National Women & Infants Health Programme

National Clinical Practice Guideline

Hyperemesis Gravidarum and Nausea/Vomiting in Pregnancy



INSTITUTE OF OBSTETRICIANS & GYNAECOLOGISTS

ROYAL COLLEGE OF PHYSICIANS OF IRELAND

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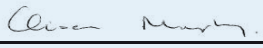
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National Clinical Guideline for Hyperemesis Gravidarum and Nausea/Vomiting in Pregnancy

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This Guideline aims to provide evidence-based recommendations for the care of women with NVP and HG as well as promoting a standardised approach nationally across all maternity units for the care of women with NVP and HG.
Description:
This national clinical practice guideline presents evidence-based recommendations for the systematic assessment and multidisciplinary management of nausea and vomiting in pregnancy (NVP) and hyperemesis gravidarum (HG). It advocates standardised severity evaluation using the PUQE instrument, stratified ambulatory or inpatient care, correction of fluid and electrolyte disturbances, stepwise pharmacological antiemetic therapy, prophylactic thiamine administration, and nutritional intervention where clinically indicated. The guideline further emphasises fetal growth surveillance, venous thromboembolism risk assessment, and trauma-informed psychological support within a coordinated model of maternity care.

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Algorithm

Algorithm 1: Management of Nausea/Vomiting in Pregnancy

Mild NVP according to modified PUQE-24 score <6, no comorbidities or clinical risks – manage at point of care

- Advise on dietary management, adequate fluid intake, comfort measures and supports as needed. Encourage oral fluids and dietary intake of small, frequent amounts of preferred foods
- Provide appropriate supportive materials such as dietary information leaflets.
- Consider prescription of first line oral anti-emetic, particularly if symptoms are affecting intake or quality of life.
- Consider the psychological impact of prolonged nausea or vomiting. Provide psychological support and offer referral to local perinatal mental health services for ongoing support as needed.
- If weight loss, dehydration, or co-morbidities, manage according to the below.

Moderate or Severe NVP (PUQE-24 score 7-12 or ≥13) or any severity of symptoms alongside any of the following conditions:

- weight loss
- clinical signs of dehydration
- on oral medications with low therapeutic window e.g. anti-epileptic medication, anti-retroviral, immunosuppression where there is concern regarding ability to tolerate oral medication)

Consult obstetric team and manage in day care unit or as per clinical judgement.

Severe NVP (PUQE-24 score ≥13) or unwell moderate NVP, may need to be managed as an inpatient. Management should be as per mild with the additional considerations for offering serial growth scans, hydration, management of complications and referral to supportive services as needed.

Severe NVP (PUQE-24 score ≥13) not suitable for daycase management, HG, significant medical comorbidity including insulin dependent diabetes – admit as inpatient

Criteria for discharge from inpatient care

- Tolerating oral intake and oral medications
- Appropriate antiemetic prescription provided
- Patient given information leaflet on diet and lifestyle management (see Appendix 4) and aware when to return to the hospital if situation changes
- On discharge from hospital arrange follow-up antenatal care to include monitoring of weight, nutritional status and fetal growth restriction and follow up appointments on the day ward as needed.

Algorithm 2: NVP Treatment Algorithm

If there is no improvement, proceed to the next step

Use of this algorithm assumes that other causes of nausea and vomiting in pregnancy have been ruled out.

Doxylamine 10mg and pyridoxine 10mg prolonged release: one capsule in the morning, one in the afternoon and two at bedtime). Adjust schedule and dose according to severity of symptoms.

Add either:

Ondansetron 4 to 8mg 8 hourly PO or (Zofran Zydis®) 4 to 8mg 8 hourly buccal (counsel the woman on safety data)

Or/And

Prochlorperazine (Stemetil®) 5mg 8 hourly PO†‡ or (Buccastem®) 3mg 12 hourly buccal

Or/And

Cyclizine (Valoid®) 50mg 8hourly PO‡

No Dehydration

If not tried previously, add any of the following:

- Promethazine (Phenergan®) 25mg up to 8 hourly PO
- Chlorpromazine 10-25 mg 6 hourly PO

Dehydration

Start IV fluid replacement with Hartmann's solution or NaCl 0.9%. **If not tried previously**, add any of the following:

- Ondansetron 4mg to 8mg 8 hourly IV*
- Prochlorperazine 12.5mg 8 hourly IM *
- Metoclopramide 5 to 10mg 8 hourly IV*
- Promethazine 12.5 to 25mg 8 hourly IM*

Consider: Hydrocortisone 100mg 12 hourly IV* change to oral Prednisolone, 40-50 mg/day PO. Taper the dose of steroids gradually until the lowest maintenance dose controlling the symptoms is reached. Given risks of long-term steroid use, seek senior advice.

Note:

- Don't use two medications which are in the same drug class
- At any stage women may require Omeprazole 20mg once daily for the management of dyspepsia or gastro-oesophageal reflux. Dose can be increased if necessary.
- Consult Summary of Product Characteristics for full prescribing data.

‡ Women should be warned of increased sedative effects possible with combination treatment.

† Extrapyramidal effects and oculogyric crises may occur with prochlorperazine.

*Only use parenteral formulations if oral products are not tolerated.

VTE risk assessment must be performed as per national clinical guidelines.

IV vitamin supplementation Pabrinex I/II® or equivelant daily for up to 3 days in women admitted (day case or inpatient) with HG; those with severe vomiting; those with limited nutritional intake for at least 5 days; and/or weight loss >10% from pre-pregnancy weight. If oral medications tolerated: Thiamine Hydrochloride 50-100mg up to 8hourly PO

Consider need for IV potassium replacement (use ready-mix bottles of NaCl 0.9% with 20mmol or 40 potassium per litre). If any abnormal electrolyte value is detected, please see Irspen Refeeding syndrome guidelines for correction (Appendix 4)

Parenteral nutrition may be required.

Key Recommendations

Definitions and Diagnosis

1. We recommend nausea and vomiting in pregnancy (NVP) be defined as nausea, vomiting and/or dry retching caused by pregnancy, with symptoms commencing in the first trimester without an alternate diagnosis. *Best practice*
2. We recommend that hyperemesis gravidarum can be diagnosed when there is onset of severe nausea and/or vomiting in early gestation (before 10-16 weeks' gestation) that affects ability to eat and drink normally and strongly limits activities of daily living, considering clinical picture and potential differential diagnoses. Signs of dehydration should be considered but are not necessary for diagnosis. *Best practice*
3. We recommend that the Pregnancy-Unique Quantification of Emesis (PUQE) scoring system is used to assess severity of nausea and vomiting in pregnancy (NVP) symptoms, alongside a thorough history. *Grade 1C.*

Initial Assessment and Investigations

4. We recommend ultrasound assessment at the appropriate timing by trained staff to outrule multiple pregnancy and molar pregnancy. *Best practice*
5. We recommend that a hydration assessment should be conducted, including fluid balance in the past 24 hours, urine colour and clinical signs of dehydration. Urine specific gravity may be considered. *Best practice*
6. We do not recommend the use of ketonuria to assess hydration. *Grade 1A*

Fluid and Electrolyte Management

7. We recommended considering intravenous (IV) provision of fluid and electrolytes if the woman cannot tolerate oral intake *Best practice*
8. We recommend caution if using dextrose-containing intra-venous (IV) fluids due to the risk of thiamine deficiency, refeeding syndrome and Wernicke's encephalopathy *Best practice*

Inpatient vs Outpatient Management and Risk Prevention

9. We recommend that consideration is given for inpatient versus outpatient management based on severity of symptoms, clinical risks, comorbidities, preferences of the woman and available resources. *Best practice*
10. We recommend regular assessment for risk factors for venous thromboembolism and consideration of thromboprophylaxis in accordance with venous thromboembolism guidelines. All patients admitted for management of hyperemesis gravidarum (HG) should have a risk assessment performed. *Best practice*
11. We recommend that pregnant women with persistent hyperemesis gravidarum (HG) should have regular fetal growth assessment, with at least one formal ultrasound to assess fetal growth in the third trimester. *Grade 1C*

Medical Management

12. We recommend that medical management is a cornerstone of the treatment of hyperemesis gravidarum (HG) and moderate-severe nausea and vomiting in pregnancy (NVP) (see algorithm). *Grade 1A*
13. We recommend that women should be encouraged to return for review if medications are not effective as they can be reassessed. *Best practice*
14. We recommend that if a woman is not responding to the medication, consider additional or changes as needed. More than one agent may be required. *Best practice*
15. We recommend avoiding the use of more than one medication from the same therapeutic class to prevent side effects. *Best practice*
16. We recommend a regular review of medications with consideration to stopping, reducing or restarting prescriptions as needed based on symptoms. Consider discontinuing any medication that is not effective for the woman, or that is causing significant side effects or complications. *Best practice*

Refeeding Syndrome Risk

17. We recommend that individual assessment for and management of refeeding syndrome is completed for women with HG, following national or local policies. *Best practice*
18. We recommend that electrolytes (at least potassium, magnesium, and phosphate) are measured and deficiencies are replaced as needed. *Best practice*
19. We recommend that Thiamine supplementation should be provided to: women admitted (day case or inpatient) with HG; those with severe vomiting; those with limited nutritional intake for at least 5 days; and/or weight loss >10% from pre-pregnancy weight. This can be provided as 250 mg IV thiamine (Pabrinex®) daily for up to 3 days; or 200-300 mg oral thiamine supplement for 10 days. *Best practice*

Nutrition Support

20. We recommend that the need for dietitian referral for comprehensive nutrition assessment should be considered for those presenting with hyperemesis gravidarum (HG). *Best practice*
21. We recommend that in appropriate settings, enteral and parenteral nutrition should be considered alongside optimisation of medical management when oral methods (food fortification, oral nutritional supplements, and dietary strategies) are not sufficient to maintain nutritional status, considering the preferences of the woman and potential complications. *Grade 2C.*
22. We recommend that enteral or parenteral nutrition should not be considered in inappropriate settings such as those without adequate equipment, training, policies or protocols for initiation and monitoring of feeding. *Best practice*
23. We recommend a multi-disciplinary approach led by the consultant obstetrician when enteral or parenteral nutrition is considered. *Best practice*
24. We recommend that clinical judgement should guide decisions about the timing of initiation or the duration of feeding. It is prudent to consider early initiation to minimise potential nutritional losses in pregnancy. *Grade 2C.*

Supplementation and Iron Management

25. We recommend that key single-nutrient supplementation should be recommended to all women throughout pregnancy. This includes folic acid (400µg/day) and vitamin D (15µg/day) at a minimum. Beyond this, an individualised approach should be taken with consideration of additional individual nutrient supplements or pregnancy multivitamins as appropriate, including iron-free formulations or products such as liquid, gummies and sprays. *Best practice.*
26. We recommend consideration on an individual basis of temporarily ceasing iron supplementation including multivitamins containing iron due to their potential to exacerbate nausea and vomiting symptoms. *Grade 1C.*
27. We recommend a prudent approach to alternative preparations such as IV infusions and consideration of their use in women with iron deficiency anaemia and HG. *Best practice*

Constipation Management

28. We recommend that women with hyperemesis gravidarum (HG) and constipation are counselled on lifestyle interventions for constipation including meeting dietary fibre recommendations (28g/day); maintaining hydration; engaging in regular physical activity and correct positioning when using the toilet. *Best practice*
29. We recommend that use of laxatives, via the oral or rectal route where appropriate, is considered (including bulk-forming, osmotic, and stimulants). *Grade 1C*

Diabetes and Endocrine Considerations

30. We recommend that the impact of nausea and vomiting in pregnancy (NVP) on blood glucose control in women with pre-gestational diabetes should be discussed as part of pre-conceptional counselling. *Best practice*
31. We recommend an individualised approach to management for women with pre-gestational diabetes throughout the course of pregnancy including close monitoring and collaborative multi-disciplinary care including input from endocrinology. *Best practice*
32. We recommend that women with type 1 diabetes should be given blood ketone testing equipment and advised to assess for ketonaemia when unwell ("sick day rules"). *Best practice*
33. We recommend that women with insulin-requiring diabetes or who are on pharmacological treatment should contact their diabetic service if vomiting. A low threshold for admission is recommended for women with insulin-requiring diabetes and NVP. *Best practice*
34. We recommend that diabetic ketoacidosis should be suspected in all women with diabetes presenting with vomiting and hyperglycaemia. *Best practice*
35. We recommend that measurement of tyroid function tests (TFTs) should be reserved for those with severe nausea and vomiting in pregnancy (NVP) or hyperemesis gravidarum (HG) or those with overt symptoms or signs of hyperthyroidism. Those with supressed thyroid stimulating hormone (TSH) should have further investigation for the underlying cause and appropriate referral to endocrinology services. *Best practice*

Psychological and Trauma-Informed Care

36. We recommend that women with hyperemesis gravidarum (HG) are routinely and periodically screened for emotional distress during and after pregnancy using validated measures and referred on to appropriate supports as needed with consent. Where indicated psychiatric assessment and intervention should be offered. *Grade 1C*

37. We recommend that clinicians consider a differential diagnosis between hyperemesis gravidarum (HG) and eating disorder-related vomiting. Provide appropriate level of care for such diagnoses (hyperemesis gravidarum, eating disorder or diagnosis of both hyperemesis gravidarum and an eating disorder). *Best practice*

38. We recommend that trauma sensitive staff training should be considered for staff interacting with women experiencing hyperemesis gravidarum (HG). In cases where clinicians do not have access to such training management should be informed so that funding can be obtained, and trauma sensitive training prioritised. *Best practice*

Delivery and Termination Considerations

39. Hyperemesis gravidarum (HG) alone is not an indication for early delivery or induction of labour, however an individualised approach taking the woman's preferences into account is recommended. *Best practice*

40. We recommend that the request for Termination of Pregnancy (TOP) should be reviewed by the appropriate members of the multidisciplinary team considering the legal criteria for TOP, the clinical situation, the best interests of the woman and her wishes. It is also important to recognise that under the 2018 Termination of Pregnancy Act women are entitled to a termination under 12 weeks without giving a reason for their decision. *Best practice*

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.[1]

1.1 Purpose

This Guideline is developed to assist the multidisciplinary team in the provision of best practice care for women with nausea and vomiting of pregnancy (NVP) and hyperemesis gravidarum (HG).

1.2 Scope

Target Users

The guideline is a resource for all clinicians providing care to women with NVP and HG in all healthcare settings. Healthcare staff including Doctors, Midwives, Nurses and Advanced Nursing and Midwifery practitioners[2], Pharmacists, and Health and Social Care Professionals involved in the care of women with NVP and HG.

Target Population

Women experiencing NVP and/or HG.

1.3 Objective

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

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. See Appendix 1 for EAG membership and Appendix 2 for Guideline Programme Process.

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1 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://assets.gov.ie/11533/2d070cb758a44fcb8b56f28784b10896.pdf

2 Nursing and Midwifery Board of Ireland (NMBI) (2018) Advanced Practice (Midwifery) Standards and Requirements. Dublin. www.nmbi.ie/NMBI/media/NMBI/Advanced-Practice-(Midwifery)-Standards-and-Requirements-2018-final.pdf

The Guideline was written in conjunction with obstetric, dietetic, pharmacy, mental health, midwifery and general practice representation.

The following were involved in the development and writing of this Guideline:

1. Dr Sarah Louise Killeen, Senior Dietitian, National Maternity Hospital, Dublin
2. Dr Nicola Whelan, Specialist Registrar Obstetrics and Gynaecology, National Maternity Hospital, Dublin
3. Dr Eileen O'Brien, Lecturer in Dietetics, Technological University Dublin, Ireland
4. Dr Tom Lynch, Senior Pharmacist, The Rotunda Hospital, Dublin
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16. Professor Mary Higgins, Consultant Obstetrician and Gynaecologist, National Maternity Hospital, Dublin
17. Professor Brian Cleary, Pharmacist Executive Manager, The Rotunda Hospital, Dublin

1.5 Stakeholder involvement

Stakeholders are people who have a common interest in improving health services. This includes persons that are responsible for delivering and those who receive services related to the clinical Guideline.

The following additional stakeholders were consulted regarding this Guideline. Consultation with Hyperemesis Ireland (HI) was done throughout the guideline process. This involved extensive review of the guideline by the HI representative Caoileann Appleby with experience of HG and update to the guideline in response to comments. The HI representative reviewed the final guideline before submission to EAG.

The following medical students are also acknowledged for their contributions including referencing and grading of evidence Shauna Galligan, Isabel Dwyer, Siofra Drohan and Nicola Lynch, alongside Jessica Meates, dietitian.

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.[3] Declaring an interest does not mean there is a conflict of interest.

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.[4]

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.[5]

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.

The Guideline Development Group have the following conflicts of interest to declare:

Brian Cleary and Eileen O'Brien are trustees of the charity Hyperemesis Ireland. Eileen O'Brien is the principal investigator on a study to investigate interventions for HG and nutritional deficiencies. Grant funding from the Bikkja trust and the Nursing and Midwifery Planning and Development unit (NMPD) were received for this work.

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.

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3 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

4 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

5 Holger J. Schünemann, Lubna A. Al-Ansary, Frode Forland, *et al.*; for the Board of Trustees of the Guidelines International Network. Guidelines International Network: Principles for disclosure of interests and management of conflicts in guidelines. Ann Intern Med. 2015;163:548-553. doi:10.7326/M14-1885. https://www.acpjournals.org/doi/10.7326/m14-1885

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 ensuring informed consent is obtained
- Provide care within 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.

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[6]. While there has been a trend to remove the word 'woman/women' and use 'gender neutral' language in policy and practice in relation to women's reproductive health and wellbeing, there is no evidence base to inform this change.[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. Finally, all those using maternal and reproductive health care and services should receive individualised, respectful care including use of the gender nouns and pronouns they prefer.[7]

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.

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1.9 Adopting a trauma-informed approach to maternity care

Many women accessing maternity services may have experienced historical or current trauma prior to, or during pregnancy – including emotional, physical, sexual abuse, rape and torture. The perinatal period (pregnancy, birth and the postpartum) can be a time when previous trauma is triggered[11]. Maternity care procedures which may seem routine and 'non-invasive' to healthcare professionals (HCPs), e.g. abdominal palpation or providing breastfeeding support can be triggering for some women with a history of trauma, as can intimate procedures such as vaginal examinations[12].

Trauma-informed care (TIC) is a developing approach to healthcare which recognises the importance of psychological safety, and the need to prevent or resist re-traumatisation of individuals[13]. It is based on 4 key principles (known as the 4Rs): (1) realisation of trauma; (2) recognition of trauma; (3) responding to trauma and (4) resisting re-traumatisation[14,]. A trauma-informed approach to maternity care means that all staff in an organisation have an understanding of the impact of trauma on individuals, families and organisations[15]. While a universal approach is yet to be agreed, within clinical practice and research, many organisations recognise the need to move towards becoming trauma-informed in the provision of maternity care[15, 16]. Such an approach requires commitment, investment and transformation within maternity services.

In simple terms, HCPs should recognise the impact of women's previous or current history of trauma (whether disclosed or not) and adopt a universally sensitive approach to care provision that recognises the impact of trauma on service users and HCPs. Examples of this include ensuring clear communication and consent is sought before any procedures/interventions, ensuring women are provided with dignity and respect at all times.

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Chapter 2: Clinical Practice Guideline

Background

Nausea and vomiting of pregnancy (NVP) affects 70-90% of pregnancies [1]. There is spectrum of severity of NVP, ranging from mild symptoms of nausea to an extreme form known as hyperemesis gravidarum. Recent consensus by the Windsor group (patients, researchers, and clinicians) defined hyperemesis gravidarum as a severe form of nausea and/or vomiting that may require treatment in hospital, an inability to eat or drink normally and a significant impact of symptoms on activities of daily living [2]. In this Guideline we will use the terms NVP and HG and will introduce tools that are used to categorise the severity of symptoms and guide treatment.

Inadequate oral intake or excessive vomiting may lead to dehydration, ketosis, electrolyte imbalance, thyrotoxicosis and in some cases vitamin deficiency in pregnancy [3]. HG is estimated to occur between approximately 0.3% and 3.6% of all pregnancies, although this figure is likely to be much higher if self-reporting is used. [4] Symptoms typically start between 5 and 10 weeks of gestation and 90% of cases will resolve by 20 weeks' gestation [5]. Up to 10% of women will continue to have symptoms for the duration of pregnancy [6].

Despite advances and improved access to medical treatment, complications of HG may occur, including nutritional deficiencies, gastrointestinal issues, neurological sequelae, electrolyte imbalances, vitamin K deficiency and Wernicke's encephalopathy [7].

A recent systematic review investigating long-term health outcomes of children born to mothers with hyperemesis gravidarum suggests a small increase in adverse outcomes in neonates including neurodevelopmental disorders such as attention deficit disorder and autism spectrum disorder and behavioural disorders [8,9].

The exact cause of nausea and vomiting in pregnancy is unknown though there are potential predictive factors. Associated factors include multiple fetus pregnancy, previous history of HG and gestational trophoblastic disease [5]. A 2019 systematic review of 308 articles of which 14 observational studies were included and involved 1400 women aimed to highlight prognostic factors associated with the development of HG [10] The included studies were highly heterogenous which meant that meta-analysis was not possible. The results of studies differed and were sometimes conflicting. There are several factors that have historically been associated with hyperemesis gravidarum, including Helicobacter pylori infection, genetic predisposition, and a history of HG in previous pregnancies. While these may represent potential risk factors, the study authors concluded that further research is required.

Recent research has highlighted other potential mechanisms that may contribute to the development of HG. The hormone GDF15 can be released because of environmental stressors as well as certain medications such as metformin [11]. GDF15 exerts its effect at the GFRAL-RET receptor located in the hindbrain, activation causes reduced food intake and loss of body weight. In pregnancy production of the GDF15 hormone can be increased dramatically by trophoblast cells causing additional symptoms such as severe nausea and vomiting. Research into specific alleles of GDF-15 has highlighted versions of the gene which result in increased risk of HG recurring by up to eight times [11]. The identification of the GDF15 hormone and GEFRAL-RET pathway has opened the door to the development of novel targeted therapeutics.

Recommendations relevant to this Guideline can also be found in:

- National Clinical Practice Guideline: Investigation and Management of Complications of Early Termination of Pregnancy [17]
- Clinical Practice Guideline: Nutrition during pregnancy [18]
- National Clinical Guideline: Fetal Growth Restriction – Recognition, Diagnosis and Management [19]
- National Clinical Practice Guideline: Prevention and Management of Venous Thromboembolism in Pregnancy [20]
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Section 1: Definitions and Diagnosis

Introduction

An appropriate diagnosis in women presenting with NVP helps to guide treatment. In addition, it is important to recognise when NVP develops into HG as this may require referral to tertiary care, regular outpatient treatment and monitoring, and at times hospital admission.

Clinical Question 2.1: What are the definitions of nausea and vomiting of pregnancy (NVP) and hyperemesis gravidarum (HG), and how are they diagnosed?

Evidence Statement

Although there is no precise definition for NVP, it is generally accepted as nausea and vomiting with an onset prior to 16 weeks' gestation for which other causes of nausea and vomiting have been excluded. The definition of HG varies but includes severity of symptoms, such as inability to tolerate oral intake due to symptoms, and limitation of activities of daily living, often with signs of dehydration [2,12]. Further criteria include weight-loss of at least 5% pre-pregnancy weight, clinical dehydration and/or electrolyte imbalance [12]. In the Windsor definition, signs of dehydration were deemed contributory but not an essential part of the definition for HG [2]. Other considerations could include objective measures of acute starvation such as carbohydrate depletion, electrolyte imbalance, and/or acid-base disturbance [12,13].

A thorough clinical assessment should be carried out to investigate other causes of NVP, particularly in those with a first presentation after 10-16 weeks' gestation, in whom an alternative diagnosis is more likely [12,14].

Clinical Practice

Potential differential diagnoses include:

- Urinary tract infection
- Gastrointestinal (for example, infection including Helicobacter pylori, reflux oesophagitis, gastritis, cholecystitis, peptic ulceration, hepatitis, appendicitis, pancreatitis, complications after bariatric surgery)
- Neurological (for example, migraine, raised Intracranial pressure, central nervous system diseases)
- Molar pregnancy
- Ear, nose, and throat disease (for example, labyrinthitis, Ménière's disease, vestibular dysfunction)
- Drugs and supplements (such as opioids and iron – some prenatal multivitamin preparations contain iron which may exacerbate NVP)
- Metabolic and endocrine disorders (such as hypercalcaemia, Addison's disease, uraemia, and thyrotoxicosis)
- Persistent vomiting in diabetic women which may suggest autonomic neuropathy
- Psychological disorders (such as eating disorders).

Recommendations

1. **We recommend NVP be defined as nausea, vomiting and/or dry-retching caused by pregnancy, with symptoms commencing in the first trimester without an alternate diagnosis.**
2. **We recommend that diagnosis of HG should be given based on onset of severe nausea and/or vomiting in early gestation (before 10-16 weeks' gestation) that affects ability to eat and drink normally and strongly impacts activities of daily living, considering clinical picture and potential differential diagnoses. Signs of dehydration should be considered but are not necessary for diagnosis.**

Clinical Question 2.2: What tools are available to determine the severity of NVP and HG?

Evidence Statement

Classification of symptom severity in NVP and HG is important to guide treatment. Identification of clinical risks can promote optimal health and guide treatment to minimise adverse effects. Validated scoring tools can be used in the assessment of women with symptoms of NVP and HG to aid in further management and appropriate level of care. The Pregnancy Unique Quantification of Emesis and Nausea) PUQE score and HELP tool are two scoring tools which may be useful in the management of NVP and HG [15,16].

The PUQE (Pregnancy Unique Quantification of Emesis and Nausea) scoring index was developed in Canada by the Motherisk group [15]. It is a condition-specific assessment tool to determine the severity of NVP based on duration of nausea, and frequency of vomiting and dry retching symptoms, and takes into account feelings of well-being [17,18]. It was originally validated against the Rhodes index of Nausea, vomiting and retching to assess nausea and vomiting over the previous 12 hours but later adapted and validated to assess 24 hours [19]. A 2023 study including 2343 women found that retrospective completion of the PUQE score based on recalling the most severe first trimester 12-hour episode of symptoms later in gestation accurately captured severity when compared to the same assessment done at the time of worst symptoms [20]. This suggests that robustness of recall of symptoms using the PUQE score across a range of time points.

The HyperEmesis Level Prediction (HELP) tool is another available resource suggested to be of value in delineating severity and managing severe symptoms however there is limited research in its validity [16 20]. The HELP tool was developed by the Hyperemesis Education Research (HER) foundation to more widely assess respondents' symptoms and prevent underestimation of disease severity. The additional questions to the PUQE of nausea and vomiting, dry-retching and wellbeing in the HELP tool include urination, weight loss, ability to work, coping, and ability to consume and retain food, fluids, and medications. It also compares symptoms to the previous week. A 2021 study which is the only study to date to compare the PUQE and HELP scores found that when compared to the PUQE scoring tool, HELP classified more women as having severe symptoms. Specifically, women who answered "nothing goes or stays down" were classed as severe in 92% of cases with HELP and 58% with PUQE [16]. Women who had an inpatient stay or self-categorised their own symptoms as severe were also more likely to be classified as severe using HELP.

The HELP tool is based on a low level of evidence from a single validation study including 445 women recruited through the foundation's social media. There was a high level of missing data and medical records were not accessed, and there is likely a high level of selection bias. It is only validated for those with severe HG and its utility in those with more mild forms of NVP is unclear. There are several studies employing the PUQE score in HG [21] showing relationships with ability to take multivitamins, suboptimal oral intake, rates of emergency room visits and hospitalisation, health costs, physical and mental well-being and healthy-related quality of life [22,23].

International guidance from the Royal College of Obstetrics and Gynaecology (RCOG), American College of Obstetrics and Gynaecology (ACOG) and the Society of Obstetric Medicine of Australia and New Zealand (SOMANZ) all recommend use of Pregnancy-Unique Quantification of Emesis and Nausea (PUQE) score for objective assessment of women with HG [19,24,25].

Clinical Practice

The PUQE score should be used to assess symptom severity. This should not be done in isolation and consideration should be given to other factors such as comorbidities, impact of symptoms on daily living and wellbeing, oral intake, fluid intake, ability to take medications (particularly those with low therapeutic window such as anti-epileptic, anti-retroviral or immunosuppressant medications), hydration status which could include objective measures of urinalysis, weight and weight loss and blood tests as indicated. The PUQE assessment tool should be readily available in clinical areas where women with NVP and HG present.

The Pregnancy-Unique Quantification of Emesis and Nausea scored over 24Hours (PUQE-24) was originally designed to assess symptoms in the last 24 hours. This may be useful in guiding hospital admissions. The modified PUQE score looks at the same questions but on "an average day". Identification of severity will aid in decision-making regarding appropriate location of further care, alongside clinical judgement, and assessment of clinical risks. Consideration could be given to the HELP tool (Appendix 3) though more research is needed. Alongside the PUQE score, the content of the HELP tool such as hydration, weight loss, quality of life and progression of symptoms should be included as part of a routine assessments of women with HG.

Figure 1: Modified PUQE Score

1. On average in a day, for how long have you felt nauseated or sick to your stomach?

Symptom	Not at all	1 hour or less	2-3 hours	4-6 hours	> 6 hours
Score	(1)	(2)	(3)	(4)	(5)

2. On average in a day, have you vomited or thrown up...

Symptom	7+ times	5-6 times	3-4 times	1-2 times	Did not throw up
Score	(5)	(4)	(3)	(2)	(1)

3. On average in a day, how many times have you had retching or dry heaves without bringing anything up?

Symptom	Not at all	1-2	3-4	5-6	7 or more
Score	(1)	(2)	(3)	(4)	(5)

Total Score from questions 1-3: _____ Key: Mild ≤ 6 Moderate 7-12 Severe ≥ 13

On a scale of 0 to 10, how would you rate your well-being?
(0= worst possible, 10 = best you felt before pregnancy)

In addition to the PUQE, a thorough history and investigation should be completed as required, including:

- Identification of comorbidities (e.g. epilepsy or diabetes mellitus) and ability to take medications (especially those with narrow therapeutic window)
- Assessment of impact of symptoms on oral intake and daily living. Note that individuals may reduce intake and activities of daily living to manage symptoms.
- Measure weight and record in chart. Ask about pre-pregnancy weight and weight loss. Record height for calculation of body mass index.
- Assess for reflux and bowel function (including constipation).
- Assess for impact of physical functioning
- Assess psychological state and well-being and need for involvement of perinatal mental health services.
- Additional assessment as needed such as mid-stream urine for urinalysis (Specific gravity for hydration, ketonuria for oral intake or culture and sensitivity – for further details refer to Clinical Question 2.3) or serum investigations (full blood count, urea and electrolytes, Calcium, Phosphate, Magnesium)
- Consider liver Function testing to exclude alternative diagnoses.

- Reserve thyroid function tests for those with clinical signs or symptoms of hyperthyroidism.
- Consider need for referral for ultrasound assessment to confirm viability and assess for multiple pregnancy or molar pregnancy.

Recommendations

3. **We recommend that the PUQE scoring system is used to assess severity of NVP and HG symptoms, alongside a thorough history.**
4. **We recommend ultrasound assessment at the appropriate timing by trained staff to outrule multiple pregnancy and molar pregnancy**

Section 2: Initial Assessment and Investigations

Introduction

Adequate hydration is essential for a healthy pregnancy, with fluid requirements estimated at approximately 2,300 mL per day [26]. However, women with HG often struggle to meet this requirement due to nausea, fluid aversions and excessive losses from vomiting or ptyalism (hypersalivation). Hydration status can be evaluated using various methods [27,28]. Rather than providing an in-depth analysis of these methods, this section offers a practical overview of clinically relevant markers that can aid in assessing hydration status in women with HG.

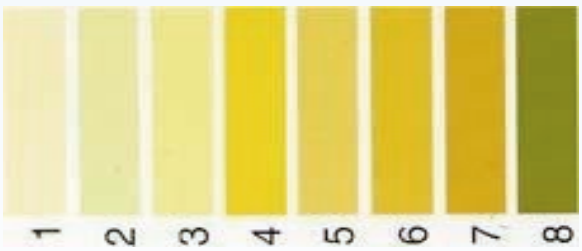
Clinical Question 2.3: How should hydration be assessed amongst those with Hyperemesis Gravidarum?

Evidence Statement

Urine colour

A prospective study of 18 pregnant and lactating women, along with 18 age-matched controls, found that urine colour from a single sample can accurately reflect 24-hour urine osmolality values indicative of dehydration (≥500 mOsm·kg^{-1}) [29]. Urine osmolality was determined using freezing point depression, while urine colour was assessed by placing the sample in a clear container against a white background and comparing it to the Armstrong urinary colour chart, a widely cited tool in hydration assessment [30], see Figure 2.

Figure 2: *Armstrong urine colour chart*



Urination frequency serves as a practical hydration marker, with a minimum of 3-4 voids per day suggesting adequate fluid intake [31]. However, relying on thirst as an indicator of hydration is unreliable, as mild dehydration can trigger thirst, making it an imprecise measure of hydration status [32].

Urine specific gravity, which measures the concentration of solutes in urine, is a well-established screening tool for dehydration in various fields [33]. It has shown strong agreement with other hydration markers, such as urine osmolality [33]. In pregnancy, urine specific gravity remains a reliable measure of hydration with minimal diurnal variation, though it may be slightly higher in individuals with a BMI >25 kg/m^2 [34]. Suggested cut-off values indicate that a urine specific gravity of ≤1.020 g·mL^{-1} reflects adequate hydration, while values ≥1.025 g·mL^{-1} suggest dehydration [34]. While standardised pregnancy-specific reference values have not been established, clinical audits from two major maternity hospitals in Dublin, The National Maternity Hospital and The Rotunda Hospital, support its use in assessing hydration among women with HG. Further research is needed in this area and limitations should be considered.

Ketone bodies are not a measure of hydration, they are the product of lipolysis, produced by the liver and used as an alternative fuel when glucose is not readily available [35]. Their presence is usually associated with starvation or suboptimal nutrition, however, ketonuria has been found to occur sporadically in about 1 in 5 pregnancies [36]. Recently a body of evidence has been published describing the inappropriate use of ketonuria for the assessment of hydration or HG severity. A meta-analysis exploring diagnostic markers of HG did not find an association between ketonuria and HG and therefore could not support its use as a diagnostic marker of HG [37]. Data from an observational study among women with HG in the Netherlands suggested that there is no association between the degree of ketonuria at admission and severity of symptoms, quality of life, maternal weight loss, or number of readmissions [38]. They were, however, associated with length of stay suggesting that healthcare professionals were using ketonuria to determine when a woman was suitable for discharge. Ketonuria may also result in symptoms such as nausea, vomiting and diarrhoea, with potential to cause/worsen dehydration. Meta-analysis has shown ketonuria is not associated with diagnosis or severity of HG, although it can give an indication of the adequacy of dietary intake [37]. Ketonuria is not a measure of hydration. Other urinary measures can be used as described above [30]. Ketones therefore are a useful assessment tool in NVP and HG, but not as a marker of hydration status specifically.

Clinical Practice

Fluid balance chart

Assess hydration status in the past 24 hours using a fluid balance chart in settings where this is feasible (e.g. inpatient settings). Input should include all oral, enteral and intravenous fluids, and output should include all fluid losses including urine and vomit volume. In outpatient settings, consider asking about fluid intake and frequency of urination.

Clinical assessment

Assessment of clinical signs of dehydration include vital signs, capillary refill time, tissue turgor and the amount and colour of the urine. Note that checking for moist mucous membranes may not be accurate as ptyalism, or hypersalivation, may be present, moistening the membranes. Urine colour may be measured by collecting a urine sample and comparing the colour of the urine sample to a colour chart, such as the Armstrong urinary colour chart in Figure 4. Urine colours range from very pale yellow to brownish green, with 1-3 indicating adequate hydration and 4-6 indicating moderate dehydration and 7-8 severe dehydration. Urine specific gravity is a clinically useful, pragmatic, and low-cost hydration assessment that can be measured with a refractometer or multipanel urine dipsticks at point of care, if available. Additional assessment as outlined in clinical question 2.2.

Recommendations

5. **We recommend that a hydration assessment should be conducted, including fluid balance in the past 24 hours, urine colour and clinical signs of dehydration. Urine specific gravity may be considered.**
6. **We do not recommend the use of ketonuria to assess hydration.**

Section 3: Fluid and Electrolyte Management

Introduction

NVP and HG are associated with dehydration. Intravenous fluids are often an integral part of management; this question aims to guide intravenous fluid rehydration.

Clinical Question 2.4: What is the recommended IV fluid rehydration schedule?

Evidence Statement

There is limited evidence describing the effectiveness of intravenous fluids in treating hyperemesis gravidarum. There is a lack of consensus as to the optimal form of intravenous fluid rehydration therapy, with each strategy having potential drawbacks. Preparations containing sodium chloride 0.9% are preferable. Higher concentrations and fast rates of infusion should be avoided in hyponatraemia as too rapid correction of sodium deficiency can cause osmotic demyelination syndrome [5,39,40]. This condition has also been described in the context of HG [41-43]. The rate of intravenous infusions can affect tolerance.

In cases where women may not be able to tolerate oral fluids due to persistent nausea and/or vomiting, they are likely to require intravenous rehydration in an ambulatory setting or as an inpatient [19,44]. There has been limited research published aiming to assess the optimal treatment strategy for dehydration in hyperemesis gravidarum. Several trials have aimed to assess the effects of different fluid regimes for rehydration and electrolyte correction in hyperemesis gravidarum. For example, 5% dextrose-0.9% saline solution has been compared against 0.9% saline solution in a double-blind trial for rehydration in hyperemesis gravidarum where 222 participants were randomised [45]. Study authors concluded that both solutions produced similar outcomes. Most recently an Indonesian double-blind randomised controlled trial included 66 women with hyperemesis gravidarum who were assigned to receive either the 5% dextrose-Ringer's lactate or Ringer's lactate by intravenous infusion at a rate of 125 mL/hour over 24 hours [46]. The authors concluded that both rehydration fluids produced similar outcomes however there was a greater mean increase in blood potassium levels in the 5% dextrose-Ringer's lactate group. Note however, there are risks to dextrose provision without adequate thiamine repletion. Starvation from persistent vomiting depletes the body of thiamine. Administration of fluids containing dextrose increases the body's demands on thiamine to metabolise dextrose. In an individual that is thiamine deficient, administration of dextrose may precipitate Wernicke's encephalopathy, a severe condition with potentially irreversible and chronic implications (see Clinical Question 2.7) [47-49]. Intravenous fluids containing dextrose should be used with caution in patients with hyperemesis gravidarum. The RCOG guidelines recommend normal saline with additional potassium chloride as the most appropriate intravenous hydration [19]. The Society of Obstetric Medicine of Australia and New Zealand (SOMANZ) recommendations for parenteral replacement of intravenous fluids and electrolytes are outlined in the table below [24].

Clinical Practice

If IV is fluid is required, commence infusion of 1,000 mL of 0.9% NaCl or Hartmann's. See fluid rehydration table below for further details. The volume of fluid administered should be sufficient to replenish any deficiencies as well as any fluid that may continue to be lost through additional vomiting. Intravenous fluids should be discontinued when the woman is able to tolerate oral fluids and when adequately hydrated. Intravenous fluids should assist women with meeting normal fluid and electrolyte requirements where possible.

An adapted table from SOMANZ recommendations is displayed below:

Table 1: *Recommendations for parenteral replacement of intravenous fluids and electrolytes, adapted from SOMANZ* [24]

Type of fluid *	Quantity/Rate	Comments
0.9% sodium chloride or Compound Sodium Lactate (Hartmann's Solution)	1-2 Litres. Initial rate 1L/hour	Further IV fluids should be given at a rate of 1L/1-2 hours or slower to correct dehydration and electrolytes (see below) Infusion rate may need to be decreased if there are tolerability issues.
Give electrolytes as required – use pre-mixed bags when possible.		
Potassium chloride	20-40 mmol/L running at 125ml/hour	Administer with caution as per local protocol and maximum concentration/infusion rates. Preferred product is premixed 20mmol potassium chloride in 0.9% sodium chloride. Use peripheral vein or central venous access as required.
Magnesium sulphate	Up to 4g (16mmol/L) of magnesium sulphate over a minimum of 4 hours	Where possible use premixed magnesium bags. Use peripheral vein or central venous access as required.
(*)5% dextrose could be considered if minimal oral intake, starvation or uncontrolled nausea but this must be used **only after correction of Thiamine deficiency** and exclusion of hyponatremia.		

Caveats to electrolyte treatment scenarios in the guidelines include the woman's ability to tolerate oral doses of electrolytes due to nausea and vomiting. Consider the tolerability of oral dosing regimens to replace electrolytes which can involve effervescent tablets which can be difficult to tolerate even without conditions such as hyperemesis. Therefore, intravenous replacement may need to be considered even in mild cases of electrolyte deficits.

Medication Safety

Potassium is a high alert medication. Ready-mixed potassium infusions should be used. Please follow local guidelines on electrolyte replacement.

Recommendations

7. We recommended considering IV provision of fluid and electrolytes if patient cannot tolerate oral intake and or clinical signs of dehydration.
8. We recommend caution if using dextrose-containing IV fluids due to the risk of thiamine deficiency, refeeding syndrome and Wernicke's encephalopathy

Section 4: Inpatient vs Outpatient Management and Risk Prevention

Introduction

The management of NVP/HG should be in a stepwise fashion, according to disease severity and individualised accordingly. Some women with milder forms of HG will be able to be managed appropriately and adequately in the community by their GP or community midwifery team, others may require early referral to tertiary care where they may be managed on an outpatient basis, and those with more severe HG or with additional medical risk factors may require hospitalisation for inpatient management for stabilisation prior to being discharged and returning to outpatient management. As HG is a condition with a wide spectrum of severity, women may go through periods where they require more intense management.

Clinical Question 2.5: How should women with HG be managed?

Evidence Statement

As most women with NVP have mild symptoms and require only oral anti-emetics it is appropriate for them to be managed in the community.

A 2017 RCT including 152 women with severe HG found that ambulatory or outpatient management was an effective alternative to inpatient management [50]. In some cases, frequent outpatient appointments for management on a day ward or similar area can offer similar results in terms of return to oral diet, reduction in PUQE score and readmission, and may be a more acceptable option to the individual rather than a prolonged admission.

Women with severe HG or persistent symptoms into the late second or third trimester are at risk of intrauterine growth restriction/small for gestational age fetal growth and low birth weight [9,51,52]. Women who have an inpatient stay are also at risk of venous thromboembolism (VTE) due to lack of mobility and hypercoagulability due to severe dehydration [19].

Clinical Practice

Clinical judgement should be used in all decision-making regarding need for admission to hospital, refer to algorithm in this Guideline for guidance.. Most women can be managed on an outpatient basis in the community, however those with more severe HG may require management on a day ward or as an inpatient. VTE risk assessment should be performed as per local or national guidelines and thromboprophylaxis prescribed if indicated. Consider if appropriate to set up frequent outpatient management where available for severe HG as it may offer similar results in hydration status and return to oral diet to admission and may be more acceptable to the woman. The PUQE score has been validated as a measure of severity of NVP and HG and is recommended as a tool to guide management decisions.

Recommendations

9. **We recommend that consideration is given for inpatient versus outpatient management based on severity of symptoms, clinical risks, comorbidities, preferences of the woman and available resources.**
10. **We recommend regular assessment for risk factors for venous thromboembolism and consideration of thromboprophylaxis as appropriate. All patients admitted for management of HG should have a risk assessment performed as per local hospital guidelines.**
11. **We recommend that pregnant women with persistent HG should have regular fetal growth assessment, with at least one formal ultrasound to assess fetal growth in the third trimester.**

Section 5: Medical Management

Introduction

There are a variety of treatment options that may reduce emesis and nausea and improve quality of life. Treatment should be offered where indicated based on severity of NVP and HG as measured by the woman's PUQE score. Concerns about the safety of medicines in pregnancy may limit willingness to prescribe or use medicines, leading to severe symptoms and potential short and long-term complications.

MBRRACE reports repeatedly include deaths in women with hyperemesis [53]. Pregnant people need clear, accurate information on the safe and effective use of medicines in pregnancy. Pregnant people obtain information on medication use for NVP and HG from a variety of sources including midwives, doctors, community pharmacists, and social media [54]. Not all will take medications, with studies reporting medication use between 12% to 39% to 72% of women with NVP [55-57]. Some may choose not to take medications for NVP and HG that are prescribed for them – in one study population-based registry study from Norway, the overall rate of filled prescriptions for NVP and HG was 7.6%, though this did increase to 10% by the end of the study period [58]. In contrast, an online study of pregnant women in Australia showed that one quarter were denied medications for NVP and HG [54]. Women who reported being denied a medication were more likely to have completed secondary school, have received a formal HG diagnosis during pregnancy and have experienced three or more pregnancies affected by severe NVP and HG.

Chronic or excessive marijuana use during pregnancy can induce Cannabis Hyperemesis Syndrome (CHS). Hyperemesis cannabinoid syndrome may lead to a cascade of medication treatments that are unlikely to be effective. Awareness and recognition of this syndrome may prompt early and effective management, avoidance of unnecessary workup and cost reduction, and reduce frustration with ineffective treatment [59,60].

Clinical Question 2.6: What medications are recommended for the management of NVP and HG?

Evidence Statement

Women with severe nausea and vomiting in pregnancy may struggle to tolerate oral dosages of medication. Therefore, alternative routes of administration may need to be explored such intravenous, subcutaneous, intramuscular or rectal [19]. A range of medications used for hyperemesis may cause acute dystonic reactions, particularly metoclopramide and prochlorperazine [61]. These reactions are characterised by involuntary contractions of muscles of the extremities, face, neck, abdomen, pelvis, or larynx in either sustained or intermittent patterns that lead to abnormal movements or postures. These reactions can be very distressing and require specialist assessment and management. Administration of procyclidine can rapidly stop an acute dystonic reaction. For complete information on adverse effects, please consult product literature.

Doxylamine/pyridoxine

Mechanism of action

Doxylamine exerts its antiemetic effect primarily through its antagonism of H1 receptors though it does also have some effect as a muscarinic receptor antagonist [62].

Background and Safety

Doxylamine-Pyridoxine was withdrawn from the market in the United States in 1983 due to concerns associating the medication with fetal anomalies. It remained on the market in other countries. The withdrawal decision was made by the company despite two independent systematic reviews showing no association with fetal anomalies [63,64]. There was no fall in the rate of fetal anomalies following withdrawal of the medication and a significant rise in the rate of hospitalisation for hyperemesis [65,66]. Later studies showed no difference in the rate of fetal abnormalities between exposed and un-exposed groups [67-70] and as a result the medication was licenced for use in pregnancy in the United States in 2014 [71] and in Ireland in 2024 [72].

Evidence for doxylamine-pyridoxine

Pyridoxine (Vitamin B6) alone [73]: Studies of pyridoxine alone show either an improvement in nausea score but no change in vomiting rate [73] or no difference in hospitalisation rate, nausea score or vomiting rate (versus placebo, both given with metoclopramide) [74] or a slightly longer hospital stay (versus placebo). A higher dose of pyridoxine (10mg) may be more effective than lower dose (1.28 mg) in reducing PUQE score [75].

Doxylamine (antihistamine) alone: One case-control study showed worse obstetric outcomes if women with NVP and HG were prescribed antihistamines [76]; while the authors suggested this may be an effect of the medications, an alternative hypothesis would be that need for medications may suggest more severe disease which in turn would predict worse outcomes. Maternal exposure to H1 antihistamines have not been shown to increase the risk of major fetal malformations, nor preterm birth, miscarriage, or stillbirth [68].

Combination doxylamine-pyridoxine: Systematic reviews have shown that doxylamine-pyridoxine improves symptoms for women with moderate symptoms compared to placebo [77]. If doxylamine-pyridoxine is taken pre-emptively prior to symptoms it reduces the recurrence risk of moderate-severe symptoms compared to waiting until symptoms begin [78]. These studies were also reported in a health economic systematic review published in 2016 [77], with two studies having a low risk of bias and overall all four studies downgraded to low quality due to clinical heterogeneity.

Improvement in symptoms with doxylamine-pyridoxine were reported in 70-80% of women, though there were no statistical differences when compared to placebo [79]. A randomised controlled trial of doxylamine-pyridoxine showed a significant fall in PUQE scores and improvement in quality of life with the medication compared to control [80].

Promethazine [81]

Mechanism of Action

Promethazine is a H1 receptor antagonist but also acts as a weak dopamine agonist [82]. It is thought to affect the vestibular system decreasing stimulation of the vomiting centre [24].

Background and Safety

There is extensive historical experience of promethazine use in NVP and HG [83,84]. More recent studies provide reassuring data on pregnancy outcomes after early pregnancy promethazine exposure [85,86].

Effectiveness

A Cochrane review examined interventions which aimed to treat hyperemesis gravidarum [87]. Treatment with promethazine was compared to other anti-emetics including metoclopramide [88], ondansetron [89] and corticosteroids [90,91]. The review could not establish the superiority of one treatment over another due to a lack of placebo-controlled trials. In one of the studies drowsiness, dizziness, dystonia and medication discontinuation were reported more frequently with promethazine in a RCT comparing interventions for NVP and HG [89]. Prescribers should be aware that promethazine may reduce the seizure threshold and therefore other anti-emetics should be chosen in patients with epilepsy [82].

Parenteral administration of promethazine has been associated with serious tissue injuries and amputations from the inadvertent arterial injection or IV extravasation. The Institute for Safe Medication Practise (ISMP) recommends removing it from hospital formularies and suggests the use of safer alternatives [92].

Prochlorperazine [93]

Mechanism of Action

Prochlorperazine is a first-generation anti-psychotic, its anti-emetic properties are mediated through its antagonism of dopamine receptors [82].

Background and safety

Data from two cohort studies with a total of approximately 1500 exposed pregnancies did not indicate that prochlorperazine exposure was associated with congenital anomalies [94]. A US study indicated that prochlorperazine is commonly prescribed in pregnancy, though less commonly than promethazine (1.1% vs. 10.9% of all deliveries) [95]. Prochlorperazine may lower the seizure threshold meaning other antiemetics should be chosen in patients with epilepsy [82]. It is also associated with acute dystonic reactions.

Effectiveness

Reviews examining the effectiveness of phenothiazines which have included prochlorperazine have demonstrated their effectiveness in treating hyperemesis gravidarum in placebo-controlled trials [67,96].

Chlorpromazine [97]

Mechanism of action

Chlorpromazine is a phenothiazine licensed for anxiety, agitation, depression, behavioural disturbances, and in the management of schizophrenia. It exerts its anti-emetic effects via its combined blockade of histamine (H1), dopamine (D2) and muscarinic (M1) receptors in the vomiting centre [98].

Background and safety

Maternal chlorpromazine use has not shown an increase in malformations in offspring, though exposure in the third trimester my cause transient complications such as dystonic reactions [96,99]. Larger register-based studies supporting the use of medications in pregnancy are lacking in comparison to other anti-emetics.

Effectiveness

The use of phenothiazines has been reviewed in both a Cochrane review [87] as well as additional reviews confirming that chlorpromazine is an effective anti-emetic in the context of hyperemesis gravidarum [96,99]. Its use tends to be reserved for cases of severe and refractory hyperemesis gravidarum where other anti-emetics have failed and there are additional psychiatric diagnoses [100].

Cyclizine [101]

Mechanism of action

Cyclizine exerts its antiemetic effect as both a H1 and muscarinic receptor antagonist.

Safety

Cyclizine is a commonly prescribed antiemetic for NVP and HG in the UK [102]. Data are available from the Swedish Medical Birth Register on pregnancy outcomes for over 2000 women who used cyclizine in early pregnancy [103]. No association between cyclizine use in early pregnancy and congenital anomalies was found.

Effectiveness

Cyclizine's effectiveness in treating NVP and HG has been documented in a Cochrane review [87] as well as additional reviews [96,99].

Ondansetron [104]

Mechanism of action

Ondansetron exerts its antiemetic effect as a selective serotonin receptor (5-HT3) antagonist acting at receptors both centrally and peripherally. Central effects are mediated in the chemoreceptor trigger zone. Peripheral effects are mediated directly by 5-HT3 action at the vagus nerve terminals [105]. As a 5-HT3 receptor antagonist, ondansetron commonly causes constipation, in cases of administration over longer time periods use has very rarely led to intestinal obstruction. It is recommended that healthcare professionals should ensure increased fluid intake and consider the use of laxatives [106,107].

Background and safety

Ondansetron is an effective antiemetic in the context of NVP and HG. A double-blind, randomised, controlled trial that randomised 36 women to either ondansetron 4 mg or doxylamine (12.5 mg)/ pyridoxine(25 mg) found that ondansetron was more effective in terms of reductions in nausea and emesis [108]. Use of ondansetron in pregnancy has been increasing over the last 20 years [109,110].

The challenges to interpreting the data relating to harms from ondansetron use in pregnancy have been well documented [111]. Several studies have provided reassuring data on gestational ondansetron exposure [112-114]. Systematic reviews have highlighted that the risk of abnormal pregnancy outcomes is low with ondansetron exposure [115-117]. Some studies have suggested an association between first trimester ondansetron exposure, cleft palate [85,118] and possibly cardiovascular defects [118-120].

More recently two large studies from the US have published conflicting results related to risk of ondansetron exposure in pregnancy and risk of various malformations. Firstly, the larger of the two studies by Huybrechts et al, which is the largest study of gestational ondansetron use to date, used US Medicaid data from more than 1.8 million pregnancies between 2000 and 2013 [121]. The study analysed the association between maternal first-trimester ondansetron use (n=88,467) and cardiac malformations or oral clefts in offspring using a retrospective cohort design. The study highlighted that ondansetron dispensing in the first trimester of pregnancy increased during the 13-year study period from less than 1% in the year 2000 and peaking at approximately 13% in 2012. The analysis found that there was no association between ondansetron exposure and cardiac or other congenital malformations. Increases in oral cleft were observed in offspring that were exposed to ondansetron in the first trimester. The increase was equivalent to three additional cases per 10,000 women when compared to unexposed pregnancies. It is unclear if this increase was due to the ondansetron or the underlying maternal condition.

Secondly, Zambelli-Weiner *et al.* examined 864,083 mother baby pairs and concluded that ondansetron use in the first trimester was associated with increased risk of both cardiac malformations as well as oral cleft compared with pregnancies without ondansetron exposure [118]. Four out of the five study authors worked at the TTi Health Research & Economics in Hampstead, Maryland. Declarations under conflicts of interest included that the 'TTi reports receiving funds from plaintiff law firms involved in ondansetron litigation and a manufacturer of ondansetron'. The study has been embroiled in controversy since it emerged that the TTi was receiving funding from a plaintiff firm whilst Zambelli-Weiner was working with the same firm as a consultant supporting allegations raised by plaintiffs in litigation against the manufacturer of ondansetron.

Furthermore, statements in the discussion of the Zambelli-Weiner *et al.* paper appear to point out that intravenous ondansetron use might increase the risk of malformations. This prompted Huybrechts *et al.* to follow up their study examining intravenous ondansetron use and congenital malformations using the same retrospective cohort study methods [122]. Analysis of the same 1.8 million pregnancy dataset indicated that intravenous ondansetron use (n= 23,866) was not associated with an increase in the risk of oral clefts, cardiac malformations or congenital malformations in the study population. The adjusted RR for cardiac malformations was 0.97 (95% CI, 0.86-1.10). For oral clefts, the adjusted RR was 0.95 (95% CI, 0.63-1.43). For malformations overall, the RR was 1.02 (95% CI, 0.96-1.08). The risk of oral clefts was lower for pregnancies exposed to intravenous ondansetron use than in the non-exposed. An advantage of studying IV ondansetron exposure is that there is a high degree of certainty that the dose was administered increasing the specificity of the findings. In comparison, dispensing claims data only highlights that the medication was claimed for after dispensing and sheds little light on adherence to oral ondansetron treatment.

Pregnancy outcomes of individuals treated with ondansetron or alternative antiemetic medications were recently examined in a multinational population-based cohort [123]. The study included 456,963 pregnancies and examined outcomes including, spontaneous abortion or stillbirth as well as congenital malformations. Ondansetron was compared to alternative antiemetic medications to minimise confounding by indication. The study found no association between ondansetron exposure during pregnancy and increased risk of fetal death, spontaneous abortion, stillbirth, or major congenital malformations in comparison to exposure to other antiemetic use.

The results of the research described above should feature as counselling points to women with NVP and HG on choice of antiemetics. Ondansetron is one of the medications with the most extensively studied safety profiles in pregnancy. Multiple population-based studies have indicated that its use in pregnancy is safe. There is a signal indicating that it may be associated with oral clefts. The biggest study to date indicated that this is equivalent to three additional cases of oral cleft per 10,000 women when compared to unexposed pregnancies. It is unclear if this increase was due to the ondansetron or the underlying maternal condition.

Ondansetron may be considered as a first-line treatment for severe NVP and HG. Guidance is available on how to contextualise potential risks of ondansetron use in pregnancy, along with visual risk communication tools [124,125]. Clinicians and patients should work together to thoughtfully work out the benefits and risks, ensuring that women who stand to benefit from ondansetron can access the treatment. This will help women to make a decision that is grounded in evidence and reflects their personal values.

Corticosteroids (oral prednisolone or intravenous hydrocortisone) [126,127]

Mechanism of action

The antiemetic effect of corticosteroids is exerted at the chemoreceptor trigger zone in the brainstem [24].

Background and safety

Corticosteroid use is generally reserved for serious presentations in which other anti-emetic medications have failed as corticosteroids have been associated with dose-related teratogenic and toxic effects in animal studies [94].

Epidemiological studies have found small associations between maternal corticosteroid use and birth defects. For example, in a prospective study by Park-Wyllie *et al.* there was no difference in the rate of major congenital anomalies between the corticosteroid-exposed (n=187) and control groups (n=188) [128]. However, as part of this prospective study a meta-analysis of 10 observational studies was conducted which found that there was an association between steroid exposure and oral clefts (OR 3.35, 95% CI 1.97-5.69). Anderka *et al.* used data from the National Births Defects Prevention Study, which is a multi-site, population based, case-control study [85]. The study aimed to assess whether NVP and HG or their treatments were associated with the most common non-cardiac birth defects. The study, which included 4524 cases and 5859 controls highlighted an association between corticosteroid use and increased risk of hypospadias, noting that this could be a chance finding.

A Swedish register analysis over a 6-year period based on prospectively collected data, examined 1,142 infants with orofacial clefts and other malformations [129]. This study did not identify a consistent association between steroid exposure and orofacial clefts. The MADRE database is a collection of information on malformed infants with a history of first trimester drug exposure (n=11,150). Analysis of the database over a 12-year period found that there was an association between in utero exposure to corticosteroids and the occurrence of cleft lip with or without cleft palate (OR 2.59, 95% CI 1.18-5.67) [130]. Most human research, does not support an association between systemic administration of corticosteroids and increased risk of orofacial clefts. On reviewing the literature the UK Teratology Information Service concluded that there is evidence of an association with cleft lip and palate in a small number of human studies and some animal models and that the available data do not support an association between in utero exposure to systemic corticosteroids and cardiac defects [131].

Effectiveness

Individual trials and case reports examining the effectiveness of corticosteroid use in treating HG have produced varying results. For example, in a randomised, double blind, placebo-controlled trial in women (n=126) that did not respond to outpatient treatment for HG, intravenous methylprednisolone was administered followed by a gradual wean from 40 mg oral prednisolone (40 mg for 1 day, 20 mg per day for 3 days, 10 mg per day for 3 days, 5 mg per day for 7 days) [132]. Both the treatment group and placebo group also received metoclopramide and promethazine for 24 hours followed by an oral regime until discharge. Receiving treatment with corticosteroids did not reduce the need for rehospitalisation in later pregnancy or affect other measured outcomes.

Other trials have found positive results associated with corticosteroid use. For example, a multicentre, double-blinded, randomised trial compared corticosteroid treatment (20 mg oral prednisolone twice daily) for HG with placebo [133]. The study indicated that steroid therapy led to an improved sense of well-being, appetite as well as increased weight when compared with placebo. However, due to the small size of the trial significant improvement in primary outcome measures could not be confirmed.

Furthermore, a case series by Taylor *et al.* documented the success in treating HG in seven women who had experienced frequent hospitalisations due to inadequate control of HG with other anti-emetics [134]. The report found that corticosteroid use was an effective treatment for intractable hyperemesis gravidarum and helped to establish normal maternal nutrition.

Corticosteroids may be considered to gain control of symptoms and allow the implementation of an effective management regimen. The known adverse effects of steroids and need for tapering should be considered in the overall risk benefit evaluation. Recommended steroid doses include Hydrocortisone 100 mg twice daily IV with a transition to prednisolone 40-50 mg daily PO once clinical improvement occurs, with the dose gradually tapered (by 5-10 mg per week) until the lowest maintenance dose that controls the symptoms is reached [19].

Metoclopramide [135]

Mechanism of action

Metoclopramide is primarily a dopamine receptor antagonist working at both central and peripheral dopamine 2 (D2) receptors in the medullary chemoreceptor trigger zone [136]. Action of metoclopramide at the D2 receptor decreases sensitivity of nerves that send information from the gastrointestinal system to the chemoreceptor trigger zone. Additionally, it has some antagonistic effect on serotonin (5-HT3 and 5-HT4) receptors. Furthermore, metoclopramide increases the rate of gastric emptying which may lead to common side effects such as diarrhoea.

Background and safety

In the previous edition of these guidelines, metoclopramide was reserved as an adjuvant in cases where other anti-emetics had been used unsuccessfully. There is evidence from a Cochrane review [87] as well as an additional systematic review [77] that metoclopramide is effective at treating NVP and HG. There is also evidence from a systematic review [137] as well as large register-based studies [138-140] that metoclopramide is safe with regards to adverse pregnancy outcomes.

In 2013, the European Medicines Agency (EMA) published new guidance on metoclopramide use primarily aimed at reducing neurological side effects such as acute dystonic reactions/extrapyramidal disorders and tardive dyskinesia [141]. It was concluded that the risks of treatment particularly in the long-term did not outweigh the potential benefits. These safety concerns mean that metoclopramide use should be reserved for cases of NVP and HG where other anti-emetics have failed or as a short-term adjuvant to help regain control of nausea. In cases where metoclopramide must be used recommendations included short term use (< 5 days) and intravenous administration should be given in a slow bolus over at least 3 minutes to avoid side effects.

A subsequent retrospective cohort study conducted in Norway from 2002-2019 examined anti-emetic treatment in women with hyperemesis gravidarum [142]. The study found that the EMA warning on metoclopramide in 2013 was followed by a dramatic although temporary drop in NVP and HG patients being provided metoclopramide prior to hospital admission.

Other pharmacotherapies that have been used but not currently recommended due to very low evidence base are detailed in Appendix 4.

Clinical Practice

Medication should be started for all women based on severity of symptoms, in a step-wise fashion according to the treatment algorithm below. It is likely that medication regimes will need to be personalised as individuals will have differing responses to anti-emetics. The mechanisms of action are different for each class of anti-emetics and therefore using combinations of anti-emetics may provide additional relief, moreover, the different drug classes may produce synergistic effects.

Assess current medications including tolerance and timings. Advise how to take medicines to maximise relief of symptoms. Women should be advised to avoid self-medication or the use of treatments outside of those recommended in the treatment algorithm. Treatment should be reviewed frequently and adjusted (adding, changing, reducing, or stopping) as required. Discharge women with a prescription for appropriate oral anti-emetic(s) and encourage taking medication regularly as prescribed to avoid worsening of symptoms and dehydration.

Steroid therapy for severe HG may be appropriate but should be a Consultant-led decision. An individual approach is needed, and alternative approaches may be available, though the following could be considered:

1. Hydrocortisone 100 mg 12 hourly IV while requiring IV fluids. The woman should be reviewed to consider switching to oral prednisolone if there is an ongoing need for IV hydrocortisone at 72 hours.
2. Change to oral prednisolone once tolerated:
    - 40-50 mg of prednisolone per day PO with the dose tapering gradually until the lowest maintenance dose that controls the symptoms is reached.

Oral prednisolone may be required to control symptoms until birth. If steroid therapy has been required for a long time, then IV hydrocortisone cover may be required for labour with tapering of oral prednisolone after the birth.

The steroid dose and protocol may need to be adjusted (increased/decreased) according to symptoms and clinical situation under consultant care.

Corticosteroid can cause hyperglycaemia, consider screening for gestational diabetes in cases of prolonged use. Women may require omeprazole 20mg once daily to prevent gastric irritation/ulceration or for the management of dyspepsia or gastro-oesophageal reflux.

NVP Treatment Algorithm

If there is no improvement, proceed to the next step

Use of this algorithm assumes that other causes of nausea and vomiting in pregnancy have been ruled out.

Doxylamine 10mg and pyridoxine 10mg prolonged release: one capsule in the morning, one in the afternoon and two at bedtime). Adjust schedule and dose according to severity of symptoms.

Add either:

Ondansetron 4 to 8mg 8 hourly PO or (Zofran Zydis®) 4 to 8mg 8 hourly buccal (counsel the woman on safety data)

Or/And

Prochlorperazine (Stemetil®) 5mg 8 hourly PO†‡ or (Buccastem®) 3mg 12 hourly buccal

Or/And

Cyclizine (Valoid®) 50mg 8hourly PO‡

No Dehydration

If not tried previously, add any of the following:

- Promethazine (Phenergan®) 25mg up to 8 hourly PO
- Chlorpromazine 10-25 mg 6 hourly PO

Dehydration

Start IV fluid replacement with Hartmann's solution or NaCl 0.9%. **If not tried previously**, add any of the following:

- Ondansetron 4mg to 8mg 8 hourly IV*
- Prochlorperazine 12.5mg 8 hourly IM *
- Metoclopramide 5 to 10mg 8 hourly IV*
- Promethazine 12.5 to 25mg 8 hourly IM*

Consider: Hydrocortisone 100mg 12 hourly IV* change to oral Prednisolone, 40-50 mg/day PO. Taper the dose of steroids gradually until the lowest maintenance dose controlling the symptoms is reached. Given risks of long-term steroid use, seek senior advice.

Note:

- Don't use two medications which are in the same drug class
- At any stage women may require Omeprazole 20mg once daily for the management of dyspepsia or gastro-oesophageal reflux. Dose can be increased if necessary.
- Consult Summary of Product Characteristics for full prescribing data.

‡ Women should be warned of increased sedative effects possible with combination treatment.

† Extrapyramidal effects and oculogyric crises may occur with prochlorperazine.

*Only use parenteral formulations if oral products are not tolerated.

VTE risk assessment must be performed as per national clinical guidelines.

IV vitamin supplementation Pabrinex I/II® or equivelant daily for up to 3 days in women admitted (day case or inpatient) with HG; those with severe vomiting; those with limited nutritional intake for at least 5 days; and/or weight loss >10% from pre-pregnancy weight. If oral medications tolerated: Thiamine Hydrochloride 50-100mg up to 8hourly PO

Consider need for IV potassium replacement (use ready-mix bottles of NaCl 0.9% with 20mmol or 40 potassium per litre). If any abnormal electrolyte value is detected, please see Irspen Refeeding syndrome guidelines for correction (Appendix 4)

Parenteral nutrition may be required.

Recommendations

12. We recommend that medical management is a cornerstone of the treatment of moderate-severe NVP and HG (see algorithm)
13. We recommend that patients should be encouraged to return for review if medications are not effective, as they can be reassessed.
14. We recommend that if a patient is not responding to the medication, consider additional or changes as needed. More than one agent may be required.
15. We recommend avoiding the use of more than one medication from the same therapeutic class to prevent side effects.
16. We recommend a regular review of medications with consideration to stopping, reducing or restarting prescriptions as needed based on symptoms. Consider discontinuing any medication that is not effective for the patient, or that is causing significant side effects or complications.

Section 6: Refeeding Syndrome Risk

Introduction

Refeeding syndrome can be defined as serious metabolic and fluid disturbances resulting in electrolyte shifts and/or clinical symptoms that can occur in starved and/or malnourished patients on recommencement of feeding, either enterally or parenterally [143,144]. It is a potentially fatal condition, but if detected early, can be managed successfully. Typically, refeeding syndrome occurs in patients with chronic malnutrition and weight loss of >10% [145].

The pathogenesis of refeeding syndrome begins with prolonged starvation or fasting which results in a reduction in glucose and energy intake. Insulin concentration falls and the body shifts towards gluconeogenesis, resulting in ketones and fatty acids becoming the primary source of fuel. Intracellular electrolytes become severely depleted; however, serum concentrations may remain normal initially due to sodium retention. Thiamine also becomes depleted. On refeeding, increased blood glucose concentration results in increased insulin production, which stimulates synthesis of fat, protein and glycogen. During this process thiamine is required as a cofactor and phosphate, magnesium, and potassium move into the cell, further depleting serum concentrations of these electrolytes [143]. Refeeding syndrome is therefore associated with electrolyte disturbances resulting in hypophosphatemia, hypomagnesaemia, hypokalaemia, thiamine deficiency, fluid and sodium retention. The consequences of refeeding syndrome can result in congestive cardiac failure, cardiac arrhythmias, neurological problems (delirium, neuropathy or seizures), respiratory failure, muscle weakness, impaired blood clotting, Wernicke's Encephalopathy and Korsakoff's Psychosis [146].

Clinical Question 2.7: How is Refeeding Syndrome managed among those with NVP and HG?

Evidence Statement

The 2018 Friedli consensus paper and 2013 Irish Society for Clinical Nutrition and Metabolism (IrSPEN) guidelines for the prevention and treatment of refeeding syndrome provide risk factors for and management of refeeding syndrome among non-pregnant populations in the acute setting in Ireland [143,144] (Appendix 5). These guidelines state that unintentional weight loss of >10%, low BMI and/or limited nutritional intake for more than five days are associated with increased risk of developing refeeding syndrome.

Additionally, the American Society for Parenteral and Enteral Nutrition (ASPEN) published consensus recommendations for refeeding syndrome, which include HG as a risk factor [147]. Women with HG are at risk of developing refeeding syndrome, especially if dietary intake is severely compromised and electrolytes become depleted, further exacerbated by loss of intestinal contents and electrolytes through vomiting. While cases of maternal and fetal deaths as a consequence of refeeding syndrome have been reported among women with HG [148-150], successful management of the condition, including reversal of the complications of Wernicke's Encephalopathy, among women with HG have also been noted in the literature [151-153].

Supplementation of thiamine will be required via oral, intravenous, or intramuscular routes.

Guidelines for the prevention of refeeding syndrome outline a need for thiamine replacement. IrSPEN recommend ≥ 250 mg IV thiamine daily for 3 days, or 200-300 mg enteral thiamine daily for 10 days [143].

- Friedli recommend Thiamine 200-300 mg on days 1-5 and multivitamin for days 1-10 commenced before initiating nutrition support [144].
- ASPEN recommends to supplement thiamine 100 mg before feeding or before initiating dextrose-containing IV fluids inpatients at risk. They also suggest supplementing thiamine 100 mg/day for 5-7 days or longer in patients with severe starvation, or other high risk for deficiency and/or signs of thiamine deficiency [147].

The 2024 RCOG guidelines for the management of HG recommend thiamine supplementation (either oral 100 mg eight hourly or intravenous as part of vitamin B complex (Pabrinex®)) should be given to all women admitted with vomiting, or severely reduced dietary intake, especially before administration of dextrose or parenteral nutrition [19].

It is not known whether women with HG, who are not at risk of refeeding syndrome, should also be advised to take a daily thiamine supplement while vomiting and/or if adequate oral intake is ongoing.

Clinical Practice

Women with HG may be at risk of developing refeeding syndrome, particularly if they have weight loss, low BMI and/or limited nutritional intake for more than five days. Individual assessment and management of women is warranted to determine risk of refeeding syndrome and management. Vigilance should be paid if commencing enteral or parenteral feeding with slow initiation of feed and close monitoring.

Any disturbances in electrolytes should be corrected as per local policy or medication protocols, seeking specialist advice as required. It should be noted that oral replacement of electrolytes may be difficult for women with severe nausea and vomiting to tolerate, and consideration should be given to intravenous replacement, even among those with mild deficiencies.

Thiamine supplementation should be provided to: women admitted (day case or inpatient) with HG; those with severe vomiting; those with limited nutritional intake for at least 5 days; and/or weight loss >10% from pre-pregnancy weight. This can be provided as 250 mg IV thiamine (Pabrinex®) daily for up to 3 days; or 200-300 mg oral thiamine supplement for 10 days. Anaphylactic reactions have been reported rarely during, or shortly after, parenteral administration of IV vitamins (e.g. Pabrinex®). Resuscitation facilities should be available.

Recommendations

17. **We recommend that individual assessment for and management of refeeding syndrome is completed for women with HG, following national or local policies.**
18. **We recommend that electrolytes (at least potassium, magnesium, and phosphate) are measured and deficiencies are replaced as needed.**
19. **We recommend that Thiamine supplementation should be provided to: women admitted (day case or inpatient) with HG; those with severe vomiting; those with limited nutritional intake for at least 5 days; and/or weight loss >10% from pre-pregnancy weight. This can be provided as 250 mg IV thiamine (Pabrinex®) daily for up to 3 days; or 200-300 mg oral thiamine supplement for 10 days.**

Section 7: Nutrition Support

Introduction

A proactive approach to nutritional management of HG is warranted given the known associations between HG and nutrition/hydration deficiencies, related poor pregnancy outcomes, including inadequate gestational weight gain, intrauterine growth restriction, small for gestational age (SGA) infant and the potential for long-term consequences for mother and child [51,52,154].

Clinical Question 2.8: What is the role of dietetics in the management of women with NVP and HG?

Evidence Statement

Nutritional deficiencies are well documented in women with severe HG and are associated with poor pregnancy outcomes including preterm delivery and SGA [51,52,155]. Substantial weight loss during early pregnancy is a common feature of HG. These women often struggle to achieve the Institute of Medicine (IOM) recommendations for gestational weight gain [156,157]. Pregnancies complicated by HG which affect the mother's gestational weight gain (i.e. inadequate total weight gain; weight loss without regain by week 13-18) or having a pre-existing low BMI (<18.5 kg/m^2) may increase the risk of fetal SGA [158].

A recent systematic review with 23 meta-analyses explored the association of maternal HG and perinatal outcomes [159]. Over 80% of included studies were fair to good quality. There was a significant association between both mild and severe HG and birth weight <1,500g, but maternal weight gain was not reported. It is not clear if more severe HG symptoms have a more significant impact on birthweights. Further research on the impact of maternal weight gain and treatment modalities are needed to inform clinical practice.

A population-based retrospective cohort study of 156,091 singleton pregnancies compared neonatal outcomes of babies born to mothers with HG (requiring admission) and poor gestational weight gain (<7kg) to mothers with HG and gestational weight gain > 7 kg and mothers without HG [155]. Mothers with HG requiring hospital admissions and total weight gain <7kg were shown to be at highest risk of delivering pre-term (before 37 weeks) and experiencing fetal SGA and low birth weight (<2,500g).

Specific considerations for women presenting with HG are documented below. Further guidance on nutrition requirements in pregnancy can be found in the HSE Clinical Practice Guideline: Nutrition for Pregnancy 2019 [32].

Clinical Practice

An accurate nutritional assessment and plan to optimise intake, carried out by a registered dietitian, is a key component of HG management. Referral to the dietitian should be made as needed considering available services. Women who warrant dietetic intervention include women already established on prescribed antiemetic medications and who despite antiemetic treatment, present with any of the following:

- A PUQE score in the severe category (>13)
- Require inpatient admission
- 5% weight loss from pre-pregnancy weight or minimal dietary intake for 3-5 days
- Women with greater nutritional needs – multiple pregnancy or pre-existing low BMI
- Inadequate gestational weight gain (as per IOM 2009) and concerns about SGA or intrauterine growth restriction
- Diabetes treated with insulin (should be prioritised) (see clinical question 2.13 for further guidance on diabetes management in HG).

The nutritional factors to consider include:

1. Medical/obstetric history – Include date of admission, gestation, gravidity/parity, history of HG, interval between pregnancies, investigations of note
2. Laboratory Medicine
    a. FBC – Hb (consider hydration status when interpreting)
    b. Urinalysis
    c. LFTs and TFTs (note changes may include raised free thyroxine levels; LFTS are abnormal in 40% of women with HG most likely due to a rise in transaminases. Bilirubin can be slightly raised but without jaundice. Amylase levels can be mildly raised. These abnormalities improve as HG resolves.
    d. Consider checking Vitamin B12, iron studies including ferritin, folate, vitamin D if severe HG for >4 weeks and minimal dietary intake or have history of nutrient deficiency.
3. Medications – Specific focus on anti-emetic medication, and medications to managed associated symptoms (antacid, proton pump inhibitor, and laxatives). May also include electrolyte supplementation and IV/prescribed micronutrient supplementation.
4. Nutrition focused physical findings
    a. PUQE score including wellbeing scale
    b. Bowel habits – Consider constipation in the setting of poor intake, early satiety, dehydration and medications
    c. Other GI – dyspepsia, gastroesophageal reflux, ptyalism
    d. Appetite – consider symptom triggers affecting appetite, e.g. hypersensitivity to smell
    e. Physical appearance
    f. Dehydration: document findings from fluid balance chart which may include positive/negative balance (if available); reduced urine frequency, dark urine colour, mucous membrane appearance (ptyalism may have a moist mouth and remain dehydrated) (refer to clinical question 2.3)

5. Anthropometric measurements & nutrition requirements

    a. Weight: on admission/pre- and post-fluids/% weight change from pre-pregnancy weight/ gestational weight gain

    b. Height and BMI: on admission or at booking

    c. Fetal assessment parameters (fetal growth centiles, intrauterine growth restriction, macrosomia or anomalies)

    d. Nutrition requirements – refer to Clinical Practice Guideline for Nutrition for Pregnancy

6. Food & nutrition related history

    a. Food, fluids, non-prescribed micronutrient supplements (ability to swallow oral tablets/ formulations), oral nutritional supplements, enteral feeding

    b. Food and nutrition related knowledge/beliefs/behaviour/motivation

    c. Factors affecting food intake/supply (functional capability, physical activity)

    d. Other:

        i. Social factors – consider impact of HG on employment, family support available, financial implications of medication and loss of earnings, and impact of same on symptoms. Consider referral to mental health or medical social worker

        ii. Sleep quality

7. Summarise nutritional issues and/or nutrition diagnosis

    Example of Summary of nutritional issues:

    - *Dietary intake is significantly reduced due to severe hyperemesis with low intake of iron rich foods, minimal protein and calcium intake. Unable to tolerate pregnancy multivitamin. Minimal gestational weight gain.*

    Example of Nutrition Diagnosis:

    - *Condition-related malnutrition related to physiological causes resulting in diminished intake as evidenced by diagnosis of hyperemesis gravidarum, unintentional weight loss of > 5% in 1 month or inadequate gestational weight gain (2nd/3rd trimester) and estimate intake < 75% of estimated energy requirements for > 1 month* [158]
    - *Inadequate protein-energy intake related to decreased ability to consume sufficient protein and energy as evidenced by diagnosis of hyperemesis gravidarum, estimate intake less than energy and protein recommended needs, weight loss of >5% in 1 month or 1-2% weight loss in 1 week or inadequate gestational weight gain* [158].

Recommendations

20. We recommend that the need for dietitian referral for comprehensive nutrition assessment should be considered for those presenting with HG.

Clinical Question 2.9: How is nutrition support provided for those with NVP and HG?

Evidence Statement

Enteral and parenteral nutrition are routinely employed in clinical situations outside of pregnancy, when oral intake is insufficient to meet nutritional requirements [160-163]. In pregnancy, and in particular in HG, despite prolonged inadequate oral intake and weight loss, evidence has highlighted that nutrition support, including enteral and parenteral nutrition, are not commonly used [164].

Malnutrition in pregnancy is poorly defined in the literature. The following conditions could be considered when making decision to initiate nutrition support: ≥ 5% weight loss; inadequate maternal weight gain (see appendix 6); intake of <50% of estimated nutritional requirements for ≥3 days or low BMI (<18.5kg/m^2) [157]. Intake of <50% of estimated nutritional requirements has been reported in the literature [165], with intakes negatively correlated with increasing PUQE score (see Table 2). Those with moderate and severe PUQE scores are most likely to meet this criterion, but some women with mild symptoms may also experience difficulties in meeting their basic energy requirements.

Table 2: Estimated Intake of Energy and Macronutrients During the First Trimester

Variable	EAR/RNI for the first trimester pregnancy/day	Mild (n=16) Mean (SD)	Moderate (n=44) Mean (SD)	Severe (n=10) Mean (SD)
Energy (kcal)	2103-2175	1616.4 (500.7)	1253.8 (566.6)	858.4 (338.7)
Carbohydrate (g)		200.4 (48.7)	166.6 (69.8)	116.6 (47.1)
Protein (g)	0.75g/kg + 6	58.6 (20.9)	42.0 (22.8)	30.6 (20.9)
Fat (g)		63.3 (28.2)	47.1 (27.7)	29.9 (20.1)

Adapted from: The Nutritional Online sUrvey for pRegnancy Induced Sickness & Hyperemesis (NOURISH) study, K Maslin *et al.* (2023) J Hum Nutr Diet. 2023 Oct;36(5):1821-1832. doi: 10.1111/jhn.13224. Epub 2023 Aug 21. PMID: 37602934. Note: Energy requirement differs per age: 19-34 year olds: 2175 kcal/day; 35-44 year olds: 2103 kcal/day

Impact of enteral nutrition support in HG

There is some low-quality evidence that nutrition support through enteral or parenteral nutrition can improve nutrition outcomes in women with HG, mostly from case reports, small case series and an observational study. A 10-year retrospective cohort study in Norway described the treatment and outcomes of 558 women with severe HG who received a variety of nutrition support regimens including intravenous fluids, peripheral nutrition, enteral nutrition, and total parenteral nutrition [166]. Women were included in the study if they met the criteria for severe HG (defined within the study as ICD-10 O21.1 Hyperemesis with metabolic disturbance), were admitted before 20 weeks of gestation and had at least two of the following factors: dehydration, weight loss, ketonuria or electrolyte disturbances. Despite greater weight loss at baseline, the women who received enteral feeding experienced similar gestational weight gain and pregnancy outcomes (preterm birth or small-for-gestational age), as the other treatment groups. The authors suggested that the results demonstrated that enteral tube feeding is a feasible treatment option resulting in sufficient maternal weight gain and favourable pregnancy outcomes [166].

There has been only one randomised controlled trial (MOTHER trial) on enteral feeding in HG, based in the Netherlands [167]. The intervention was at least seven days of enteral nutrition support, commenced between five-20 weeks' gestation, compared to standard care. No difference was found in the primary outcome of birthweight or secondary outcomes including gestational weight gain. There are several limitations worth noting, including lack of statistical power, poor "per protocol" delivery of the intervention, inclusion of participants with variable HG symptoms, limited duration of feeding and short-term outcome measurement. Authors highlighted that women who received the intervention according to the protocol had lost more weight at baseline and were more likely to tolerate feeding, suggesting potential benefit in more severe cases [167].

Perspectives of women with HG

In a qualitative study of 13 women with HG, women who received nasogastric tube feeding (n=8) highlighted benefits including preventing severe weight loss, reducing dehydration or hospital admissions, and nutrition provision to meet requirements for the baby [168]. Conversely, those who did not receive enteral nutrition support reported they wished they had. In other literature, however, reports of tube removal due to discomfort and emotional distress have been reported [167,169].

Hyperemesis symptoms

While there is currently no high-quality evidence that enteral or parenteral nutrition can improve symptoms of HG, it should be emphasised that the role of nutrition support is to meet nutritional requirements, and not as a strategy to reduce symptoms of HG. While older, low-quality studies report reduced symptoms with enteral feeding, more recent studies, including the MOTHER trial [167], highlight continued nausea and vomiting during enteral feeding, although this is not always a limitation to feeding. Appropriate medical management to reduce nausea and vomiting should remain the cornerstone of the management of HG symptoms and, importantly, medications should be optimised prior to initiation of enteral feeding.

Complications

Gastrointestinal (diarrhoea, nausea and vomiting, constipation); mechanical (aspiration, tube related positioning issues, tube obstruction); and metabolic (hypo- and hyper-natraemia, dehydration, hyperglycaemia) complications [170]. Among HG populations the observational study by Stokke *et al.* observed over half (54%) of the women with nasojejunal tubes had tube removal due to forceful vomiting (n=46) and clogging (n=4) [166]. Additionally, eight women (7%) asked for tube removal due to discomfort. Despite this, they reported no cases of aspiration. In the MOTHER trial, there were similar rates of other complications in the intervention arm, with nose-throat irritation reported in 26 (44.1%) and tube dislocation in 23 (39.0%) [167]. Despite this, there were no difference in outcomes, including maternal morbidity, and there were no serious adverse effects. Along with following appropriate routine protocols for placing and monitoring tubes, strategies to help reduce the risk in nasogastric/jejunal feeding in pregnancy, such as fixation clips or ultrasound placement, may be helpful, however evidence of benefit for these additional strategies is currently lacking in HG [171,172]. Percutaneous endoscopic gastrostomy (PEG) feeding may reduce the risk of tube dislodgement, radiation exposure during confirmation of nasogastric tube replacement via x-ray and potentially some complications, but this is not guaranteed [163,173,174]. Several case series have reported administration of enteral nutrition through PEG or PEG-jejunostomy tubes in women with severe HG, which have resulted in positive pregnancy outcomes [162,169,175]. A potential complication includes superficial wound infection because of tube placement [176], and management of tubes and stomas with anatomical changes as pregnancy progresses needs consideration.

Parenteral nutrition

Parenteral nutrition bypasses the gut, potentially avoiding some of the associated complications in enteral feeding. Despite this, parenteral nutrition in HG has been associated with more complications than nasal enteral tubes or medications alone [177]. There have been reports of total parenteral nutrition in pregnancy and HG, but its use has been associated with significant morbidity, especially in central catheters [166,178,179]. Total parenteral nutrition has been used in HG to provide adequate maternal nutrition when there is limited tolerance for food or enteral nutrition provision [180,181]. Levine *et al.* describe use of total parenteral nutrition in severe HG, provided nocturnally at home to allow oral intake during the day [182]. Due to high risks associated with total parenteral nutrition, including thrombosis, pneumothorax, obstruction, metabolic disturbances, and infectious complications (including sepsis), it should be considered as a method of feeding only after weighing up these risks [166,178,183]. The provision of total parenteral nutrition requires strict aseptic technique and healthcare professional competence in line management, and this should inform decisions about when and where it is used.

Peripheral nutrition (method of delivering partial parental nutrition via a smaller, peripheral vein) may provide an alternative to total parenteral nutrition in pregnancy [184,185]. A combination of enteral and peripheral parenteral nutrition could be considered. In a study by Stokke *et al.*, all women received intravenous rehydration with saline or 5% glucose, the latter being a potential option to provide some calories, if electrolytes and risk of refeeding are managed appropriately [166]. If inadequate oral intake persisted after rehydration, women received peripheral nutrition (1000kcal) for a median of two days (n=177). This was employed due to persistent inadequate oral food intake up to three days after rehydration with IV fluids. Additional women who were provided with enteral feeding received supplemental peripheral nutrition while waiting to achieve their target feeding rate and nine women who received nasojejunal support also received total parenteral nutrition. Nutritional and pregnancy outcomes were similar across a group in this study, although those who received enteral nutrition support had lost more weight at the start of nutrition therapy.

The optimal timing for initiation and duration of nutritional support has not been established and should be based on clinical judgment. Several reports start feeding around 20-25 weeks' gestation, while others, including the case series of 30 women by Gulley *et al.*, report early feeding in the first trimester [169,174,183,186]. In the two highest-quality studies mentioned above, enteral feeding commenced at about 8-9 weeks gestation [166,167]. Of note, the qualitative study by Van Vliet *et al.* highlighted the impact that delayed interventions had on women, and the potential benefit of early tube feeding from the perspective of women with HG [168]. Stokke *et al.* described enteral nutrition use four to six days after hospitalisation [166]. Feed was provided for up to 41 days (median five days during hospitalisation). Women were encouraged to consume orally while receiving tube feeding and were discharged home once they were competent in feed delivery. In the MOTHER trial, women continued tube feeding for at least seven days, or until they could maintain an intake of 1000 calories/day [167]. There have been reports of cases of enteral feeding right up to delivery, with tube dislodgement(s) and replacement(s) during this time [173,183].

Clinical Practice

Enteral and parenteral nutrition should not be considered as a treatment for HG, rather they can be considered a potential means to maintain nutritional status while optimising medical and supportive management. Oral nutritional supplements and oral methods such as food fortification or dietary counselling should be tried in advance of considering enteral or parenteral feeding. Appropriate use of oral nutritional supplements can help to reverse weight loss and reduce the risk of malnutrition. Oral nutritional supplements come in a variety of formulations, volumes, and flavours, providing energy, protein, vitamins, minerals, and hydration.

An appropriate clinical environment is required for enteral and parenteral nutrition for women with HG. This includes sufficiently trained staff, multidisciplinary involvement, including dietitian and medical oversight from a consultant obstetrician. In addition, the clinical setting should have in place; adequate equipment, training, policies or protocols for initiation and monitoring of feeding. Enteral and parenteral nutrition may be considered, alongside optimisation of medical management, when oral methods (food fortification, oral nutritional supplements, and dietary strategies) are not sufficient to maintain nutritional status, considering the preferences of the woman and potential complications. The timing, initiation and duration of feeding requires clinical judgement, but early initiation, rather than delaying feeding to a point where the woman is malnourished, will minimise potential nutrition losses.

Recommendations

21. **We recommend that in appropriate settings, enteral and parenteral nutrition could be considered alongside optimisation of medical management when oral methods (food fortification, oral nutritional supplements, and dietary strategies) are not sufficient to maintain nutritional status, considering the preferences of the woman and potential complications.**
22. **We recommend that enteral or parenteral nutrition only be considered in appropriate settings with adequate equipment, training, policies or protocols for initiation and monitoring of feeding.**
23. **We recommend a multi-disciplinary approach led by the consultant obstetrician when enteral or parenteral nutrition is considered.**
24. **We recommend that clinical judgement should guide decisions about the timing of initiation or the duration of feeding. It is prudent to consider early initiation to minimise potential nutritional losses in pregnancy.**

Section 8: Supplementation and Iron Management

Introduction

Women with HG are at risk of malnutrition, including relative micronutrient deficiencies of iron, folate and other micronutrients, posing risk of complications for both mother and baby.

Iron deficiency anaemia in pregnancy is common, especially in the second and third trimester [199]. According to the World Health Organisation (WHO) approximately 37% of pregnant women are affected by anaemia [200]. Iron deficiency is the leading cause of anaemia globally and in pregnancy. The WHO Global nutrition targets for 2025 are aiming for a 50% reduction in the prevalence of anaemia in women of reproductive age. Iron deficiency has been associated with negative health outcomes including pre-term delivery, impaired cognitive development, low birth weight and maternal mortality [201-204].

Clinical question 2.10: What antenatal micronutrient supplements are recommended for those with Hyperemesis Gravidarum?

Evidence Statement

Women with hyperemesis gravidarum are at risk of poor nutritional intake, leading to potential malnutrition including micronutrient deficiencies of key nutrients for pregnancy [187]. Recent data highlight that women with HG have inadequate intakes of nearly all nutrients [187,188]. A scoping review was performed including four articles (three hospital case control studies, one observational women's cohort study). Data was reported on 314 women across four countries (Turkey, South Africa, Norway and the United Kingdom). Quality assessment of the studies was not included. Nutrient intake across all studies was found to be significantly lower in the HG group compared to controls. The authors concluded that nutritional intake of those with severe HG symptoms is estimated at less than 50% for most nutrients. Severity of symptoms is thought to be inversely related to oral intake and weight gain [187].

The NOURISH study in 2023 used an online dietary survey (3 days) and PUQE score to determine dietary intakes of 166 participants in the United Kingdom with HG in their first trimester [165]. Of those who completed the dietary survey (n=70); 22.9% had mild, 62.9% moderate and 14.2% severe symptoms, based on PUQE scores. Women in the severe category had significantly lower intakes of energy, protein, fat, carbohydrate, iron, thiamine, folate and vitamin C compared to the mild category. The moderate category had significantly lower intakes of energy, fibre, iron, thiamine, folate and vitamin C compared to the mild category. The results of this study, conducted in the United Kingdom, are comparable to our population in Ireland due to the significant demographic and cultural similarities between the two countries. Further research is needed to investigate the dietary habits of people living with HG on the Island of Ireland. Table 3 shows the proportion of participants with HG not meeting the lower reference nutrient intakes (LRNIs) for key vitamins and minerals in pregnancy.

Table 3: Percentage of Women in each category of PUQE Not Meeting LRNI of Key Nutrients (from food) in Pregnancy (n=70)

Variable	Mild PUQE (n=16)	Moderate PUQE (n=44)	Severe PUQE (n=10)
Iron	18.8	59.1	60
Folate	25	78.2	60
Vitamin B12	12.5	35.4	40
Calcium	18.8	56.8	60
Iodine	68.7	77.3	70
Thiamine	0	13.8	30
Riboflavin	33.3	63.6	60
Vitamin C	6.3	29.5	50
Vitamin A	43.8	56.8	60
Zinc	56.3	68.3	70

Adapted from: The Nutritional Online sUrvey for pRegnancy Induced Sickness & Hyperemesis (NOURISH) study, K Maslin *et al.* (2023) J Hum Nutr Diet. 2023 Oct;36[5]:1821-1832. doi: 10.1111/jhn.13224. Epub 2023 Aug 21. PMID: 37602934. Data is percentage of women within each category not meeting the LRNI for each nuitreint, for example, 18.8 refers to n=3/16 participants in the mild PUQE category not meeting the LRNI for iron while 59.1 refers to 26/44 women within the moderate PUQE category not meeting the LRNI for the same nutrient (Iron).

Research suggests that a large proportion of women discontinue prenatal multivitamins despite the importance of folic acid in the first trimester [189]. Reasons may include tablet size and pre-existing gastrointestinal conditions and/or symptoms which can worsen NVP and HG [190]. Maslin *et al.* found 22.9% of women with HG discontinued their pregnancy multivitamin due to sickness [165]. It has been suggested that antenatal multivitamins which contain iron can precipitate symptoms of NVP and HG [191].

Folic acid (vitamin B9) supplementation pre-conception and during pregnancy is important to reduce the risk of neural tube defects (NTD) in the developing fetus [32]. All pregnant women should be advised to supplement with 400 µg folic acid throughout pregnancy and lactation if applicable [32]. Women planning another pregnancy should be encouraged to start folic acid 400 µg at least 6 weeks, but ideally at least 3 months, prior to trying to conceive (RCPI, 2019). Individuals with an increased risk of NTDs should be prescribed high dose folic acid (5mg) daily pre-conception and during the first trimester, followed by 400µg from the second trimester onwards.

High dose supplementation may be prescribed for the first trimester in some circumstances including: previous pregnancy complicated by a NTD, pre-gestational diabetes Type 1 or 2, first degree relative with a NTD, taking certain medications, moderate or severe obesity (BMI > 34.9 kg/m^2). Some women suffering with HG are at increased risk of thiamine deficiency and refeeding syndrome (see clinical question 2.7: How is refeeding syndrome managed in those with HG?).

Rates of vitamin D deficiency (serum 25(OH)D concentrations <30 nmol/L) in the adult population across Europe have been described as an "epidemic" with total population deficiency rates at 13% in 2020 [192-194]. Certain ethnicities, medical conditions, cultural practices and medications may increase the risk of vitamin D deficiency [194]. Low vitamin D status has been linked to pre-eclampsia, birth weights and miscarriage [195]. In pregnancy, Vitamin D insufficiency (<75nmol/L) is associated with uteroplacental dysfunction, increased risk of pre-eclampsia and small for gestational age (SGA) [196].

The Food Safety Authority of Ireland (FSAI) and Health Service Executive (HSE) currently recommends for pregnant women, of all ethnicities, in Ireland, to supplement 15µg (600 international units) Vitamin D3 daily throughout the year [197]. This is in line with the recommendations set out by EFSA [198]. The tolerable upper intake level of vitamin D3 in pregnancy as defined by EFSA is 100 µg/4,000 international units per day) [198].

Clinical Practice

Multivitamins

Pregnancy multivitamins are a convenient way to meet most micronutrient requirements during pregnancy. Pregnancy-specific multivitamins that cover key nutrients, folic acid (400 µg), and vitamin D (15 µg) can be encouraged with acknowledgment that generic products tend to be more cost-effective. Women should be encouraged to discuss suitable and available supplementation options with their healthcare professional such as doctor, midwife, pharmacist or dietitian.

If antenatal multivitamins are discontinued a reason should be explored and possible alternatives discussed. Women should be recommended to start folic acid (400µg), vitamin D (15µg) or an iron-free multivitamin. Alternatively, liquid, spray or chewable forms of antenatal vitamins can be explored if swallowing or tolerance issues are present, however there may be limited availability of alternative preparations in hospital settings. Once symptoms are alleviated, antenatal multivitamin consumption should be re-considered particularly if the diet is lacking in key food groups or nutrients.

Individuals with co-existing conditions or at risk of nutrient deficiency should be referred to a dietitian, for example: post-bariatric surgery, IBD, cystic fibrosis, restricted dietary practices (vegetarian, vegan), poor access to food (homeless, asylum seeker). Special consideration should also be given to individuals with additional nutritional needs including high BMI (≥35kg/m^2), multiple pregnancies and adolescents.

Folic Acid

All pregnant women should be advised to supplement with 400 µg folic acid throughout pregnancy and lactation if applicable. Women planning another pregnancy should be encouraged to start folic acid 400 µg at least 6 weeks but ideally three months prior to trying to conceive. Individuals with an increased risk of NTDs should be prescribed high dose folic acid (5mg) daily pre-conception and during the first trimester, followed by 400µg from the second trimester onwards.

Vitamin D

In the case of sufficient serum concentrations, advise 15µg (600 international units) vitamin D3 per day. Of note, several multivitamins containing vitamin D3 and single nutrient vitamin D3 products provide 10µg (400 international units) per serving. In the case of vitamin D3 deficiency, follow local policy to replenish serum concentration. Do not exceed the tolerable upper intake level of vitamin D3 in pregnancy. Additionally, regular intake of vitamin D-rich foods should be encouraged, e.g. oily fish, eggs and fortified products such as breakfast cereals, milk, yogurt, butters and spreading fats. Special consideration should also be given to individuals at greater risk of deficiency such as individuals with darker skin; gastrointestinal disease, e.g. inflammatory bowel disease, post-bariatric surgery; those who cover their skin for religious or other reasons; and those on certain medications, e.g. some antiretrovirals/antifungals/antiseizure medications and glucocorticoids; as these populations are at increased risk of deficiency.

Recommendations

25. **We recommend that key single-nutrient supplementation should be recommended to all women throughout pregnancy. This includes folic acid (400µg/day) and vitamin D (15µg/day) at a minimum. Beyond this, an individualised approach should be taken with consideration of additional individual nutrient supplements or pregnancy multivitamins as appropriate, including iron-free formulations or products such as liquid, gummies and sprays.**

Clinical Question 2.11: How is Iron deficiency anaemia prevented and treated in HG?

Evidence Statement

Iron deficiency anaemia in pregnancy is diagnosed using blood tests to assess serum haemoglobin and ferritin concentrations. The British Society for Haematology (BSH) have published guideline recommendations on haemoglobin (Hb) targets in each trimester of pregnancy. Anaemia in pregnancy is defined as a haemoglobin <11 g/dL in trimester 1, a haemoglobin <10.5 g/dL in trimesters 2 and 3, and a haemoglobin <10 g/dL immediately post-partum [199].

Evidence investigating the relationship between iron deficiency anaemia and hyperemesis gravidarum is lacking. There is ongoing debate as to which serum ferritin concentration to use as threshold to diagnose iron deficiency [205]. In the UK, the majority of clinicians are familiar with using a serum ferritin level <30 µg/l [199,206]. It may be appropriate to use a higher cut-off in the HG population, but as of yet there is no data to support this in pregnancy. The guideline group encourage continued use of a serum ferritin level <30 µg/l until good quality evidence suggesting another cut-off emerges.

The population reference intake (PRI) for iron in pregnant and lactating women is 16mg per day [207]. Current Irish guidelines recommend iron supplementation in the form of a general antenatal multivitamin (16-20mg) alongside a balanced diet to maintain adequate iron status in healthy cohorts and prevent anaemia [32]. These supplements are not recommended to treat iron-deficiency. Anecdotal evidence suggests that low-dose iron supplements (16-50mg) may precipitate nausea and vomiting in pregnant women with HG [208]. Although, pregnant women without HG do not seem to experience heightened gastrointestinal symptoms with 20-50mg daily dose of iron [209]. In a Canadian prospective cohort study, two-thirds of 97 women who discontinued prenatal iron-containing multivitamin supplements (27-60mg) reported improvement in their severity of NVP and HG [191].

Higher dose oral iron supplements are required to treat iron deficiency in pregnancy [199]. Recommendations for the optimal dose of elemental iron to treat iron deficiency vary. The British Society of Haematology recommend a dose of 40-80mg elemental oral iron daily [199]. The Irish guideline recommends a dose of 100-200mg elemental iron daily to correct iron-deficiency [32].

Due to the inhibitory effects of endogenous hepcidin circulation following oral iron supplementation, alternate day dosing has been proposed to optimise iron absorption and mitigate gastrointestinal side-effects [210].

A Cochrane systematic review published in 2015 explored the impact of alternate day iron dosing in pregnancy compared to consecutive, daily iron [211]. The review included 21 papers, most of which are low or very-low quality evidence. Most studies (14/21) compared intermittent iron and folic acid supplements (2-3 times weekly) to daily iron and folic acid supplements. The weekly dose of iron (intermittent group) ranged from 80-300mg elemental iron. The weekly dose of iron (consecutive group) ranged from 280-840mg elemental iron. Iron supplements were given in the form of ferrous sulphate or ferrous fumarate. Alternate day dosing was concluded to cause fewer gastrointestinal side effects, such as nausea, as well as lower risk of haemoglobin >130g/L in second or third trimester, compared to consecutive dosing. No significant differences were found between groups for maternal anaemia at term or infant birthweights.

The British Society for Haematology recommend considering parenteral iron from the second trimester onwards and postpartum period in women with iron deficiency anaemia who fail to respond to, or are intolerant of, oral iron [199]. Systematic reviews and meta-analyses found that pregnant women receiving intravenous (IV) iron, compared with oral iron, achieved the target Hb more often, had an increased Hb after 4 weeks and had fewer side effects [212,213].

Clinical Practice

At the initial booking visit, FBC should be assessed with follow-up testing at 28 weeks' gestation. Serum iron studies including ferritin should be tested in women with increased risk of deficiency, including hyperemesis gravidarum, coeliac disease, malabsorption, vegetarian diet, multiparous pregnancies and post-bariatric surgery patients. Women with anaemia and/or iron deficiency (serum ferritin <30 µg/l) should be offered oral iron supplementation. The national guideline recommendations for treating iron-deficiency or anaemia should be followed. Oral elemental iron 100-200 mg daily should be recommended, which is equivalent to products containing 305 mg ferrous fumarate or 325 mg ferrous sulphate such as readily available Galfer or Ferrograd C. Those commenced on iron supplementation should be offered repeat FBC after 2-3 weeks to monitor response to oral treatment.

Barriers to consuming oral iron tablets should be explored with patients experiencing a limited response to oral iron supplementation. Iron supplements should be taken on an empty stomach first thing in the morning. Check the manufacturer instructions of iron supplements to assess whether a source of vitamin C should be encouraged at the same time as supplementation to improve absorption, i.e. a glass of orange juice or handful of berries. Oral iron products may include vitamin C as a combined supplement. It is advised to wait at least 60 minutes after taking an iron supplement to have food or tea/coffee. Alternate day dosing should be considered if adverse gastrointestinal (GI) side effects occur. If nausea and vomiting impact the woman's ability to tolerate oral iron, advise adjusting the timing of supplementation and educate on the potential for reduced absorption, e.g. alongside a snack or just after eating. Liquid preparations of iron-supplements may be explored, e.g. Galfer liquid.

Intravenous iron may be required in patients after the first trimester with anaemia and limited response to oral supplementation, proven malabsorption, total non-compliance with oral supplementation or inability to tolerate the supplementation. It may also be considered when a rapid Hb improvement is required. IV iron should be prescribed under the instruction and guidance of a senior obstetrician with considerations of adverse side effects such as iron staining and anaphylaxis. Contraindications include a history of anaphylaxis or serious reactions to parenteral iron therapy, first trimester of pregnancy, active acute or chronic bacteraemia and decompensated liver disease. Facilities and staff trained in management of anaphylaxis should be available. The patient must be informed of the risks associated with IV iron. Consider risk of hypophosphataemia associated with IV iron (especially ferrous carboxymaltose) in the context of poor PO intake and risk of re-feeding syndrome in this population.

Dietary advice should be provided by registered dietitians to educate women on the increased nutrient needs during pregnancy. Personal preference and food aversions must be considered. Dietary recommendations can be found in the national clinical guideline Nutrition During Pregnancy. Women recommended oral iron should also be offered advice to prevent constipation relating to fluid and dietary fibre intake (see clinical question 2.12 on constipation).

Recommendations

26. **We recommend consideration on an individual basis of temporarily ceasing iron supplementation including multivitamins containing iron due to their potential to exacerbate nausea and vomiting symptoms.**
27. **We recommend a prudent approach to alternative preparations such as IV infusions and consideration of their use in patients with iron deficiency anaemia and HG**

Section 9: Constipation Management

Introduction

Constipation is a common symptom experienced during pregnancy. Constipation is defined as difficulty in passing stool and reduced frequency of bowel movements that is not secondary to an underlying cause [215]. It is characterised by discomfort, excessive straining, hard or lumpy stools, a sensation of incomplete evacuation, and infrequent defecation [216]. Pregnancy predisposes to bowel dysfunction and constipation, with an estimated prevalence of up to 40% [217]. Pregnancy-related constipation is likely influenced by a combination of factors including increased progesterone levels, anatomical changes from the growing fetus, changes in physical activity and dietary habits [217]. Constipation can be a common complication of NVP and HG due to lack of dietary input, dehydration and side effects of some antiemetics. Constipation during pregnancy is an unpleasant symptom that may have an additional negative effect on quality of life [218]. It can also cause haemorrhoids and pelvic floor dysfunction, which may manifest as faecal or urinary incontinence, overactive bladder or pelvic organ prolapse [219].

Clinical Question 2.12: How should constipation be managed in HG?

Evidence Statement

A prospective cohort study in Finland investigated dietary & lifestyle habits influence on rate of constipation in pregnancy [220]. A questionnaire was completed by 173 participants during each trimester. The questionnaire included questions pertaining to current and past dietary habits, fluid intake, GI symptoms and lifestyle characteristics. Interestingly, a combination of low fibre (<22g/day) and low fluid (1300mL) intake increased risk of constipation during pregnancy. Lifestyle habits of women living with HG and constipation are not documented in the literature. As discovered by Maslin et al, it is likely for these individuals to have significantly decreased intake of all nutrients, including fibre [165]. Risk of inadequate fluid intake and dehydration in this population is well documented [221].

Lifestyle interventions for managing constipation include meeting dietary recommendations for fibre and consuming adequate liquid daily. Current adult dietary guidelines for fibre suggest maintaining an intake of 28g/day [222]. The fluid recommendations for adults during pregnancy are 2,300mL daily [32]. Meeting the national adult recommendations for physical activity is encouraged for adults to manage constipation (150 minutes of moderate intensity exercise each week). Although, ability to exercise with HG is likely hindered. Counselling individuals on treatment of this condition is crucial to reduce risk of psychological complications including frustration and low mood [223-225]. Counselling should include the appropriate time frame for use of medications given certain types (such as stimulant laxatives) are not recommended for long term use [226].

Medical interventions

There is extremely limited evidence to assess the effectiveness and safety of interventions for treating constipation in pregnancy. A Cochrane review identified few studies with small sample size and did not perform any meta-analyses [221]. The review found that stimulant laxatives appeared to be more effective in improvement of constipation relative to bulk forming laxatives but are accompanied by an increase in diarrhoea and abdominal discomfort and no difference in women's satisfaction. Additionally, fibre supplementation appeared to increase frequency of stools compared with no intervention. There were no data for a comparison of other types of interventions, such as osmotic laxatives, stool softeners, lubricant laxatives and enemas and suppositories.

Clinical Practice

Women should be treated based on their individual needs.

Dietary fibre

Women should be counselled to include a variety of soluble and insoluble fibre daily to meet increased requirements of 28g/day. Women with HG tend to consume a diet higher in carbohydrates due to its tolerability in comparison to protein and fat-containing foods. Encourage individuals to choose high-fibre options outlined below.

- Soluble fibre, e.g. porridge oats, beans, lentils, pulses, flesh of fruit
- Insoluble fibre, e.g. whole grains, skin of fruit and vegetables, nuts and seeds
- Milled flaxseed, milled linseed and wheat bran can be added to cereal, porridge, yoghurt, puree fruit or smoothies. It is recommended to start with 2 teaspoons daily and increase every 2 days until improvement is noticed. Encourage adequate hydration is maintained.

Hydration

Dehydration through external losses (vomiting) and reduced tolerance of fluids may exacerbate constipation. Estimated losses should be calculated and added to daily fluid requirements. Please see clinical question *'How should dehydration be assessed and managed'*. Refer to Appendix 7: Practical tips on diet with HG.

Physical activity

Once able individuals should aim to meet the recommended amount and intensity of physical activity for adults (150 minutes moderate intensity per week).

Medical Interventions

Medical interventions should be considered when lifestyle modifications are not effective. The aim of medical treatment of constipation is to restore a normal bowel movement so laxatives are best tried in the following order:

- Bulk-forming laxatives (e.g. ispaghula – Fybogel® and sterculia – Normacol®) increase the bulk of the stools and moisture in stool, stimulating bowel activity. Taken with plenty of water or fruit juice, they are usually effective in 24 hours, but may take 2-3 days of regular treatment
- Osmotic laxatives (e.g. lactulose – Duphalac®, Laxose and macrogols – Movicol®) increase the water content of stools. When taken on an empty stomach, they are effective in 24-48 hours.
- Stimulant laxatives (e.g. sodium picosulfate (Dulcolax Pico®), senna (Senokot®) and bisacodyl (Dulcolax®) increase peristalsis and intestinal secretions by stimulating the myenteric plexus and Auerbach plexus. Sometimes they can be ineffective unless they are combined with an osmotic or stimulant laxative. Not recommended for long term use. These products stimulate the bowel and should be effective in 6-12 hours. They are best taken at bedtime. This group should be used occasionally, regular use is not recommended.

Products such as magnesium salts, suppositories and enemas may be used occasionally but are not for regular use. Suppositories or enemas should be considered if the woman has not had a bowel evacuation for 5 or more days to treat severe constipation or in the case of faecal impaction.

Liquid paraffin is not recommended.

Castor oil should be avoided in pregnancy as it was traditionally used to induce labour.

Recommendations

28. We recommend that women with HG and constipation are counselled on lifestyle interventions for constipation including meeting dietary fibre recommendations (28g/day); maintaining hydration and engaging in regular physical activity.
29. We recommend that use of laxatives, via the oral or rectal route where appropriate, is considered (including bulk-forming, osmotic, and stimulant laxatives).

Section 10: Diabetes and Endocrine Considerations

Introduction

The effect of NVP and HG on women with endocrine disorders can be significant. Women with diabetes can have more challenging management of glucose control due to lack of ability to predict absorption; women with thyroid disorders can have difficulty absorbing medications.

Clinical Question 2.13: How are NVP/HG and endocrine disorders in pregnancy managed?

Evidence Statement

Endocrine disorders are the most commonly associated comorbidities in women admitted with NVP and HG [227]. NICE guidelines state the importance of educating women with pre-gestational diabetes pre-conceptually about the impact of nausea and vomiting of pregnancy on blood glucose control [228]. The HSE guideline for the management of pre-gestational and gestational diabetes mellitus from preconception to the postnatal period also includes the importance of assessing all women with diabetes and vomiting for Diabetic Ketoacidosis (DKA) [229]. International guidelines recommend all pregnant women with DKA should be admitted to HDU level care [228].

There is a relationship between HG and thyroid dysfunction due to the structural similarity of TSH and HCG [230]. Physiological gestational hyperthyroidism is a transient biochemical hyperthyroidism which normalises by the middle of the second trimester without any treatment. Clinically overt hyperthyroidism and thyroid antibodies are usually absent [231]. TSH should only be measured in women with HG refractory to treatment or in those with milder symptoms who have symptoms/signs of thyrotoxicosis [12]. It is not recommended to routinely check thyroid function testing for all women with NVP and HG [24,25,232].

Women who have HG and are managing diabetes during pregnancy (GDM, type 1 diabetes, type 2 diabetes and other forms of diabetes such as CF related diabetes, etc.) require specialist input from the multidisciplinary team (MDT) diabetes in pregnancy team in conjunction with those who are involved in the management of HG. This includes the endocrinologist, advanced midwife practitioner and dietitian, obstetric team and others as needed [229]. All staff should be aware of the potential for DKA in early pregnancy, and the significant fetal and maternal morbidity which is associated with DKA in pregnancy [233]. Women with diabetes or diabetes in pregnancy should be advised on the effect of nausea and vomiting on blood glucose control [228].

Clinical Practice

All women with insulin-requiring diabetes should be educated pre-conceptually regarding the potential impact of nausea and vomiting of pregnancy on blood glucose control.

An individualised approach is required as the severity of symptoms and the treatment plan of HG can vary. For those with GDM, lifestyle intervention through appropriate food choices and activity is the first line treatment. This may be difficult to implement depending on what foods are being tolerated by the person due to hyperemesis. If glycaemic control is not optimised by lifestyle and dietary changes, pharmacological treatment will be required.

Close monitoring will be required for those taking insulin to manage their diabetes during pregnancy, as there may be an increased risk of hypoglycaemia. For women who are using Continuous subcutaneous insulin infusion (CSII) (insulin pump) and/or CGM (continuous glucose monitor) and individualised approach will be needed to review settings on these devices.

Other factors to consider are weight loss and/or inadequate gestational weight gain and the need for oral nutrition support to optimise nutritional intake and the effect this may have on glycaemic control.

A MDT approach will be required and will need to be reviewed regularly during the course of the pregnancy.

People with diabetes who require glucose infusion must be given thiamine concurrent with or immediately after commencing dextrose/glucose infusion. Thiamine deficiency followed by glucose infusion poses a risk for Wernicke's encephalopathy.

Women with diabetes and women with diabetes in pregnancy (type 1, type 2, GDM) who are on pharmacological treatment should be advised to contact their diabetes service at any gestation if they have vomiting.

Pregnant women with type 1 diabetes should be offered blood ketone tests and a meter and advised to test for ketonaemia and seek urgent medical attention if they become unwell or notice rise in ketones.

There should be a low threshold for inpatient management of women with diabetes and NVP. There should be early involvement from the diabetic team and endocrinology.

Women with diabetes who are admitted for management of HG should have serum electrolytes monitored at least daily.

Women with type 1 diabetes mellitus who have a suspected DKA in pregnancy should have blood ketones measured, full blood count, urea and electrolytes, liver function tests, and an arterial blood gas to assess for acidosis. Management of DKA involves correction of dehydration, insulin deficit and electrolyte abnormalities. Local guidelines for management of DKA should be followed.

If thyroid function is abnormal, further assessment should be guided by possible causes. The most common alternative diagnosis to gestational hyperthyroidism is Grave's disease, in which TSH receptor antibody (TRAB) is positive. TSH should be measured in women with refractory NVP and HG and those with clinical signs of hyperthyroidism. If TSH is suppressed below the appropriate gestational range, repeat TSH, T3 and T4 should be taken along with thyroid antibodies. An ultrasound of the thyroid should be arranged if there is a goitre.

Recommendations

30. We recommend that pre-conceptional planning should advise women with pre-gestational diabetes of the potential impact of NVP and HG on blood glucose control.
31. We recommend an individualised approach to management for women with pre-gestational diabetes throughout the course of pregnancy including close monitoring and collaborative multi-disciplinary care including input from endocrinology.
32. We recommend that women with type 1 diabetes should be given blood ketone testing equipment and advised to assess for ketonaemia when unwell ("sick day rules").
33. We recommend that women with insulin-requiring diabetes or who are on pharmacological treatment should contact their diabetic service if vomiting. A low threshold for admission is recommended for patients with insulin-requiring diabetes and NVP/HG.
34. We recommend that diabetic ketoacidosis should be suspected in all women with diabetes presenting with vomiting and hyperglycaemia.
35. We recommend that measurement of TFTs should be reserved for those with severe, refractory NVP and HG, or those with overt symptoms or signs of hyperthyroidism. Those with supressed TSH should have further investigation for the underlying cause and appropriate referral to endocrinology services.

Section 11: Psychological and Trauma-Informed Care

Introduction

HG is a severe and debilitating condition that extends beyond physical symptoms, significantly impacting the mental health and quality of life of affected women. Women with HG experience significant distress associated with the condition. HG can affect every aspect of a woman's life and impair her ability to function on a day-to-day basis as well as affect the rest of her family. Recent studies highlight the broad-reaching effects of HG and suggest gaps in the knowledge-base particularly in relation to the role of psychological support.

Clinical Question 2.14: What is the impact of NVP and HG on mental health?

Evidence Statement

Numerous studies confirm that women with HG are at greater risk for emotional distress, anxiety, and depression than those with uncomplicated pregnancies [234,235]. One longitudinal study [234] measuring emotional distress at 17 and 32 weeks of gestation, as well as at six months postpartum found that women with HG experienced significantly higher distress at all three time points compared to controls, though the difference diminished by 18 months postpartum.

Impact on Quality of Life and Relationships

Quality of life has unsurprisingly been shown to be lower in women with HG, as is acceptance of pregnancy and motherhood [236,237]. The severity of vomiting correlates with a greater impact on quality of life and sense of psychological burden. Additionally, the emotional distress experienced by women with HG is often amplified by social and economic pressures, including isolation, financial stress, work absence, lack of support, and healthcare providers inadequate response [238,239]. In addition, HG has been shown to impact a woman's sense of self, her identity and it can contribute to a perception that she is dying and a feeling of being unable to care for self and others [240].

The impact of HG on women, families, and society is substantial. Poursharif *et al.* found that more than 80% of women with HG reported negative psychosocial effects, including socioeconomic burdens, relationship difficulties, and psychological sequelae [241]. Lacasse *et al.* report that Health Related Quality of Life (HRQOL) of women with moderate to severe nausea and vomiting of pregnancy was like HRQOL of women with breast cancer and myocardial infarction [242]. Hyperemesis and NVP has also been found to have a significant impact on paternal anxiety [243] and has an impact on family planning and decision making regarding future pregnancies [244]. Studies differ on whether bonding with the infant is impacted by HG with Beirne *et al.* indicating that there is an ongoing impact postnatally [245] while other studies suggest that bonding difficulties resolve once the baby is born [246].

Impact on Mental Health

Several studies have documented an increased rate of mental health difficulties in women with HG. One study of 200 women with HG compared to women without HG showed that 35% had mild depression, 26% moderate and 17.8% had severe, compared to 95% in the control group with no depression [247]. A systematic review of 59 articles and meta-analysis of 12 of these articles by Mitchell-Jones *et al.* showed a significantly increased frequency of depression and anxiety in women with HG [235]. Another study showed a high rate of depression and elevated anxiety scores as well as sleep disorders, with 60.9% having severe sleep disorders compared to 7.7% in the control group [248]. Paid employment has been shown to be a risk factor for anxiety associated with HG, and previous miscarriage a risk factor for depression associated with HG [249].

The findings regarding the link between eating disorders and hyperemesis gravidarum (HG) have been inconsistent. One study found no difference in body image scores or eating attitude test scores, suggesting that HG is associated with depression and anxiety rather than changes in eating attitudes and body image [250]. In their sample of over 38,000 women, Torgersen and colleagues found a link between NVP and HG and eating disorders but not between eating disorders and HG [250]. However, other research (Mantel 2020, Kouba, 2005) suggests that women with eating disorders may be at higher risk for developing HG [251,252]. More recent research has shown that women with a history of eating disorders are more likely to experience HG during pregnancy, and those who develop HG without a prior eating disorder diagnosis are more prone to developing an eating disorder afterward [253].

In some cases, recovery from HG results in an amelioration of mental health whereby women with HG demonstrated rates of depression falling from 19% during hospitalisation to 4% in the third trimester, anxiety fell from 69% to 19% and stress from 21% to 4% [237]. All three conditions were lower in the third trimester compared to the controls, which the authors concluded may be a "rebound" phenomenon of improved psychological wellbeing after physical recovery from HG, when only 15% of women had ongoing nausea and 9.9% had ongoing vomiting. However, Nijsten *et al.* indicate that multiple HG pregnancies or longer durations of symptoms can exacerbate the mental health burden, leading to an increased risk of anxiety disorders or PTSD [244]. Research shows that post-traumatic stress symptoms are prevalent in 18% of women after HG pregnancies and are associated with negative life outcomes [254]. In a study of 5,071 women, 74% self-reported HG, and 52% considered termination of pregnancy

(TOP) due to their symptoms [255]. 25.5% reported occasional suicidal ideation, and 6.6% reported regular suicidal thoughts, which were linked to more severe illness, perceptions of poor care, and lower functional status.

The Role of Healthcare Providers and Barriers to Care

Research indicates that healthcare professionals' reluctance to recognise and treat NVP and HG can worsen both physical and mental health outcomes [240]. Women who undergo termination of pregnancy due to HG have been found to be three times more likely to describe their healthcare providers as uncaring compared to those who do not terminate [241]. Studies suggest that improving care would involve addressing symptoms holistically while considering the woman's life situation [242,245]. McCormack *et al.* emphasised that the World Health Organization (WHO) recommends psychological interventions for patients whose physical illnesses contribute to mental distress, yet many HG patients report difficulty accessing appropriate mental health care [256].

Psychological Interventions: Current Evidence and Future Directions

While evidence for psychological interventions in HG remains limited and of low quality [257], some small studies suggest potential benefits from mindfulness-based interventions, cognitive-behavioural therapy (CBT), and progressive muscle relaxation [19]. Faramarzi *et al.* conducted an RCT comparing pharmacotherapy alone vs. pharmacotherapy plus a three-week mindfulness-based stress reduction intervention [258]. Women in the mindfulness group experienced significantly lower nausea and vomiting episodes and reduced anxiety symptoms. Gawande *et al.* found that women who practiced progressive muscle relaxation alongside pharmacotherapy showed greater clinical improvement than those receiving pharmacotherapy alone [259]. Fletcher *et al.* compared a holistic assessment and individualised care plan to standard care, finding that while nausea and vomiting severity did not significantly differ, women in the holistic care group had shorter hospital stays [260]. Evidence for Eye Movement Desensitisation and Reprogramming (EMDR) is insufficient to ascertain whether it is an effective management tool with only one study indicating that it can help ameliorate the symptoms of HG [261]. A review of 45 studies on the use of hypnosis for NVP and HG found that all studies reported positive outcomes but the quality of the evidence was insufficient to accurately assess the efficacy of hypnosis [262].

International guidelines indicate that psychological support should be provided [24]. McCormack *et al.* identify the importance of developing a targeted intervention designed to prevent and/or treat mental health difficulties associated with HG [256]. There is a lack of research as to which psychological interventions would be beneficial in either reducing symptomatology associated with HG or reducing the emotional impact wrought by HG on a woman and her family. Lee and Saha point to the lack of understanding of the role that psychotherapy can play [263]. Future studies should confirm whether better treatment of HG can prevent or improve depression, anxiety and PTSD symptoms [244].

Researchers advocate for a shift towards a holistic biopsychosocial model of care for HG [245,264], and in their conclusions, Mitchell Jones *et al.* highlight the need for service development for women with HG that includes provision of psychological care and support [246]. Other researchers, for example Castillo and Phillippi suggest that given the lack of data to guide recommendations and the gravity of psychosocial morbidity, psychological therapy should be view as not essential to treatment, but appropriate for women who are interested and find it helpful [265]. Given the status of the evidence base it may be more helpful to view psychological therapy as a means of reducing stress and distress, and a way of accessing additional internal and interpersonal support. While the research base is building it is suggested that clinicians explore the use of techniques that feel acceptable to the woman and look to research in areas such as intractable vomiting following chemotherapy for direction. For example, a systematic review of psychological interventions for chemotherapy-induced nausea and vomiting among women with breast cancer found that cognitive-behavioural therapy, progressive muscle relaxation training, guided imagery, and yoga alleviated symptoms [266].

A recurrent theme in the research is that HG can escalate to the point that a woman may consider a termination of pregnancy and suicidal ideation has also been associated with HG [255,267]. The immediate and long term mental and social consequences and complications of HG on a pregnant person's body, the effects on a person's (and their families) quality of life, effects on mental health, efficacy of psychotherapy and access to psychotherapy have all been identified as priorities for HG research in an international patient clinician partnership [264].

Health care professionals should adopt a holistic and compassionate approach to assessment in HG [245,268]. Researchers suggest that further education is required to improve practitioner awareness and management of the condition [237]. Patients report a large contributor to distress is difficulty accessing treatment or feeling to have to fight for adequate treatment of their condition [242]. Practitioners should address the severity of a woman's symptoms in relation to her quality of life and social situation and offer adequate treatment of HG that is acceptable to the patient to ease and avoid psychological distress.

Psychological screening could utilise routine evaluation instruments, for example the EPDS [269] and Whooley Question [270], quality of life instruments such as the SF12 [271] or instruments specific to HG, such as the Hyperemesis Impact of Symptoms Questionnaire (HIS) [272].

Involvement of a mental health team in the care of a woman with HG may improve her quality of life and the ability to cope with the pregnancy [273]. Emotional support and psychological or psychiatric care may be required with targeted interventions specifically designed to treat mental health issues in HG, which are a result of HG rather than a cause [254,256].

With regard to employed women, flexible work schedules including breaks and assistance from families with daily duties in the household may help to relieve fatigue and may consequently help to relieve nausea and vomiting and improve Health Related Quality of Life in these women [274].

Clinical Practice

Addressing Symptoms and Quality of Life

Practitioners should evaluate the severity of a woman's symptoms in relation to her quality of life and social circumstances.

Psychological Assessment

When assessing women with Hyperemesis Gravidarum (HG), a psychological evaluation should focus on the woman's mental health, quality of life, and social support network. The HIS (Hyperemesis Impact Scale) is a validated 10-item self-administered questionnaire that can provide insight into the physical and psychosocial impact of HG. It includes questions on daily activities and psychosocial stress, which can help in creating a comprehensive, compassionate care plan.

Psychological Interventions

Where appropriate, clinicians should offer evidence-based psychological interventions. Although specific research on HG is limited, interventions should be tailored to the woman's level of distress. Clinicians must remain flexible and adjust interventions to suit the individual's capacity. Approaches such as cognitive-behavioural therapy (CBT), progressive muscle relaxation, guided imagery, and yoga may help alleviate symptoms. These techniques can be discussed with pregnant women to assess acceptability and trial them as treatments for distress associated with HG.

Referral for Psychological Support

If necessary and with consent, consider referring the woman to a psychologist within a perinatal or community setting for further support.

Partner and Family Support

Psychological support can also provide a safe space for the woman and her partner to identify resources to assist them during the pregnancy, especially if children are involved.

Rest and Family Support

Women should be encouraged to rest as needed to manage symptoms. Families should be supported in facilitating this. A flexible work schedule and breaks within the household may also be beneficial.

Recommendations

36. **We recommend that women with NVP and HG are routinely and periodically screened for emotional distress during and after pregnancy using validated measures and referred on to appropriate supports as needed with consent. Where indicated psychiatric assessment and intervention should be offered.**
37. **We recommend that practitioners consider a differential diagnosis between HG and eating disorder-related vomiting. Provide appropriate level of care for such diagnoses (HG, eating-disorder or diagnosis of both HG and an eating disorder).**
38. **We recommend that trauma sensitive staff training should be considered for staff interacting with women experiencing HG. In cases where clinicians do not have access to such training management should be informed so that funding can be obtained, and trauma sensitive training prioritised.**

Section 12: Delivery and Termination Considerations

Introduction

For people where NVP and HG persists throughout pregnancy, birth can represent a time that may result in relief of symptoms. Timing and mode of birth can be assessed as part of the wider context of the woman's wishes, her previous obstetric history, co-morbidities, mental wellbeing and care to date. In very rare cases where HG is severe and complications present, early delivery may be recommended in the interest of maternal health.

Almost 5% of women with HG will terminate a wanted pregnancy due to severity of symptoms, and some women may feel termination of pregnancy is the best option for their wellbeing [268]. In other cases complications of HG may be life-threatening and termination of pregnancy may be recommended in maternal interest.

Clinical Question 2.15: Should women with HG be offered early delivery, and when should this be considered?

Evidence Statement

There is a lack of literature regarding recommendations surrounding early delivery or induction of labour based on a diagnosis of hyperemesis. This may be associated with the understanding that symptoms most commonly subside later in pregnancy and would be resolved by the third trimester. Guidance from RCOG and SOMANZ does not discuss early delivery based on HG alone, but support individualised care [19,24].

Clinical Practice

While HG alone is not typically an indication for induction of labour, in severe refractory cases not responding to treatment, early delivery may be considered in maternal interest, following multidisciplicary input. In cases where HG is severe and persistent into the third trimester, delivery may be considered when fetal maturity is reached at 37 weeks, on an individualsied basis and taking the woman's wishes into account.

Recommendations

39. **HG alone is not an indication for early delivery or induction of labour, however an individualised approach taking the woman's preferences into account is recommended.**

Clinical Question 2.16: Should termination of pregnancy due to HG be discussed and when?

Evidence Statement

Many women report having considered termination of pregnancy on the grounds of symptoms of HG. A prospective study involving 215 women involved in the MOTHER trial found 40% of those that had a subsequent pregnancy delayed this due to HG, one patient had a termination of pregnancy due to recurrent HG, and eight women (23%) considered a termination due to a recurrence of symptoms [267]. Women report poor care experience and difficulty accessing medication as risk factors for termination of pregnancy and suicidal ideation. In a UK survey of more than 5000 patients with HG, 52.1% considered a termination due to their symptoms [255,268]. RCOG state that all therapeutic measures should have been tried before offering termination of a wanted pregnancy for HG symptoms [19]. Common reasons for TOP in the study included feeling unable to care for family and believing a TOP was the only way to avoid suicidal ideation [255].

Clinical Practice

Women in Ireland may request a TOP for a variety of reasons. It is good practice that reasonable therapeutic measures are tried before considering TOP of wanted pregnancy specifically for management of HG symptoms. Under the current legal criteria for TOP, women with NVP and HG may access TOP care under section 12 (under 12 weeks without having to give a reason), section 9 (significant risk to mental or physical health or risk to life) or Section 10 (in an emergency). Section 11 applies to pregnancies where the fetus has an anomaly that means they are likely to die within 28 days of childbirth, i.e. the indication is fetal rather than maternal.

Recommendation

40. **We recommend that the request for TOP should be reviewed by the appropriate members of the multidisciplinary team considering the legal criteria for TOP, the clinical situation, the best interests of the woman and her wishes. It is also important to recognise that under the 2018 Termination of Pregnancy Act women are entitled to a termination under 12 weeks without giving a reason for their decision**

Clinical Question 2.17: Can recurrence of HG be prevented in subsequent pregnancies?

Evidence Statement

The recurrence rate of hyperemesis gravidarum has not been formally established but due to the proposed genetic nature of the condition, recurrence of HG has been studied [267, 275, 276] (multiple references). The MOTHER randomised control trial in the Netherlands assessed whether early enteral tube feeding in addition to standard care for women admitted with HG improved neonatal and maternal outcomes [167]. As a follow-up, women were asked to complete a self-directed questionnaire exploring maternal outcomes (n=73) [267]. High recurrence risk of 89% was found and 40% of women postponing pregnancy due to their previous experience. Termination was considered in 25% of women and one woman terminated. 63% of women who did not have another pregnancy avoided pregnancy due to HG.

Clinical Practice

This is an opportunistic time for women to correct any nutritional deficiencies which may have been exacerbated by previous HG pregnancy.

Key vitamins and minerals such as iron, vitamin B12, folic acid and vitamin D should be assessed during pre-conception care and corrected prior to conception. When planning an additional pregnancy, women should be encouraged to take 400µg/day folic acid at least 3 months prior to conception.

Women should be encouraged to know their pre-pregnancy weight to support identifying weight loss and risk of malnutrition in future pregnancies.

Online resources and support groups should be encouraged such as Hyperemesis Ireland.

Recommendations

41. **Women who were admitted to hospital for HG in previous pregnancy should be considered high risk of HG recurrence.**
42. **Pre-conception planning should include nutrition assessment of key nutrients such as iron and folic acid, with folic acid 400µg per day supplementation advised 3 months prior to conception.**

Chapter 3: Development of Clinical Practice Guideline

3.1 Literature search strategy

The evidence to support this recommendation is largely derived from journals and textbooks as well as from research exploring clinicians' knowledge and decision-making in the area of hyperemesis gravidarum. To inform the development of this guideline, existing policies and the recently published international guidelines from two professional bodies on nausea and vomiting in pregnancy and hyperemesis gravidarum were also reviewed.

A comprehensive literature review was undertaken in January of 2023 which included national and international publications. This involved searches of various databases including EMBASE and PubMED and Cochrane dating from 1954-present. A primary search string was made and combined with various different facets depending on the clinical question and speciality involved. The primary search string was hyperemesis gravidarum OR hyperemesis OR morning sickness, and in the case of pharmacy was combined with one separate facet "antiemetic agent or Pyridoxine/doxylamine or cyclizine or metoclopramide or ondansetron or chlorpromazine or prochlorperazine or promethazine or domperidone or hydrocortisone or dexamethasone or prednisolone". Search terms varied based on the question asked, and results were reviewed by those responsible for each clinical question and were rejected or included by an appraisal of the evidence provided. Priority was given to evidence from randomised-controlled trials, meta-analyses and systematic reviews.

Additional research was identified after the initial search, up until end of Dec 2025 through individual author searches as deemed necessary to fully address each clinical question and respond to feedback from external review.

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.

Several evidence-based recommendations for management of nausea and vomiting or hyperemesis gravidarum 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 8) as recommended by the Department of Health in the 'How to Develop a National Clinical Guideline: a manual for guideline developers', 2019[22].

22 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/

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 literature search was completed by NW, EOB and TL, identifying relevant research. Evidence was categorised and each category was reviewed by the relevant subject experts as part of the wider guideline author group. Additional research was identified through individual author searches as deemed necessary to full address each clinical question.

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.[23]

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.[24] (Appendix 9).

3.6 Future research

An important outcome of the Guideline development process is in highlighting gaps in the evidence base. Future research should continue to build on evidence for optimal medical management, nutrition support, psychological interventions and mental health services, and overall research in the management and impact of hyperemesis specifically. A James Lind Priority Setting Partnership has assessed research priorities in this context. We endorse the research priorities that were identified through this process [264].

23 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.

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. doi: 10.1016/j.ajog.2013.07.012.

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 (GPT). 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[25] for developing Policies, Procedures, Protocols and Guidelines (2023) and under supervision of the Guideline Programme Team.

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 10 for list of CAG members.

4.3 Copyright/Permission sought

HER foundation: The Guideline Developers sought permission from Kimber MacGibbon on 31/05/24. Permission granted by Kimber on 13/06/24.

25 Health Service Executive (2023). How to develop HSE National Policies, Procedures, Protocols and Guidelines (PPPGs).

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[26].

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 and supporting documents available to all employees through standard networks. Electronic versions available on the https://www2.healthservice.hse.ie/organisation/national-pppgs/ and RCPI websites https://www.rcpi.ie/faculties/obstetricians-and-gynaecologists/national-clinical-guidelines-in-obstetrics-and-gynaecology/ and other communication means can be used to maximise distribution.

In the case of this Guideline, it will be shared with Hyperemesis Ireland and nationally through medical and other relevant organisations.

26 Department of Health (2018). NCEC Implementation Guide and Toolkit. Available at: https://www.gov.ie/en/collection/cd41ac-clinical-effectiveness-resources-and-learning/?

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 Guideline 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

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

General barriers to implementation of the guideline include access to services and staff training. This guideline aims to address that by providing clear algorithms to support healthcare professionals in practice, including how to assess severity, nutrition and hydration and medication management. Resource barriers exists such as lack of facilities and trained staff to trial enteral or parenteral nutrition safely in the maternity setting and variable access to resources such as dayward hydration services and supportive services such as dietetics and mental health. Individual providers should consider what is possible to offer within their setting and identify areas for increased resource and training as appropriate.

Access to care barriers may also exist for women who may not be able to attend the hospital or community healthcare providers, or may have limited health literacy or language barriers that limit their engagement with healthcare services. Maternity healthcare professionals supporting women with nausea and vomiting should be aware of the multiple factors that may limit a woman's ability to seek and engage with care so that support can be provided according. Clear, accessible and appropriate advice should be made available to women on how and when to take medications, the other strategies that can support management such as diet, fluids and rest, and when/where to seek help.

People with HG face significant barriers in accessing psychological support:

- Services are often hospital focused; while the larger maternity units have specialist perinatal mental health teams, smaller centres cannot access these services and often have limited access to other sources of psychological support. Limitations in funding mean psychological input is often under-resourced with restrictions on the level of support that can be accessed by people unless they are experiencing moderate to severe mental health disorders. Stigma and misunderstanding or invalidation of HG can minimise the severity of psychological distress and heighten the experience of invalidation for service users. For many the nature of the condition itself acts as a significant barrier to attendance as people cannot get to appointments or implement strategies in between sessions.

Strategies to address these challenges:

- Embed routine mental health screening within services so psychological need is identified early and referrals can be made to the appropriate service.
- Include HG as a condition requiring mental health input and ensure that this is included within the resource allocations of the mental health services and referenced in the revision of the perinatal model of care.
- Allocate resources to capacity building within the workforce so that multi-disciplinary clinicians supporting women with HG feel competent to provide psychoeducation about the condition and teach strategies to aid in symptom management.
- Support researchers to develop and validate online tools that women can access when they feel able. Develop a HSE approved website offering online tools and access to targeted online support such as bibliotherapy that can be accessed nationwide.
- Consider requesting funding for additional psychology and mental health midwifery posts within maternity hospitals so that clinicians are available to attend antenatal clinics and respond to a person's need when they present rather than having to go through a referral pathway and wait on an outpatient appointment.
- Train staff involved in the care of women with HG in trauma informed models so that they can communicate with women in a way that is validating. Support continuity of care between inpatient and community care.
- Offer online sessions to support attendance and offer text-based check-ins with clinicians when women are unable to attend due to illness.

Ways around barriers:

- Allocate specific funding to the psychological care of women with HG and build the requirement for psychological screening and referral pathways into the national maternity strategy.
- Encourage organisations to invest in trauma informed care training for all staff. As a first step staff should complete the trauma informed care module on HSEland.
- Research into the use of psychological treatments for symptoms of HG should be supported.

Addressing barriers for people with HG will require system-level investment in opening up access to psychological care and ensuring that services are adequately resourced to support women on an individual level and to offer capacity building for clinicians working in both hospital and community settings. A stepped-care, evidence-based model that uses technology such as apps where appropriate, and embedding the importance of psychological care for this vulnerable group of service users within national policy is the means to consistently support the needs of these women.

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 the care of the woman. 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, as detailed in Appendix 11.

Auditable standards for this Guideline include:

1. Calculation and documentation of PUQE score of women attending care for treatment of nausea and vomiting (initial and subsequent presentations or daily on ward).
2. Assessment of medication prescribing practices with reference to the treatment algorithm.
3. Appropriate ultrasound Scans, bloodwork, correction of electrolyte imbalances, VTE assessments, fluid replacement, and intake/output assessment.
4. Number of women with NVP and HG attending the perinatal mental health team.
5. Number of attendances per patient to ED, Day Ward, inpatient admissions, and outpatient appointments

Where electronic health records are available, collaboratively-developed routine reports should be used to describe and audit the management of this population.

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.[27]

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.

27 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.[28]

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.

28 Health Service Executive (2023). How to develop HSE National Policies, Procedures, Protocols and Guidelines (PPPGs).

Chapter 9: **References**

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Supporting Evidence

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

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

Glossary

ACOG American College of Obstetrics and Gynaecology

AGREE Appraisal of Guidelines for Research and Evaluation

BNF British National Formulary

BMI Body Mass Index

CAG Clinical Advisory Group

CF Cystic Fibrosis

CGM Continuous glucose monitor

CSII Continuous Subcutaneous Insulin Infusion

D2 Dopamine

DKA Diabetic Ketoacidosis

EAG Expert Advisory Group

EFSA European Food Safety Authority

EMA European Medicines Agency

FBC Full Blood Count

FSAI Food Safety Authority of Ireland

FIGO International Federation of Gynaecology and Obstetrics

GDM Gestational Diabetes Mellitus

GI Gastrointestinal Losses

GPT Guideline Programme Team

GRADE Grading of Recommendations, Assessments, Developments and Evaluations

Hb Haemoglobin

HCG Human Chorionic Gonadotropin

HCPs Health Care Practitioners.

HDU High Dependency Units

HELP HyperEmesis Level Prediction

HER Hyperemesis Education and research

HG Hyperemesis gravidarum

H1 Histamine

HIS Hyperemesis Impact of Symptoms Questionnaire

HIQA Health Information and Quality Authority

HRQOL Health Related Quality Of Life

HSE Health Service Executive

INDI Irish Nutrition and Dietetic Institute

IOG Institute of Obstetricians and Gynaecologists

IrSPEN Irish Society for Clinical Nutrition & Metabolism

IV Intravenous

ISMP The Institute for Safe Medication Practise

LC-PUFAs Long chain polyunsaturated fatty acids

LFTs Liver Function Tests

M1 muscarinic

MDT Multidisciplinary Team

MOTHER Maternal Opioid Treatment: Human Experimental Research

MUAC Mid-upper arm circumference

NCEC National Clinical Effectiveness Committee

NICE National Institute for Clinical Evidence

NTD Neural Tube Defects

NVP Nausea and Vomiting of pregnancy

NWIHP National Women and Infants Health Programme

PEG Percutaneous Endoscopic Gastrostomy

PPPG Policy, Procedures, Protocols and Guidelines

PTSD Post-Traumatic Stress Disorder

Ptyalism Hypersalivation

PUQE Pregnancy Unique Quantification of Emesis and Nausea

RCOG Royal College of Obstetrics and Gynaecology

RCPI Royal College Of Physicians of Ireland

SOMANZ Society of Obstetric Medicine of Australia and New Zealand

SWS Southampton Women's Survey

T3 Triiodothyronine

T4 Thyroxine

TFTs Thyroid Function Tests

TOP Termination of Pregnancy

TSH Thyroid Stimulating Hormone

UK United Kingdom

US United States

WHO World Health Organisation

Appendix 1:
Expert Advisory Group Members 2021-

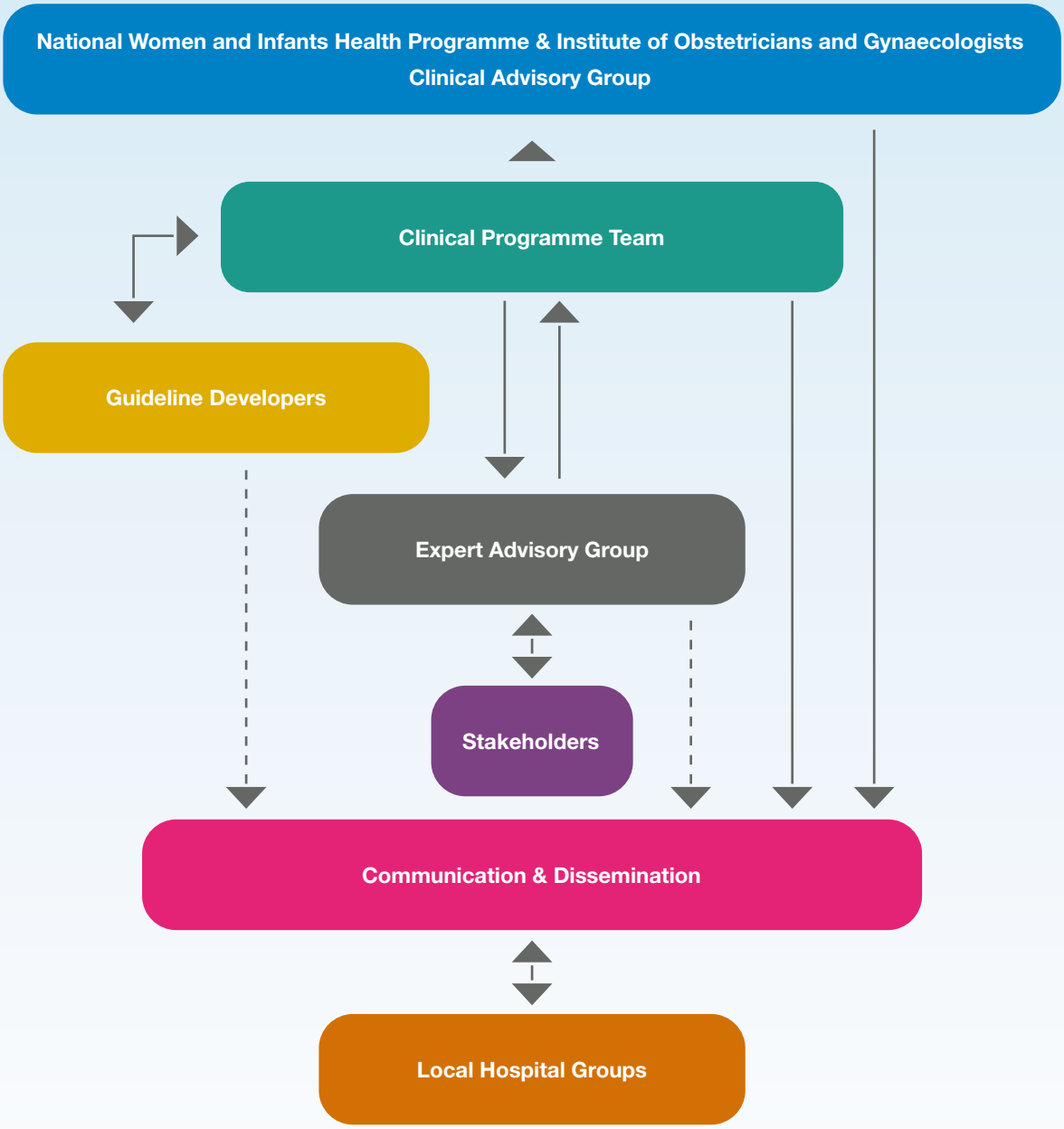
Member	Profession	Location
Dr Mairead Butler	Consultant Obstetrician and Gynaecologist	University Hospital Waterford
Dr Nicholas Barrett	Consultant Anaesthesiologist, Lead for Obstetric Anaesthesiology services	Limerick University Hospital
Dr Venita Broderick	Consultant Obstetrician and Gynaecologist	National Maternity Hospital Dublin
Ms Siobhan Canny	Group Director of Midwifery	Saolta University Health Care Group
Ms Triona Cowman	Director of the Centre for Midwifery Education	Centre for Midwifery Education, Coombe Women & Infants University Hospital
Ms Marie Culliton	Lab Manager/Chief Medical Scientist	National Maternity Hospital Dublin
Ms Niamh Connolly-Coyne *And* Ms Mandy Daly *(Shared nomination)*	Board of Directors Members	Irish Neonatal Health Alliance
Ms Jennifer Dempsey	Clinical Tutor in Midwifery	University College Dublin
Ms Sinéad Curran	Dietician Manager	National Maternity Hospital
Dr Niamh Conlon	Consultant Histopathologist	Cork University Hospital
Ms Georgina Cruise	National Manager	Patient Advocacy Service
Dr Orla Donohoe	Specialist Registrar, Obstetrics and Gynaecology and SWEC Fellow	St George Hospital, Sydney, Australia
Ms Alana Dineen	Senior Clinical Pharmacist	Cork University Maternity Hospital
Prof. Maeve Eogan	Consultant Obstetrician and Gynaecologist National Clinical Lead SATU (HSE)	Rotunda Hospital Dublin
Dr Brendan Fitzgerald	Consultant Perinatal Pathologist	Cork University Hospital

Member	Profession	Location
Dr Daniel Galvin	Specialist Registrar, Obstetrics and Gynaecology	Cork University Maternity Hospital
Ms Stacey Grealis	Patient Research Partner	Independent Living Movement Ireland
Ms Fiona Hanrahan	Director of Midwifery and Nursing	Rotunda Hospital Dublin
Ms Laura Harrington	Principal Medical Social Worker	National Maternity Hospital Dublin
Dr Caroline Joyce	Principal Clinical Biochemist Adjunct Clinical Lecturer PhD Candidate	Cork University Hospital University College Cork
Dr Chaitra Jairaj	Consultant Perinatal Psychiatrist	Coombe Women & Infants University Hospital, Dublin Midland Regional Hospital Portlaoise
Dr Cathy Monteith	Consultant Obstetrician and Gynaecologist	Our Lady of Lourdes Hospital Drogheda
Oana Marian	PhD, Post-Doctoral Researcher	Pregnancy Loss Research Group, INFANT Centre, University College Cork
Prof. John Murphy	Consultant Neonatologist Clinical Lead for the National Clinical Programme for Paediatrics and Neonatology	National Women and Infants Health Programme
Ms Janet Murphy	Advanced Midwifery Practitioner	University Hospital Waterford
Dr Jill Mitchell	Specialist Registrar, Obstetrics and Gynaecology	Cork University Maternity Hospital
Dr Aisling McDonnell	Specialist Registrar, Obstetrics and Gynaecology	Mater Misericordiae University Hospital Dublin
Dr Ciara McCarthy	General Practitioner ICGP and NWIHP Women's Health Lead	Irish College of General Practitioners
Ms Orla McCarthy	Clinical Specialist Physiotherapist in Pelvic Health	Cork University Maternity Hospital
Dr Sarah Nicholson	Locum Consultant Obstetrician and Gynaecologist	Sligo University Hospital

Member	Profession	Location
Dr Donough J. O'Donovan	Director Neonatal Intensive Care Unit Consultant Neonatologist/Paediatrician	University College Hospital Galway
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
Dr Gillian Ryan	Consultant Obstetrician and Gynaecologist	University Hospital Galway
Ms Nora Vallejo	Advanced Midwife Practitioner	Coombe Women & Infants University Hospital, Dublin

Member 2021-2025	Profession	Location
Dr Katherine Astbury	Consultant Obstetrician and Gynaecologist	University Hospital Galway
Dr Richard Duffy	Consultant Perinatal Psychiatrist	Rotunda Hospital Dublin
Ms Clare Farrell	Physiotherapy Manager	Coombe Women & Infants University Hospital, Dublin
Ms Marie Finn	Medical Social Work Counsellor	Saolta University Health Care Group
Prof. Declan Keane	Consultant Obstetrician, Gynaecologist, Professor of Obstetrics and Gynaecology	National Maternity Hospital Dublin, Royal College of Surgeons in Ireland
Ms Áine Kelly	Physiotherapy Manager	Coombe Women & Infants University Hospital, Dublin
Dr Fergus McCarthy	Consultant Obstetrician, Gynaecologist	Cork University Maternity Hospital, University College Cork
Dr Sarah Petch	Specialist Registrar, Obstetrics and Gynaecology	National Maternity Hospital Dublin
Ms Margaret Quigley	National Lead for Midwifery	Office of Nursing and Midwifery Services Director
Prof. Valerie Smith	Chair of Midwifery	University College Dublin
Ms Marita Hennessy	Post-Doctoral Researcher	Pregnancy Loss Research Group, INFANT Centre, University College Cork

Appendix 2:
Guideline Programme Process



Appendix 3:
HELP Tool – published with permission from the HER foundation

HELP (HyperEmesis Level Prediction) SCORE

Name: _____ Date: _____ Gestational Age: _____ SCORE: _____

TODAY'S Weight: _____ LAST WEEK'S Weight: _____ Change: _____% PREVIOUS SCORE: _____

Meds: ☐ Ondansetron ☐ Granisetron ☐ Diclegis ☐ Promethazine ☐ Metoclopramide ☐_____

Mark ONE box in EACH ROW that describes symptoms over the last 24 hours unless specified otherwise.

My nausea level most of the time:	0	1 (Mild)	2	3 (Moderate)	4	5 (Severe)
I average __ vomiting episodes/day:	0	1-2	3-5	6-8	9-12	13 or more
I retch/dry heave __ episodes daily:	0	1-2	3-5	6-8	9-12	13 or more
I am urinating/voiding:	Same	More often due to IV fluids; or light color	Slightly less often, and normal color	Once every 8 hours; or slightly dark yellow	Less than every 8 hours or darker	Rarely; dark or bloody; or foul smell
Nausea/vomiting severity 1 hour after meds OR after food/drink if no meds:	0 or No Meds	1 (Mild)	2	3 (Moderate)	4	5 (Severe)
Average number of hours I'm unable to work adequately at my job and/or at home due to being sick has been:	0	1-2 (hours are slightly less)	3-4 (can work part time)	5-7 (can only do a little work)	8-10 (can't care for family)	11+ (can't care for myself)
I have been coping with the nausea, vomiting and retching:	Nor-mal	Tired but mood is ok	Slightly less than normal	It's tolerable but difficult	Struggling: moody, emotional	Poorly: irritable depressed
Total amount I have been able to eat/drink AND keep it down: Medium water bottle/large cup = 2 cups/500mL.	Same; no weight loss	Total of about 3 meals & 6+ cups fluid	Total of about 2 meals & some fluid	1 meal & few cups fluid; or only fluid or only food	Very little, <1 meal/minimal fluids; or frequent IV	Nothing goes or stays down, or daily **IV/TPN/NG**
My anti-nausea/vomiting meds stay down or are tolerated:	No meds	Always	Nearly always	Sometimes	Rarely	Never/**IV/SQ** (SubQ pump)
My symptoms compared to last week:	Great	Better	About Same	Worse	Much Worse	So Much Worse!!!
Weight loss over last 7 days: ___%	0%	1%	2%	3%	4%	5%
Number of Rx's for nausea/vomiting*	0	1	2	3	4	5+
	0 pts	**1 pt/answer**	**2 pts/answer**	**3 pts/answer**	**4 pts/answer**	**5 pts/answer**
TOTAL each column = (#answers in column) x (# points for each answer)	0	____	____	____	____	____
TOTAL for ALL columns: _____	**None/Mild ≤ 19**			**Moderate 20-32**		**Severe 33-60**

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Weight Loss % = (Amount lost ÷ Pre-pregnancy weight) x 100
(Weight loss calculation optional for home use)
* Number of Rx's = Number of Rx medications for HG (not doses)

HER Foundation

info@hyperemesis.org
www.hyperemesis.org
www.HelpHER.org

Support:
help@hyperemesis.org

HER Foundation
10117 SE Sunnyside Road F8
Clackamas, OR 97015 USA

Reprints:
www.hyperemesis.org/tools

Appendix 4: Medications that have been used to treat HG but are not recommended due to low quality evidence base

Gabapentin

Mechanism of Action

The exact mechanism by which gabapentin exerts it's anti-emetic effect is not known (1). Gabapentin's antiemetic properties were first reported when associations were noticed between delayed chemotherapy induce nausea and vomiting in women with breast cancer (2,3).

Background and safety

Gabapentin treatment in animals was associated with fetal growth impairment as well as developmental delay. There are human reports of normal and abnormal pregnancy outcomes following gabapentin therapy however controlled studies have not yet suggested an association or risk of malformations. Most of the research has focused on Epilepsy and the safety evidence is conflicting. There is limited evidence for Gabapentin in hyperemesis and is therefore not recommended (1,2, 4,-9)

Mirtazapine

Mechanism of action

Mirtazapine is primarily used as an antidepressant. It exerts it's antidepressant effects as a noradrenergic and specific serotonergic antidepressant (NaSSA) that acts by antagonising the adrenergic alpha2-autoreceptors and alpha2-heteroreceptors as well as by blocking 5-HT2 and 5-HT3 receptors (10). Its activity at the 5-HT3 receptor is how its anti-emetic effects are mediated in a similarly way to ondansetron.

Background and safety

Maternal mirtazapine exposure during pregnancy is not expected to increase the risk of congenital abnormalities (reprotox). Mirtazapine exposure in pregnancy has systematically reviewed with study authors concluding that it is safe in pregnancy (11). Furthermore, a recent Danish registry based study including 1,650,649 pregnancies from 1997-2016 found no association between mirtazapine exposure and major congenital malformations, spontaneous abortion, stillbirth or neonatal death. Study authors advised that mirtazapine is safe in pregnancy (12).

Effectiveness

There is limited evidence in the literature of mirtazapine's effectiveness as a sole treatment for hyperemesis gravidarum. Research is limited to several case reports although a protocol for a randomised controlled trial has been published which aims to validate the effect of ondansetron and mirtazapine in treating hyperemesis gravidarum (13).

The case reports describe severe presentations of hyperemesis in which the patient has not responded to other anti-emetic medications and may also be suffering from anxiety or depression related to nausea and vomiting. Studies generally report positive outcomes associated with Mirtazapine use (14-17).

Further research is required to establish the effectiveness of mirtazapine in treating hyperemesis in comparison with other anti-emetics. The safety data available in pregnancy is so far reassuring. Mirtazapine should be reserved in cases whereby traditional anti-emetics have been unsuccessful and there is a requirement to treat a depressive episode (17).

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Appendix 5: Fluid and Electrolyte Monitoring – Adapted from Friedli and IrSPEN

Potassium replacement (from IrSPEN)

Initial potassium infusions should not use glucose if possible as this may cause an intracellular shift in potassium and further depletion. Cardiac monitoring is required if the rate exceeds 10mmol K^+/hour or concentration greater than 40mmol K^+/L. *Concentrations exceeding 40mmol K^+/L should be given via a central line to avoid pain, phlebitis and extravasation injury. Baseline ECG is necessary if serum K^+ <3mmol/L. If serum K^+<3.3mmol/L, magnesium level should be checked (41). For fluid restricted patients, maximum concentration 40 mmol/500ml (800mmol/L).

Serum potassium level	Guideline for repletion
Critical deficit K^+ <2mmol/L or K^+ <2.5mmol/L with ECG changes characteristic of hypokalaemia	Likely to require replacement in intensive setting, seek specialist advice
Severe deficit K^+ 2-2.5mmol/L without critical conditions or ECG changes	Intravenous replacement via peripheral line 1. 40mmol K^+/1L premixed solution of potassium and fluid, given at 125mL per hour dependent on fluid status of patient. 2. Check serum potassium after 8 hours of commencement of infusion. 3. If serum potassium not corrected to normal levels, repeat step 1. Correct serum potassium to normal levels. Total supplementation of 80mmol K^+ often required in cases of severe deficit.
Moderate deficit K^+ 2.5-3.0mmol/L	Intravenous replacement via peripheral line 1. 40mmol K^+/1L in premixed solution at 125mL per hour, dependent on patient fluid status. 2. Check serum potassium level after 8 hours. 3. If not corrected to normal levels, give further 20mmol K^+/500mL fluid. 4. Check serum potassium level 4 hours after last dose. Repeat infusion at step 3 as necessary to correct serum potassium to normal level.

Serum potassium level	Guideline for repletion
Mild deficit K^+ 3.1-3.5mmol/L	Oral replacement: Slow K® – 2 tabs tds (8mmol K^+/tablet) **Sando K 2 to 4 tablets daily in divided doses. Each Sando-K® tablet contains potassium 470 mg (12 mmol of K+) and chloride 285 mg (8 mmol of Cl-).** Kay-Cee-L® – 10mL bd (1mmol K^+/mL) or Intravenous replacement with premixed solution of 20mmol K^+/500mL.

Magnesium replacement

Serum magnesium level	Guideline for repletion
Acute or severe hypomagnesaemia Mg^{2+} <0.7mmol/L + symptoms or Mg^{2+} <0.4mmol/L	10mL magnesium sulphate 50% injection (5g in 10mL) diluted in 500mL Sodium Chloride 0.9%. Infuse over a minimum of 5 hours for 3 to 5 days, depending on serum levels. Often requires oral magnesium to maintain at normal serum levels. Use ready-mixed intravenous magnesium products if available.
Mild hypomagnesaemia Mg^{2+} 0.5-0.7mmol/L no symptoms	Give by mouth 20 to 24mmol Mg^{2+} per day in divided doses for 5 days. Magnesium Verla® 2 sachets bd 1 sachet (5g) = 5mmol Mg^{2+}.

Intravenous administration

- Symptomatic hypomagnesaemia is usually associated with a deficit of 0.5-1mmol/kg Mg2+. Since 50% of the administered dose is excreted in the urine, even in severe deficiency, up to 160mmol over 5 days may be required. The maximum dose per day should not exceed 40mmol.
- Serum magnesium levels should be checked daily, 6 to 8 hours following intravenous doses.
- Magnesium sulphate available as 50% solution (1g in 2mL, 2.5g in 5mL, or 5g in 10mL). 1g magnesium sulphate = 4mmol Mg2+. Ready-mixed bags are also available with 4g in 50ml or 4g in 100ml.
- Maximum concentration for infusion is 20% (200mg/mL or 0.8mmol/mL) and can be given peripherally or centrally.
- Maximum rate of infusion is 150mg (0.6mmol) per minute, rapid infusion of intravenous magnesium may lead to respiratory depression and reduced tidal volume.

Chronic hypomagnesaemia:

- If losses are ongoing consider oral maintenance therapy, 4-12mmol Mg2+ per day

Phosphate replacement

Serum phosphate level	Guideline for repletion
Severe hypophosphataemia with refeeding syndrome	Intravenous therapy 50mmol $PO4^{3}$ – over 6 – 12 hours. (i.e. Phosphate Polyfusor®)
Severe deficit **PO4 $^{3-}$<0.4mmol/L**	Intravenous replacement via peripheral line. 1. Calculate phosphate requirement of 0.16mmol/kg and administer over 6 hours in patients who are unwell or have multiple risk factors for hypophosphataemia., e.g. in 70kg patient, give 20mL potassium phosphate or sodium phosphate injection diluted in 500mL Sodium Chloride 0.9% or Glucose 5% over 6 hours. 2. In critically unwell patients, increase to 0.24mmol/kg over 6 hours., e.g. in 70kg critically ill patient, give 28mL sodium phosphate injection diluted in 500mL Sodium Chloride 0.9% or Glucose 5% over 6 hours. 3. Recheck serum phosphate after 6-12 hours following infusion and repeat if necessary. Maximum of 50mmol PO4 $^{3-}$ in 24 hours. 4. Check serum phosphate levels daily for 48 hours following infusion. 5. Stop infusions when serum phosphate levels > 0.8mmol/L.
Moderate deficit **PO4 $^{3-}$ = 0.41-0.6mmol/L**	Intravenous replacement via peripheral line. 1. Calculate phosphate requirement of 0.08mmol/kg over 6 hours in patients who are unwell or have multiple risk factors for hypophosphataemia., e.g. in 70kg patient, give 10mL of potassium phosphate or sodium phosphate injection diluted in 500mL Sodium Chloride 0.9% or Glucose 5% over 6 hours. 2. Recheck serum phosphate after 6-12 hours following infusion and repeat if necessary. Maximum of 50mmol PO4 $^{3-}$ in 24 hours. 3. Check serum phosphate levels daily for 48 hours following infusion. 4. Stop infusions when serum phosphate level > 0.8mmol/L.
Mild deficit **PO4 $^{3-}$ = 0.61-0.79mmol/L**	Oral replacement therapy 1000mg phosphorus/day (32.2mmol/day) Phosphate – Sando® 1 tablet bd can go up to 6 tablets daily in divided doses.

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1. Initial Risk Assessment

Minor risk factors	Major risk factors	Specific patient populations at high risk
• BMI <18.5 kg/m²	• BMI <16 kg/m²	(careful assessment is recommended)
• Unintentional weight loss >10% in the past 3–6 mo	• Unintentional weight loss >15% in the past 3–6 mo	• Hunger strike, chronic severe dieting
• Little or no nutritional intake for >5 d	• Little or no nutritional intake for >10 d	• History of bariatric surgery, short bowel syndrome
• History of alcohol abuse or drugs including insulin, chemotherapy, antacids, or diuretics	• Low baseline levels of potassium, phosphate, or magnesium before feeding	• Tumor patients, frail elderly patients with chronic debilitating disease

2. Prevention of RFS During Nutritional Therapy

	No Risk	Low Risk	High Risk	Very High Risk
Risk stratification for RFS		1 minor risk factor	1 major or 2 minor risk factors	• BMI <14kg/m² • Weight loss >20% • Starvation >15 d
Preventive measures before/during nutritional therapy	Careful restoration of fluid balance to avoid fluid overload (see Table 1): % dehydration x BW (kg) = volume to be replaced in L (rough estimate of fluid loss)			
	No other preventive measures needed	**Depending on the risk, consider electrolyte substitution** if lower than normal/in low normal range* with daily adaption according to serum levels: 1–1.5 mmol/kg/d potassium, 0.2–0.4mmol/kg/d magnesium, 0.3–0.6 mmol/kg/d phosphate **Depending on the risk, consider other measures:** use of thiamine (200–300 mg on days 1–5), Multivitamins during days 1–10, replace specific deficiency of trace elements, sodium restriction (<1 mmol/kg/d) for days 1–7		
Days 1–3†	Energy (by all routes): Full requirements (40–60% carbohydrates, 30–40% fat, 15–20% proteins)	Energy (by all routes): 15–25 kcal/kg/d (40–60% carbohydrates, 30–40% fat, 15–20% proteins)	Energy (by all routes): 10–15 kcal/kg/d (40–60% carbohydrates, 30–40% fat, 15–20% proteins)	Energy (by all routes): 5–10 kcal/kg/d (40–60% carbohydrates, 30–40% fat, 15–20% proteins)
Day 4†		Energy (by all routes): 30 kcal/kg/d (40–60% carbohydrates, 30–40% fat, 15–20% proteins)	Energy (by all routes): 15–25 kcal/kg/d (40–60% carbohydrates, 30–40% fat, 15–20% proteins)	Energy (by all routes): 10–20 kcal/kg/d (40–60% carbohydrates, 30–40% fat, 15–20% proteins)
Day 5†		Energy (by all routes): full requirements (40–60% carbohydrates, 30–40% fat, 15–20% proteins)		
Day 6†			Energy (by all routes): 30 kcal/kg/d (40–60% carbohydrates, 30–40% fat, 15–20% proteins)	
Days 7–9†			Energy (by all routes): full requirements (40–60% carbohydrates, 30–40% fat, 15–20% proteins)	Energy (by all routes): 20–30 kcal/kg/d (40–60% carbohydrates, 30–40% fat, 15–20% proteins)
>10 d†				Energy (by all routes): full requirements (40–60% carbohydrates, 30–40% fat, 15–20% proteins)
Fluids	No restriction in fluids	Fluids to maintain zero balance, approx. 30–35mL/kg/d	Fluids to maintain zero balance, days 1–3 25–30mL/kg/d, >days 4 30–35mL/kg/d	Fluids to maintain zero balance, days1–3 20-25mL/kg/d, days 4–6 25–30mL/kg/d, >days 7 25–35mL/kg/d
Salt	No restriction in salt intake	No restriction in salt intake	Restrict Na to <1 mmol/kg/d (days 1–7)	Restrict Na to <1 mmol/kg/d (days 1–10)
Iron	No iron substitution within the first 7 d even if patients have iron deficiency			
Monitoring	• Assessment of serum electrolyte levels daily up to day 3, then every 2–3 d • Daily clinical examination focusing on hydration status (1–2 times per day) • Continuous monitoring of the cardiac rhythm or electrocardiogram daily in patients at very high risk for RFS			

3. Reassessment and Diagnosis During Nutritional Therapy

(for all risk categories)

Diagnosis of RFS

Shift in electrolytes within 72 h after start of nutrition therapy:
- Decrease of *phosphate* from baseline >30% or <0.6 mmol/L
- Or *any 2 other electrolyte* shifts below normal range (Mg <0.75 mmol/L, PO_4 <0.80 mmol/L, K <3.5 mmol/L)

NO ↓ | YES ↓

No RFS

No change of therapy algorithm.

Substitution of electrolytes if they drop below reference range.

Associated with clinical symptoms‡?

NO ↓ | YES ↓

Imminent RFS

Start and/or adapt electrolyte substitution. Repeat assessment every 2–3 d.

Manifest RFS

Increase electrolyte substitution and treat clinical conditions adequately. Adapt nutrition therapy as in high-risk patients. Repeat assessment every day.

Appendix 6: Recommended weight gain for pregnancy by pre-pregnancy BMI

BMI category	Rate of weight gain in kilograms per week in 2nd and 3rd trimester	Recommended total weight gain
Singleton		**Kilograms**
Underweight (< 18.5 kg/m^2)	0.4-0.5	12.7-18.2
Normal weight (18.5-24.9 kg/m^2)	0.4-0.5	11.4-15.9
Overweight (25.0-29.9 kg/m^2)	0.2-0.4	6.8-11.4
Obesity (≥ 30.0 kg/m^2)	0.2-0.3	5-9
Twins		
Underweight (< 18.5 kg/m^2)	0.7-0.8	No weight gain guidelines are available because of insufficient data
Normal weight (18.5-24.9 kg/m^2)	0.6-08	16.8-24.5
Overweight (25.0-29.9 kg/m^2)	0.5-0.7	14-22.7
Obesity (≥ 30.0 kg/m^2)	0.3-0.6	11.4-19
Triplets		
Any BMI	0.6-0.7	23

*rate of gain/week rounded to the nearest 0.1 decimal place

Sources:

BMI categories from WHO 1995, 2000 and 2004.

Food and Nutrition Board, Institute of Medicine. *Nutrition During Pregnancy.*

Washington DC: National Academy Press, 1990.

Brown JE, Carlson M. Nutrition and multifetal pregnancy. J Am Diet Assoc, 2000: 100: 343-348.

Food and Nutrition Board, Institute of Medicine. Rasmussen KM and Yaktine AL, editors. *Weight Gain During Pregnancy: Re-examining the Guidelines.* Washington DC: National Academy Press, 2009.

Appendix 7:
Practical tips on diet with HG

Dietary goals in pregnancies affected by nausea and vomiting:

- When struggling to eat or drink enough, the aim is to eat little and often of whatever foods are tolerated and needed to remain nourished, avoid weight loss and manage symptoms.
- As symptoms ease, aim to eat a wider variety of foods and food groups within tolerances in line with general healthy eating in pregnancy advice and at least a folic acid and vitamin D supplement (RCPI & HSE, 2017)(Institute of Obstetricians and Gynaecologists, Royal College of Physicians of Ireland and Directorate of Clinical Strategy and Programmes, Health Service Executive, 2019).

Practical tips on what to eat/drink with nausea and vomiting

Drink plenty of liquids:

- It is important to not become dehydrated.
- Aim to sip on 100-200ml of liquid every hour. It can be useful to set goals or reminders to drink throughout the day.
- Consuming liquids separately to food may be easier.
- Using a straw or different containers may help.
- Try liquids other than still water if needed, e.g. sparkling water, flavoured water, water with squash, sugary or non-sugary fizzy drinks, flavoured or regular milks or milk shakes, sports or vitamin drinks, juices, smoothies, savoury drinks (e.g. Bovril/marmite) or hot drinks such as decaffeinated or regular tea/coffee or hot chocolate.
- Different temperatures may work better. Try exploring room temperate or cold by adding ice to drinks, freezing a half bottle of liquids and topping the rest up or sucking ice-cubes/frozen grapes.
- Some foods have high water content and can be useful to improve hydration(e.g. melon, tinned fruit, soup, jelly, yogurt, mousses, cucumber, grapes, custard and ice lollies).
- It is very important that women attend their doctor if they are unable to drink enough or if they are unable to hold down liquids.

Eat little and often:

- Eating a small meal or snack every 1-2 hours rather than trying to have 3 larger meals can help manage symptoms by avoiding the stomach getting too empty or too full.
- Aim to eat 100-200 calories every hour, e.g. crackers, a handful of nuts, rice pudding, yoghurt, dried fruit, oat cakes/biscuits/bars, toast, glass of milk or bowl of cereal.
- Eating a small snack before going to sleep at night may prevent nausea in the morning.
- If nauseated in the morning, eating a light snack and waiting 15-20 minutes before getting out of bed can help to ease symptoms. Have suitable snacks at bedside such as jelly pots, crackers, popcorn, biscuits or other according to tolerances.

- It can help tolerance to have food and drinks separately.
- Some textures and tastes may work better than others. Reflect on what foods work better and consider foods with similar tastes/textures to try, e.g. sour/bitter, sweet, salty, bland, spicy, earthy, dry, wet, crunchy, hot and cold.
- Temperature may affect tolerance. Consider if cold, room temperature or hot works better and focus on that until symptoms improve.
- Be aware of nausea-free times and take advantage of these times. If feeling well, aim to eat until feeling satisfied, then come back to eating if desired after an hour or two. This may help avoid exacerbating symptoms by becoming too full at any one time.
- Note what times of the day symptoms tend to worsen and try to eat something small if they feel hungry before it turns into nausea.
- Keeping a symptom and food diary can help increase awareness of symptoms, triggers and tolerances.
- It can be useful to have food prepared (sandwiches/ready meals/frozen batch cooked meals) and snacks available in bags, at work or at the bedside to make the most of the nausea-free opportunity. Keeping the cupboard stocked with easy meals, e.g. cheese and crackers, beans, bread, milk, nut butters, tinned soup and packet noodles is also useful.

Aim to take folic acid and vitamin D in line with public health recommendations. In short term, consider a break from a multivitamin if it makes symptoms worse. If a multivitamin is desired, consider liquids/chewable options if tablets are not tolerated.

Appendix 8: AGREE II checklist[29]

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	

29 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 9: **Grades of Recommendation**[30]

Grade of recommendation	Clarity of risk/ benefit	Quality of supporting evidence	Implications	Suggested Language
1A. 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…

30 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
1B. 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…
1C. 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...

Grade of recommendation	Clarity of risk/ benefit	Quality of supporting evidence	Implications	Suggested Language
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...
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 10:
NWIHP/IOG CAG membership (2026-)

Dr Cliona Murphy (Chair, 2023-). Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital. Clinical Director, National Women and Infants Health Programme.

Dr Suzanne O'Sullivan (2023-). Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Director of Education and Training, Obstetrics and Gynaecology, Institute of Obstetricians and Gynaecologists. Chair, Institute of Obstetricians and Gynaecologists.

Dr Venita Broderick (2024-). Clinical Lead Gynaecology, National Women and Infants Health Programme.

Dr Brian Cleary (2023-). Chief Pharmacist, Rotunda Hospital. Medications Lead, Maternal and Newborn Clinical Management System Project.

Angela Dunne (2023-). Director of Midwifery, National Women and Infants Health Programme.

Prof. Seán Daly (2023-). Master, Consultant Obstetrician and Gynaecologist, Rotunda Hospital.

Prof. Maeve Eogan (2023-). Consultant Obstetrician and Gynaecologist, Rotunda Hospital. Clinical Lead, Sexual Assault Treatment Units, National Women and Infants Health Programme.

Prof. Richard Greene (2023-). Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Director, National Perinatal Epidemiology Centre, University College Cork.

Prof. John Higgins (2023-). Cork University Maternity Hospital, Consultant Obstetrician and Gynaecologist, Clinical Director, Ireland South Women and Infants Directorate.

Prof. Shane Higgins (2023-). Master, Consultant Obstetrician and Gynaecologist, National Maternity Hospital.

Dr Mendinaro Imcha (2023-). Clinical Director, Consultant Obstetrician and Gynaecologist, University Maternity Hospital Limerick.

Prof. John Murphy (2023-). Clinical Lead Neonatology, National Women and Infants Health Programme.

Dr Aoife Mullaly (2023-). Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital. Clinical Lead, Termination of Pregnancy Services, National Women and Infants Health Programme.

Prof. John Morrison (2023-). Consultant Obstetrician and Gynaecologist, University Hospital Galway. Clinical Director, Saolta Maternity Directorate.

Kilian McGrane (2023-). Director, National Women and Infants Health Programme.

Prof. Keelin O'Donoghue (2023-). Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Lead, National Guidelines, National Women and Infants Health Programme.

Prof. Mike O'Connell (2023-). Master, Consultant Obstetrician and Gynaecologist, Coombe Women and Infants University Hospital.

Dr Vicky O'Dwyer (2023-). Consultant Obstetrician and Director of Gynaecology, Rotunda Hospital.

Dr Mairead O'Riordan (2024-). Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital.

Dr Fergal O'Shaughnessy (2025-) Senior Pharmacist, Rotunda Hospital.

Prof. Nóirín Russell (2023-). Consultant Obstetrician and Gynaecologist, Cork University Maternity Hospital. Clinical Director, Cervical Check.

Dr Carmen Regan (April 2024). Clinical Lead Obstetrics, National Women and Infants Health Programme.

Dr Orla Shiel (2024-). Consultant Obstetrician and Gynaecologist, National Maternity Hospital.

Ms Clare Thompson (2023-). Consultant Gynaecological Oncologist, The Mater, Dublin.

Appendix 11: **Audit Tool**

Two to three charts of women with NVP who attend the Emergency Room (ER) and/or are admitted to Day Care or Gynaecology Ward will be reviewed quarterly to ensure the guideline is being implemented. The auditor will be a member of the implementation team.

Parameter	Yes	No
Was the PUQE score performed and documented in this treatment episode?		
Was the patient treated in accordance with the NVP treatment algorithm?		
If there was a deviation from the guideline, is this recorded and rationale for same explained?		
Was a clear and concise plan of care documented?		

At the time of the chart review the auditor will interview midwifery, nursing and/or obstetric staff in ER, Day Care or Gynaecology Ward at random:

Parameter	Yes	No
Are you aware that a NVP guideline exists?		
Are you aware of the PUQE scoring tool?		
Do you have access to the guideline?		
Have you read the guideline?		

Auditor: _____

Ward (circle one): ER Day Care Gynaecology

Staff interviewed (circle one): Midwifery Nursing Obstetrics