INFANT Centre, University College Cork
Ms Niamh Connolly-Coyne *And* Ms Mandy Daly *(Shared nomination)*	Board of Directors	Irish Neonatal Health Alliance
Ms Caroline Joyce	Principal Clinical Biochemist PhD Candidate	Cork University Hospital University College Cork
Dr Richard Duffy	Consultant Perinatal Psychiatrist	Rotunda Hospital Dublin
Ms Clare Farrell	Physiotherapy Manager	Coombe Women & Infants University Hospital
Ms Fiona Dunlevy *And* Ms Sinéad Curran *(Shared nomination)*	Dietician Manager	Coombe Women & Infants University Hospital National Maternity Hospital
Dr Nicholas Barrett	Lead for Obstetric Anaesthesiology services	Limerick University Hospital
Dr Brendan Fitzgerald	Consultant Perinatal Pathologist	Cork University Hospital
Dr Niamh Conlon	Consultant Histopathologist	Cork University Hospital
Ms Georgina Cruise	Service Manager	Patient Advocacy Ireland

Appendix 2: **Guideline Programme Process**

Guideline Programme Process



Appendix 3: **AGREE II checklist**[23]

AGREE Reporting Checklist 2016

This checklist is intended to guide the reporting of Clinical Practice Guidelines.

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
DOMAIN 1: SCOPE AND PURPOSE		
1. OBJECTIVES *Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.*	☐ Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) ☐ Expected benefit(s) or outcome(s) ☐ Target(s) (e.g., patient population, society)	
2. QUESTIONS *Report the health question(s) covered by the guideline, particularly for the key recommendations.*	☐ Target population ☐ Intervention(s) or exposure(s) ☐ Comparisons (if appropriate) ☐ Outcome(s) ☐ Health care setting or context	
3. POPULATION *Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.*	☐ Target population, sex and age ☐ Clinical condition (if relevant) ☐ Severity/stage of disease (if relevant) ☐ Comorbidities (if relevant) ☐ Excluded populations (if relevant)	
DOMAIN 2: STAKEHOLDER INVOLVEMENT		
4. GROUP MEMBERSHIP *Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/ rating the evidence and individuals involved in formulating the final recommendations.*	☐ Name of participant ☐ Discipline/content expertise (e.g., neurosurgeon, methodologist) ☐ Institution (e.g., St. Peter's hospital) ☐ Geographical location (e.g., Seattle, WA) ☐ A description of the member's role in the guideline development group	

23 AGREE Reporting Checklist is available on the AGREE Enterprise website, a free and open access resource to support the practice guideline field (www.agreetrust.org).

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
5. TARGET POPULATION PREFERENCES AND VIEWS *Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.*	☐ Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) ☐ Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) ☐ Outcomes/information gathered on patient/public information ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	
6. TARGET USERS *Report the target (or intended) users of the guideline.*	☐ The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) ☐ How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)	
DOMAIN 3: RIGOUR OF DEVELOPMENT		
7. SEARCH METHODS *Report details of the strategy used to search for evidence.*	☐ Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) ☐ Time periods searched (e.g., January 1, 2004 to March 31, 2008) ☐ Search terms used (e.g., text words, indexing terms, subheadings) ☐ Full search strategy included (e.g., possibly located in appendix)	
8. EVIDENCE SELECTION CRITERIA *Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.*	☐ Target population (patient, public, etc.) characteristics ☐ Study design ☐ Comparisons (if relevant) ☐ Outcomes ☐ Language (if relevant) ☐ Context (if relevant)	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
9. STRENGTHS & LIMITATIONS OF THE EVIDENCE *Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.*	☐ Study design(s) included in body of evidence ☐ Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) ☐ Appropriateness/relevance of primary and secondary outcomes considered ☐ Consistency of results across studies ☐ Direction of results across studies ☐ Magnitude of benefit versus magnitude of harm ☐ Applicability to practice context	
10. FORMULATION OF RECOMMENDATIONS *Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.*	☐ Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) ☐ Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) ☐ How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)	
11. CONSIDERATION OF BENEFITS AND HARMS *Report the health benefits, side effects, and risks that were considered when formulating the recommendations.*	☐ Supporting data and report of benefits ☐ Supporting data and report of harms/side effects/risks ☐ Reporting of the balance/trade-off between benefits and harms/side effects/risks ☐ Recommendations reflect considerations of both benefits and harms/side effects/ risks	
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE *Describe the explicit link between the recommendations and the evidence on which they are based.*	☐ How the guideline development group linked and used the evidence to inform recommendations ☐ Link between each recommendation and key evidence (text description and/or reference list) ☐ Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
13. EXTERNAL REVIEW *Report the methodology used to conduct the external review.*	☐ Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) ☐ Methods taken to undertake the external review (e.g., rating scale, open-ended questions) ☐ Description of the external reviewers (e.g., number, type of reviewers, affiliations) ☐ Outcomes/information gathered from the external review (e.g., summary of key findings) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)	
14. UPDATING PROCEDURE *Describe the procedure for updating the guideline.*	☐ A statement that the guideline will be updated ☐ Explicit time interval or explicit criteria to guide decisions about when an update will occur ☐ Methodology for the updating procedure	
DOMAIN 4: CLARITY OF PRESENTATION		
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS *Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.*	☐ A statement of the recommended action ☐ Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) ☐ Relevant population (e.g., patients, public) ☐ Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply) ☐ If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline	
16. MANAGEMENT OPTIONS *Describe the different options for managing the condition or health issue.*	☐ Description of management options ☐ Population or clinical situation most appropriate to each option	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
17. IDENTIFIABLE KEY RECOMMENDATIONS *Present the key recommendations so that they are easy to identify.*	☐ Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms ☐ Specific recommendations grouped together in one section	
DOMAIN 5: APPLICABILITY		
18. FACILITATORS AND BARRIERS TO APPLICATION *Describe the facilitators and barriers to the guideline's application.*	☐ Types of facilitators and barriers that were considered ☐ Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) ☐ Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the population receive mammography) ☐ How the information influenced the guideline development process and/or formation of the recommendations	
19. IMPLEMENTATION ADVICE/TOOLS *Provide advice and/or tools on how the recommendations can be applied in practice.*	☐ Additional materials to support the implementation of the guideline in practice. For example: • Guideline summary documents • Links to check lists, algorithms • Links to how-to manuals • Solutions linked to barrier analysis (see Item 18) • Tools to capitalize on guideline facilitators (see Item 18) • Outcome of pilot test and lessons learned	

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
20. RESOURCE IMPLICATIONS *Describe any potential resource implications of applying the recommendations.*	☐ Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) ☐ Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) ☐ Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	
21. MONITORING/ AUDITING CRITERIA *Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.*	☐ Criteria to assess guideline implementation or adherence to recommendations ☐ Criteria for assessing impact of implementing the recommendations ☐ Advice on the frequency and interval of measurement ☐ Operational definitions of how the criteria should be measured	
DOMAIN 6: EDITORIAL INDEPENDENCE		
22. FUNDING BODY *Report the funding body's influence on the content of the guideline.*	☐ The name of the funding body or source of funding (or explicit statement of no funding) ☐ A statement that the funding body did not influence the content of the guideline	
23. COMPETING INTERESTS *Provide an explicit statement that all group members have declared whether they have any competing interests.*	☐ Types of competing interests considered ☐ Methods by which potential competing interests were sought ☐ A description of the competing interests ☐ How the competing interests influenced the guideline process and development of recommendations	

From: Brouwers MC, Kerkvliet K, Spithoff K, on behalf of the AGREE Next Steps Consortium. The AGREE Reporting Checklist: a tool to improve reporting of clinical practice guidelines. BMJ 2016;352:i1152. doi: 10.1136/bmj.i1152.

For more information about the AGREE Reporting Checklist, please visit the AGREE Enterprise website at http://www.agreetrust.org.

Appendix 4: **Grades of Recommendation**[24]

Grade of recommendation	Clarity of risk/ benefit	Quality of supporting evidence	Implications	Suggested Language
1 A. Strong recommendation, high-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Consistent evidence from well-performed randomised, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk	Strong recommendations can apply to most patients in most circumstances without reservation. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present	We strongly recommend… We recommend that …should be performed/ administered… We recommend that … is indicated/ beneficial/ effective….
1 B. Strong recommendation, moderate-quality evidence	Benefits clearly outweigh risk and burdens, or vice versa	Evidence from randomised, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate	Strong recommendation and applies to most patients. Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present	We recommend… We recommend that … should be performed/ administered… We recommend that … is (usually) indicated/ beneficial/ effective…

24 SMFM adopts GRADE (Grading of Recommendations Assessment, Development, and Evaluation) for clinical guidelines. Society for Maternal-Fetal Medicine (SMFM), Chauhan SP, Blackwell SC. Am J Obstet Gynecol. 2013 Sep;209(3):163-5. https://pubmed.ncbi.nlm.nih.gov/23978245/

Grade of recommendation	Clarity of risk/ benefit	Quality of supporting evidence	Implications	Suggested Language
1 C. Strong recommendation, low-quality evidence	Benefits appear to outweigh risk and burdens, or vice versa	Evidence from observational studies, unsystematic clinical experience, or from randomised, controlled trials with serious flaws. Any estimate of effect is uncertain	Strong recommendation that applies to most patients. Some of the evidence base supporting the recommendation is, however, of low quality	We recommend… We recommend that … should be performed/ administered… We recommend that … Is (maybe) indicated/ beneficial/ effective…
2A. Weak recommendation, high-quality evidence	Benefits closely balanced with risks and burdens	Consistent evidence from well-performed randomised, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk	Weak recommendation: best action may differ depending on circumstances or patients or societal values	We suggest… We suggest that … may/might be reasonable…
2B. Weak recommendation, moderate-quality evidence	Benefits closely balanced with risks and burdens, some uncertainty in the estimates of benefits, risks and burdens	Evidence from randomised, controlled trials with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence of some other research design. Further research (if performed) is likely to have an impact on our confidence in the estimate of benefit and risk and may change the estimate	Weak recommendation; alternative approaches likely to be better for some patients under some circumstances	We suggest… We suggest that … may/might be reasonable…

Grade of recommendation	Clarity of risk/ benefit	Quality of supporting evidence	Implications	Suggested Language
2C. Weak recommendation, low-quality evidence	Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens	Evidence from observational studies, unsystematic clinical experience, or from randomised, controlled trials with serious flaws. Any estimate of effect is uncertain	Very weak recommendation: other alternatives may be equally reasonable.	We suggest… is an option We suggest that … may/might be reasonable.
Best practice	A recommendation that is sufficiently obvious that the desirable effects outweigh undesirable effects, despite the absence of direct evidence, such that the grading of evidence is unnecessary			We recommend… We recommend that … should be performed/ administered… We recommend that … Is usually) indicated/ beneficial/effective

Appendix 5: **Policies, Procedures, Protocols and Guidelines checklist**

The PPPG Checklists were developed to assist staff to meet standards when developing Clinical PPPGs.

Standards for developing clinical PPPG	
Stage 1 initiation	**Checklist**
The decision making approach relating to the type of PPPG guidance required (policy, procedure, protocol, guideline), coverage of the PPPG (national, regional, local) and applicable settings are described.	☐
Synergies/co-operations are maximised across departments/organisations (Hospitals/ Hospital Groups/Community Healthcare Organisations (CHO)/National Ambulance Service (NAS)), to avoid duplication and to optimise value for money and use of staff time and expertise.	☐
The scope of the PPPG is clearly described, specifying what is included and what lies outside the scope of the PPPG.	☐
The target users and the population/patient group to whom the PPPG is meant to apply are specifically described.	☐
The views and preferences of the target population have been sought and taken into consideration (as required).	☐
The overall objective(s) of the PPPGs are specifically described.	☐
The potential for improved health is described (e.g. clinical effectiveness, patient safety, quality improvement, health outcomes, quality of life, quality of care).	☐
Stakeholder identification and involvement: The PPPG Development Group includes individuals from all relevant stakeholders, staff and professional groups.	☐
Conflict of interest statements from all members of the PPPG Development Group are documented, with a description of mitigating actions if relevant.	☐
The PPPG is informed by the identified needs and priorities of service users and stakeholders.	☐
There is service user/lay representation on PPPG Development Group (as required).	☐
Information and support is available for staff on the development of evidence-based clinical practice guidance.	☐

Stage 2 development	**Checklist**
The clinical question(s) covered by the PPPG are specifically described.	☐
Systematic methods used to search for evidence are documented (for PPPGs which are adapted/ adopted from international guidance, their methodology is appraised and documented).	☐
Critical appraisal/analysis of evidence using validated tools is documented (the strengths, limitations and methodological quality of the body of evidence are clearly described).	☐
The health benefits, side effects and risks have been considered and documented in formulating the PPPG.	☐
There is an explicit link between the PPPG and the supporting evidence.	☐
PPPG guidance/recommendations are specific and unambiguous.	☐
The potential resource implications of developing and implementing the PPPG are Identified e.g. equipment, education/training, staff time and research.	☐
There is collaboration across all stakeholders in the planning and implementation phases to optimise patient flow and integrated care.	☐
Budget impact is documented (resources required).	☐
Education and training is provided for staff on the development and implementation of evidence- based clinical practice guidance (as appropriate).	☐
Three additional standards are applicable for a small number of more complex PPPGs:	☐
Cost effectiveness analysis is documented.	☐
A systematic literature review has been undertaken.	☐
Health Technology Assessment (HTA) has been undertaken.	☐
Stage 3 governance and approval	**Checklist**
Formal governance arrangements for PPPGs at local, regional and national level are established and documented.	☐
The PPPG has been reviewed by independent experts prior to publication (as required).	☐
Copyright and permissions are sought and documented.	☐
Stage 4 communication and dissemination	**Checklist**
A communication plan is developed to ensure effective communication and collaboration with all stakeholders throughout all stages.	☐
Plan and procedure for dissemination of the PPPG is described.	☐
The PPPG is easily accessible by all users e.g. PPPG repository.	☐

Stage 5 implementation	**Checklist**
Written implementation plan is provided with timelines, identification of responsible persons/ units and integration into service planning process.	☐
Barriers and facilitators for implementation are identified, and aligned with implementation levers.	☐
Education and training is provided for staff on the development and implementation of evidence- based PPPG (as required).	☐
There is collaboration across all stakeholders in the planning and implementation phases to optimise patient flow and integrated care.	☐
Stage 6 monitoring, audit, evaluation	**Checklist**
Process for monitoring and continuous improvement is documented.	☐
Audit criteria and audit process/plan are specified.	☐
Process for evaluation of implementation and (clinical) effectiveness is specified.	☐
Stage 7 revision/update	**Checklist**
Documented process for revisions/updating and review, including timeframe is provided.	☐
Documented process for version control is provided.	☐

To view in full refer to website:
https://www.hse.ie/eng/about/who/qid/nationalframeworkdevelopingpolicies/

Appendix 6: **NWIHP/IOG CAG Membership 2022**

Dr Cliona Murphy (Chair). Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital. Clinical Director, National Women and Infants Health Programme.

Dr Sam Coulter-Smith. Consultant Obstetrician and Gynaecologist, Rotunda Hospital. Chair, Institute of Obstetricians and Gynaecologists.

Angela Dunne. Director of Midwifery, National Women and Infants Health Programme.

Kilian McGrane. Director, National Women and Infants Health Programme.

Dr Peter McKenna. Clinical Lead, Obstetric Event Support Team, National Women and Infants Health Programme.

Prof John Murphy. Clinical Lead Neonatology, National Women and Infants Health Programme.

Prof Maeve Eogan. Consultant Obstetrician and Gynaecologist, Rotunda Hospital. Clinical Lead, Sexual Assault Treatment Units, National Women and Infants Health Programme.

Dr Aoife Mullaly. Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital. Clinical Lead, Termination of Pregnancy Services, National Women and Infants Health Programme.

Prof Keelin O'Donoghue. Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Lead, National Guidelines, National Women and Infants Health Programme.

Prof Nóirín Russell. Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Director, Cervical Check.

Prof Richard Greene. Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Director, National Perinatal Epidemiology Centre, University College Cork.

Prof John Morrison. Consultant Obstetrician and Gynaecologist, University Hospital Galway. Clinical Director, Saolta Maternity Directorate.

Dr Suzanne O'Sullivan. Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Director of Education and Training, Obstetrics and Gynaecology, Institute of Obstetricians and Gynaecologists.

Prof John Higgins. Cork University Maternity Hospital, Consultant Obstetrician and Gynaecologist, Clinical Director, Ireland South Women and Infants Directorate.

Dr Mendinaro Imcha. Clinical Director, Consultant Obstetrician and Gynaecologist, University Maternity Hospital Limerick.

Prof Shane Higgins. Master, Consultant Obstetrician and Gynaecologist, National Maternity Hospital.

Prof Mike O'Connell. Master, Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital.

Dr Brian Cleary. Chief Pharmacist, Rotunda Hospital. Medications Lead, Maternal and Newborn Clinical Management System Project.

Prof Seán Daly. Master, Consultant Obstetrician and Gynaecologist, Rotunda Hospital.

Ms Clare Thompson. Consultant Gynaecological Oncologist, The Mater, Dublin.

Dr Vicky O'Dwyer. Consultant Obstetrician and Director of Gynaecology, Rotunda Hospital.