Guideline

Identification and management of nausea and vomiting of pregnancy and hyperemesis gravidarum

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Revision History

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August 2021 SWSLHD_GL2021_024	Publication of guideline.

1. Introduction

There has been a lack of clear guidance in the Australian context for the management of nausea and vomiting in pregnancy (NVP) and hyperemesis gravidarum (HG). This guideline aims to provide consistent information in the identification and management of NVP and HG, aiming to assist with management in ambulatory and community services. This guideline aligns with the Society of Obstetric Medicine of Australia and New Zealand (SOMANZ) guideline for identification and management of NVP and HG released in 2019.

Definitions of NVP and HG vary and their causes are largely unknown.[1,9] SOMANZ proposes a definition of NVP as "nausea, vomiting and/or dry retching caused by pregnancy, with symptoms commencing in the first trimester, without an alternate diagnosis."[5] This is consistent with the definition stated in the Royal College of Obstetricians and Gynaecologists (RCOG) Green top Guideline no.69.[6] The definition of hyperemesis gravidarum offered by SOMANZ is "nausea and/or vomiting caused by pregnancy leading to significant reduction of oral intake and weight loss of at least 5% compared with pre-pregnancy, with or without dehydration and/or electrolyte abnormalities."[4] This definition is consistent with the Matthews *et al*[5] Cochrane review, which further expands on this to include the potential for hospital admission.

NVP is usually experienced between six and 16 weeks gestation although some women (20%) experience NVP up to 20 weeks or longer.[5] NVP and HG have the potential to adversely affect quality of life, workforce participation and health care costs.[1]

The prevalence of NVP is reported as high as 50-80% [1-3,5,9] of pregnant women and retching as high as 50%.[1,5] Between 15-81% of women who have had NVP previously have an incidence of NVP in subsequent pregnancies.[1] HG has a reported incidence of 0.3-3.6%[1,5,6] and has been stated as the leading cause of hospital admission in early pregnancy.[9]

In view of the high prevalence of NVP, health professionals and women require clear and consistent information around safe and effective management in order to improve women's experience of health care in early pregnancy.[5] Implementing consistent classification and definitions of NVP and HG using the Pregnancy-Unique Quantification of Emesis (PUQE-24) scale and appropriate management algorithms, will lead to efficient and effective experiences of integrated care in early pregnancy.

Between 1st of January 2019 and the 2nd of March 2020, 2092 pregnant women presented to Emergency Departments (EDs) across SWSLHD. They ranged in age from 15 to 49 years (mean 29.11 years). 633 (30%) of these women presented with nausea and vomiting. Of these women, 456 (21.8%) had a diagnosis of NVP or HG. In the remaining 177 (8.5%) nausea and vomiting was caused by other factors.

The disposition across SWSLHD of women with NVP or HG was:

- 285 (62.5%) went home
- 113 (24.8%) were admitted
- 53 (11.6%) left against medical advice

- 4 (0.9%) did not wait to be seen
- 1 was transferred to another facility.

Women who presented with NVP or HG were more likely to re-present four or more times in their pregnancy.

The risk addressed by this guideline:

- Missed or misdiagnosis of hyperemesis gravidarum.
- Inappropriate care provision contrary to SOMANZ guidelines and evidence based practice.

2. The Aims / Expected Outcome of this guideline:

To ensure:

- Accepted district-wide definition of NVP and HG
- Evidenced-based investigations of NVP or HG
- Evidence-based treatment strategies for NVP and HG
- Evidence-based management strategies for NVP and HG
- Improved quality of life for women with NVP and HG
- Appropriate admission of women with severe NVP and HG
- Appropriate use of community based and ambulatory care services
- Appropriate identification of adverse reactions/complications.

Aims:

- In consultation with women, identify those with mild to moderate NVP who can be appropriately managed in the community or ambulatory care settings
- Appropriately determine the need for inpatient treatment of severe NVP and HG.
- In consultation with women, establish appropriate review and follow up.
- Improve NVP and HG health literacy.

3. Procedure

Women presenting to the Emergency Department will be triaged according to the Australasian Triage Scale and allocated a triage category and treatment location aligning with the presenting complaint and symptomatology.

Clinical assessment by the appropriate medical officer or nurse practitioner will include utilisation of the PUQE-24 score and investigations as per table below.

A history (using an interpreter as required, as per PD2017_044) and physical examination should be undertaken as per usual practice. The assessment should be directed towards the potential identification of any alternate diagnosis. The physical examination should include:

- Temperature, pulse and BP
- Abdominal examination and an assessment of hydration status
- CNS assessment for any signs of raised intracranial pressure or meningism
- PUQE-24 score (Attachment 2 or search PUQE-24 in pre completed notes in eMR*)
- Urinalysis.

If there are any signs or symptoms of thyrotoxicosis (e.g. heat intolerance, palpitations, new anxiety, tremor, weight loss or lid lag), a thyroid stimulating hormone (TSH) assay should be performed.

Once other diagnoses are excluded, women with mild to moderate nausea and vomiting of pregnancy (PUQE-24 score 3 to 12) do not need any further investigations performed. All women should be given the 'Sickness (nausea) and vomiting in pregnancy' information sheet (which includes the 'My sickness in Pregnancy Plan') in the appropriate available language and English.

Women with severe NVP or HG (PUQE-24 which is 13 to 15) should have the following investigations undertaken:

- Electrolytes, Urea & Creatinine (EUC), Calcium, Magnesium, Phosphate (CMP)
  - In pregnancy a creatinine of >70umol/L suggests significant dehydration.
- Liver function tests (LFT)
  - Elevated in NVP and HG due to starvation, but rarely more than 4 times the upper limit of normal (ULN). Further investigation may be required if above this level.
- Obstetric ultrasound (US):
  - This should be undertaken to assess for multiple gestation or trophoblastic disease unless an US has recently been undertaken.
- Thyroid stimulating hormone (TSH):
  - Should only be measured in those with HG or NVP which is refractory to treatment or where there are signs or symptoms of thyrotoxicosis
  - If abnormal FT4 and FT3 will need to be assessed.
- Tests to exclude alternate diagnoses as suggested by the clinical assessment (see table in section 4.1 regarding differential diagnosis).

*** PUQE – 24 SCORING template in eMR**

1. Open required patient on eMR
2. Select **documents**
3. Select +**ADD** (new note)
4. Select **pre completed**
5. Search **PUQE – 24** (this will appear in title or select in search)
6. Add to **favorites** for future use
7. Select **OK** to continue as a patient note

3.1. Differential diagnosis of nausea and vomiting in pregnancy

Gastrointestinal	Gastroenteritis Gastro-oesophageal reflux disease Hepatitis Pancreatitis Biliary tract disease Peptic ulcer disease - Helicobacter pylori Bowel obstruction Gastroparesis Appendicitis Peritonitis
Genitourinary	Urinary tract infection including pyelonephritis Ovarian torsion Nephrolithiasis
Metabolic or Toxic	Drugs-including pregnancy vitamins Use and/or withdrawal of cannabinoids or other illicit drugs Diabetic ketoacidosis Addison's disease Thyrotoxicosis Non-infectious hepatitis Hypercalcemia Eating Disorders
Central nervous system disease	Migraine Infection Tumours Raised intracranial pressure Vestibular system pathology: Labyrinthitis, Meniere's Disease

Source: Lowe et al, 2019

3.2. Investigations to be undertaken according to PUQE-24 score

<table>
<tr><td colspan="6">Investigations aim to exclude alternate diagnosis from history and examination.
Assess hydration, nutritional status and weight.
Attend PUQE-24.</td></tr>
<tr><td>PUQE-24 score:
3 to 12
Mild to moderate nausea or vomiting of pregnancy and no suspicion of alternate diagnosis</td><td>No investigations required.</td><td>TSH if signs and symptoms of thyrotoxicosis.</td><td colspan="3">Consider management at home.</td></tr>
<tr><td>PUQE-24 score:
13 to 15
Severe NVP or HG</td><td>Sodium, potassium, chloride, bicarbonate, calcium, magnesium, urea and creatinine (EUC, CMP)</td><td>Bilirubin, ALT, AST, Albumin (LFTs)</td><td>Obstetric ultrasound (exclude multiple pregnancy or trophoblastic disease)</td><td>TSH if treatment for NVP/HG is providing no relief</td><td>Consider admission if community manage-ment is not feasible.</td></tr>
</table>

Source: Lowe et al, 2019.

Women who may require admission are those who have severe HG (PUQE-24 score 13 to 15) or have:

- Underlying medical issues e.g. Type 1 diabetes mellitus, high risk conditions (short bowel syndrome or previous bariatric surgery) or those requiring continuity of essential medications (e.g. severe epilepsy or renal transplant patient)
- Severe electrolyte disturbances
- Acute kidney injury (creatinine >90umol/L)
- Malnutrition, or starvation ketoacidosis
- Other associated complications needing inpatient management e.g. Mallory Weiss tear

Optimally women with a PUQE- 24 score 3 to 12 can be managed in the community with ongoing care. For those women who require ongoing IVF, this is best managed in an ambulatory care, hospital-in-the-home or day stay setting as relevant to each hospital within the SWSLHD.

3.3. Management

The overarching principles of therapy are that a holistic approach achieves the best results. This is comprised of a management plan that addresses:

1. Interventions to reduce nausea, retching and vomiting (Tables 1.1 to 1.3)
2. Gastric dysmotility, GORD (Table 2)
3. Constipation (Table 3)
4. Maintenance of hydration and electrolyte replacement

The targets of therapy are the ability to eat and drink adequately – **complete resolution** of symptoms is less likely in the short term. There is some evidence that ceasing prenatal vitamins helps with NVP symptoms; however, if possible, folic acid (0.5mg/day) and iodine (150ug/day) should be continued.

As a general rule, if an antiemetic is not effective at maximal dose, discontinue before commencing an alternate agent. If partially effective, optimise dosing before adding a second agent.

Use the 'Sickness (nausea) and vomiting in pregnancy' information sheet in the appropriate language and English to assist with management of symptoms in the community after discharge.

Pharmacological management of NVP & HG:

- Mild to moderate NVP:
  - Treatment can commence with ginger, with or without B6.
  - An oral antihistamine or dopamine antagonist can be added if required.
- If the response to initial therapy is inadequate or NVP is moderate to severe:
  - Consider IV or IM antihistamine or dopamine antagonist.
- If sedation is considered excessive or NVP is not brought to acceptable levels:
  - Add or substitute an oral or IV serotonin antagonist during the day
  - Include acid suppression.
- If NVP or HG remains refractory:
  - Consider corticosteroids along with antiemetics
  - Increase acid suppression
  - IV Thiamine (prevention of Wernickes encephalopathy).
- Manage and prevent constipation.
- Management is guided by the severity of symptoms. It would be reasonable to commence a therapy, but if it does not improve the patient symptoms, then the agent should be ceased and another commenced.
- Inform the woman about ongoing care and self-assessment with provision of patient handout (available in four languages: English, Vietnamese, Arabic and Cambodian).

Suggested regimens for commencement of therapy based on severity are as follows:

Table 1.1 Interventions to reduce nausea, retching and vomiting if PUQE-24 score 3 to 12 (mild-moderate NVP)

Medication	Mechanism	Evidence	Contraindications	Dose	MIMS AIDH link
Ginger	Increases Gastro intestinal (GI) motility	Reduces N but not V (LOE II)	Increase risk of bleeding and hypoglycaemia	Up to 1200mg /day (250mg qid)	Therapeutic Research Centre – Natural medicines
Vit B6 (pyridoxine)	Inhibits H1 receptor, acts indirectly on vestibular system. Muscarinic inhibition decreases vomiting centre stimulation.	Reduces N but not V (LOE I)		12.5-25mg tds/qid Up to 200mg/day **OR** 37.5mg with ginger 600mg bd	
Antihistamines	Indirect vestibular system decreases vomiting centre stimulation.	Doxylamine, reduces N (LOE II) Dimenhydrinate or Diphenhydramine or Cyclizine (LOE III)	Anticholinergic effects may worsen – GI and bladder obstruction	Varied (Doxylamine 6.25-25mg PO or Cyclizine 12.5-50mg PO/IV)	AMH

Metoclopramide	Increases upper GI motility. Acts on CNS vomiting centre.	equal to ondansetron for N but less effective for V (LOE II)	Phaeochromocytoma Parkinson's disease Epilepsy (can induce an extrapyramidal movement disorder)	10mg tds	AMH eMIMS
Prochlorperazine	Central and peripheral Dopamine antagonist	Superior to placebo for NVP (LOE I)	CNS depression Parkinson's disease	5-10 mg tds	AMH eMIMS Drugs in Pregnancy and Lactation(Briggs)
Chlorpromazine	Central and peripheral Dopamine antagonist	LOE III	CNS depression Bone marrow depression Phaeochromocytoma	10-25mg tds	AMH eMIMS Drugs in Pregnancy and Lactation (Briggs)

Table 1.2 Interventions to reduce nausea, retching and vomiting if PUQE-24 score 13 to 15 (severe NVP)

Medication	Mechanism	Evidence	Contraindications	Dose	MIMS AIDH link
Ondansetron	Central & peripheral serotonin receptor blocker	Superior to Doxylamine/B6 for reduces N&V. Superior to Metoclopramide for reduced V but not N in HG.	Phenylketonuria. Use with Apomorphine is contraindicated, avoid if QT prolonged	4-8mg up to tds	AMH eMIMS
Corticosteroids (if critically unwell with intractable vomiting and not responding to above measures)	Anti-emetic effect on chemoreceptor trigger zone in brain stem.	No difference in readmission or LOS compared to placebo. = to promethazine, reduced side effects. (LOE I). Superior to IV Metoclopramide (LOE I)	Phaeochromocytoma Myasthenia gravis Precaution: Latent TB Peptic ulcer disease	Prednisone 40-50 mg/day IV hydrocortisone 100mg bd	AMH eMIMS

IV Fluid administration is in its own right is an important adjunct to therapy for both inpatients and outpatients. Studies have demonstrated a significant improvement in nausea with IVF alone, without the use of antiemetics. Below are some recommended fluid regimens for the replacement of IV fluids and electrolytes.

Table 1.3 IV fluid administration

IV fluid	Volume and rate	Comment
sodium chloride 0.9%	1-2 L. 1st litre 1 L/hr	Following IV fluids can be given at 1-2L/hr or slower to correct dehydration and electrolytes.
sodium chloride 0.18% and dextrose 4% or dextrose 5%	1 L. 1st litre 1 L/2 hours	**Exclude hyponatremia and correct thiamine deficiency prior to commencing**. Consider if unable to tolerate oral fluids, starvation or nausea is uncontrolled.
Add electrolytes as required		
Potassium chloride	Administer as per local protocol with caution.	Premixed 1L bag of 30mmol in sodium chloride 0.9% is preferred. Use a large peripheral vein or central venous access only.
Magnesium sulphate	10-20mmol/day, infused at 10mmol/hr.	Magnesium can be added to IV fluid or diluted in 100ml of sodium chloride 0.9%. Use a large peripheral vein or central venous access only.

If IV Dextrose is used give IV Thiamine prior to IVF to prevent Wernicke's encephalopathy in women with thiamine deficiency.

Table 2. Acid suppression and gastric dysmotility therapeutic options

Medication	Mechanism	Evidence or pregnancy classification	Contraindications	Dose	MIMS AIDH link
1st line **Mg,Ca,Al Antacids**	Neutralise hydrochloric acid secreted by gastric parietal cells	TGA listed as Cat A	Renal insufficiency; accumulation of absorbed magnesium ion, may lead to CNS depression and other symptoms of hypermagnesemia	10-20mL PO PRN	AMH UpToDate
2nd line **H2 Antagonists**	Inhibition of pentagastrin induced gastric acid secretion	TGA listed as Cat B1		Varied e.g. Famotidine 20-40mg PO daily	AMH eMIMS
3rd line **Proton pump inhibitors**	Inhibition of H+/K+-ATPase, leads to the suppression of basal and stimulated gastric acid secretion	TGA listed as Cat B3	Proton pump inhibitors (PPIs) may decrease the absorption of certain human immunodeficiency virus (HIV) protease inhibitors.	Varied e.g. Omeprazole 20-40mg PO daily	eTG eMIMS UpToDate

Table 3. Bowel management therapeutic options

Medication	Mechanism	Evidence	Contraindications	Dose	MIMS AIDH link
1st line **Dietary fibre**	Absorb water in the colon to increase faecal bulk, stimulating peristaltic activity		-Intestinal obstruction, partial or complete -Colonic atony **Avoid Use:** -Dysphagia - oesophageal obstruction may occur -Fluid restriction, immobility	Varied e.g. Psyllium husk powder (Metamucil) 2 spoonsful 1-3 times daily	AMH eMIMs
2nd Line **Stool softeners**	Softens stool by assisting mixture of water into faeces. May also increase intestinal fluid secretion	TGA listed as Cat A	Prolonged use may lead to dependence	Varied e.g. Docusate 50–150mg once or twice daily (up to 500mg/day)	AMH eMIMs
3rd line **Stimulant laxatives**	Increase intestinal motility	TGA listed as Cat A	Intestinal obstruction, partial or complete -Acute abdominal conditions, e.g. appendicitis -Inflammatory bowel condition **Precaution:** Dehydration, hypokalaemia	Varied e.g. Bisacodyl 5-15mg at night	AMH eMIMs

3.4. Disposition Planning:

PUQE-24: score less than or equal to ≤12 (3 to 12)			
and IV fluid not required	Discharge with GP follow up.	Discuss booking into local birthing hospital	Electrolytes if conditions worsens
and repeat IV fluids required	Discharge home with Ambulatory care or HITH follow up.	Daily electrolytes until stable	If liver enzymes are more than 4 times the upper limit of normal for pregnancy, conduct further investigations and seek specialist referral.
Women with diabetes or other significant pre-existing condition	+/- Admission. Refer to dietician.	Daily electrolytes	
PUQE-24: score 13 to 15			
Admission	Admit to ward	Daily electrolytes until stable. Refer to dietician	If liver enzymes are more than 4 times the upper limit of normal for pregnancy, conduct further investigations and seek specialist referral.

3.5. Local Management

Please refer to your local ambulatory care or HITH guidelines.

4. Definitions and Acronyms

Term	Definition
ACOS	Ambulatory Care Outpatient Service
ALT	Alanine Aminotransferase test
AMH	Australian Medicines Handbook
AST	Aspartate transaminase test
bd	Twice a day
BP	Blood pressure
CKD	Chronic kidney disease
CMO	Career Medical Officer
CMP	Calcium, magnesium, phosphate
CNS	Central nervous system
ED	Emergency Department
eMIMS	MIMS Online
eMR	Electronic Medical Record
EPIC	Emergency Protocol Initiating Care
eTG	Therapeutic Guidelines
EUC	Electrolytes, urea, creatinine
GI	Gastrointestinal
GORD	Gastro-oesophageal reflux disease
GP	General Practitioner
HG	Hyperemesis gravidarum
HITH	Hospital In The Home
HIV	Human immunodeficiency virus
IM	Intramuscular
IMI	Intramuscular injection
IV	Intravenous
IVF	Intravenous fluid
LFT	Liver function test

LOE	Level of evidence
LOS	Length of stay
MACS	Macarthur Ambulatory Care Service
MCHS	Multi-cultural health services
mg	Milligram(s)
mmol	Millimole
N	Nausea
NVP	Nausea and vomiting of pregnancy
O&G	Obstetrics and Gynaecology
PO	Oral
PPIs	Proton pump inhibitors
PRN	*Pro re nata* (as required)
PUQE	Pregnancy-Unique Quantification of Emesis
qid	Four times a day
RCOG	Royal College of Obstetricians and Gynaecologists
SOMANZ	Society of Obstetric Medicine of Australia and New Zealand
TB	Tuberculosis
tds	Three times a day
TGA	Therapeutic Goods Administration
Triple I	Intake Information and Intervention
TSH	Thyroid stimulating hormone
ug	Microgram
ULN	Upper limit of normal
umol	Micromole
US	Ultrasound
V	Vomiting
Vit	Vitamin
WHITU	Women's Health Initiative Translational Unit

5. References and Links

.Related Policy Directives / Guidelines

MoH – PD2012_022	Maternity – Management of Early Pregnancy Complications	Link
MoH – PD2019_008	The First 2000 Days Framework	Link
MoH – GL2015_011	Maternity- Rh (D) Immunoglobulin (Anti D)	Link
MoH – PD2017_044	Interpreters – Standard Procedures for Working with Health Care Interpreters	Link

References

1. ACOG Practice Bulletin No. 189: Nausea and Vomiting Of Pregnancy. Obstetrics & Gynecology January 2018;131(1):e15-e30 Online ACOG Publications.	Link
2. Campbell, K., Rowe, H., Azzam, H & Lane, CA. 2016, 'The management of nausea and vomiting of pregnancy', *Journal of Obstetrics and Gynaecology Canada,* Vol.38, No. 2, pp 1127-1137.	Link
3. Ebrahimi, N., Maltepe, C., Bournissen, F.G. & Koren, G. 2009, 'Nausea and Vomiting of Pregnancy: Using the 24-hour Pregnancy-Unique Quantification of Emesis (PUQE-24) Scale', Journal of Obstetrics and Gynaecology Canada, vol. 31, no. 9, pp. 803-7.	Link
4. Lowe SA, Bowyer L, Beech A, Robinson H, Armstrong G, Marnoch C, & Grzeskowiak L. 2019, Guideline for the management of Nausea and vomiting in pregnancy and Hyperemesis gravidarum Executive Summary SOMANZ Society of Obstetric Medicine of Australia and New Zealand	Link
5. Matthews, A., Haas, D.M., O'Mathuna, D.P. & Dowswell, T. 2015, 'Interventions for nausea and vomiting in early pregnancy', Cochrane Database Syst Rev, no. 9, p. CD007575.	Link
6. RCOG The Management of Nausea and Vomitting in Pregnancy and Hyperemesis Gravidarum. Green-top Guide No.69, July 2016.	
7. Tsakiridis, I., Mamopoulos,A., Athanasiadis, A., & Dagklis, T. 2019, 'The Management of Nausea and Vomiting of Pregnancy: A Synthesis of National Guidelines', Obsterical and Gynecological Survey, vol. 74, no. 3.	Link

Articles / Research / Resources

South Western Sydney Primary Health Network, HealthPathways.	Link
NSW Health, Having a Baby.	Link
South Eastern Sydney Local Health District (SESLHD), Mothersafe.	Link
Fiaschi, L., Nelson-Piercy, C, Deb, C, King, R, & Tataa,L,J. 2019, 'Clinical management of nausea and vomiting in pregnancy and hyperemesis gravidarum across primary and secondary care: a population-based study', BJOG, pp. 1201-12.	Link
NICE 2019, Doxylamine pyridoxine NICe evidence review 2019	Link

NICE 2008, Antenatal care for uncomplicated pregnancies, National Institute for Health Care Excellence, UK	Link

6. Forms

The following forms are available by following the link:

Form Number	Name of Form	Link or paper
	PUQE-24	Attachment 2 and on eMR
AMR065.024	Ambulatory Care Maintenance Plan: Nausea or Vomiting of Pregnancy and Hyperemesis Gravidarum	Link

7. Resources

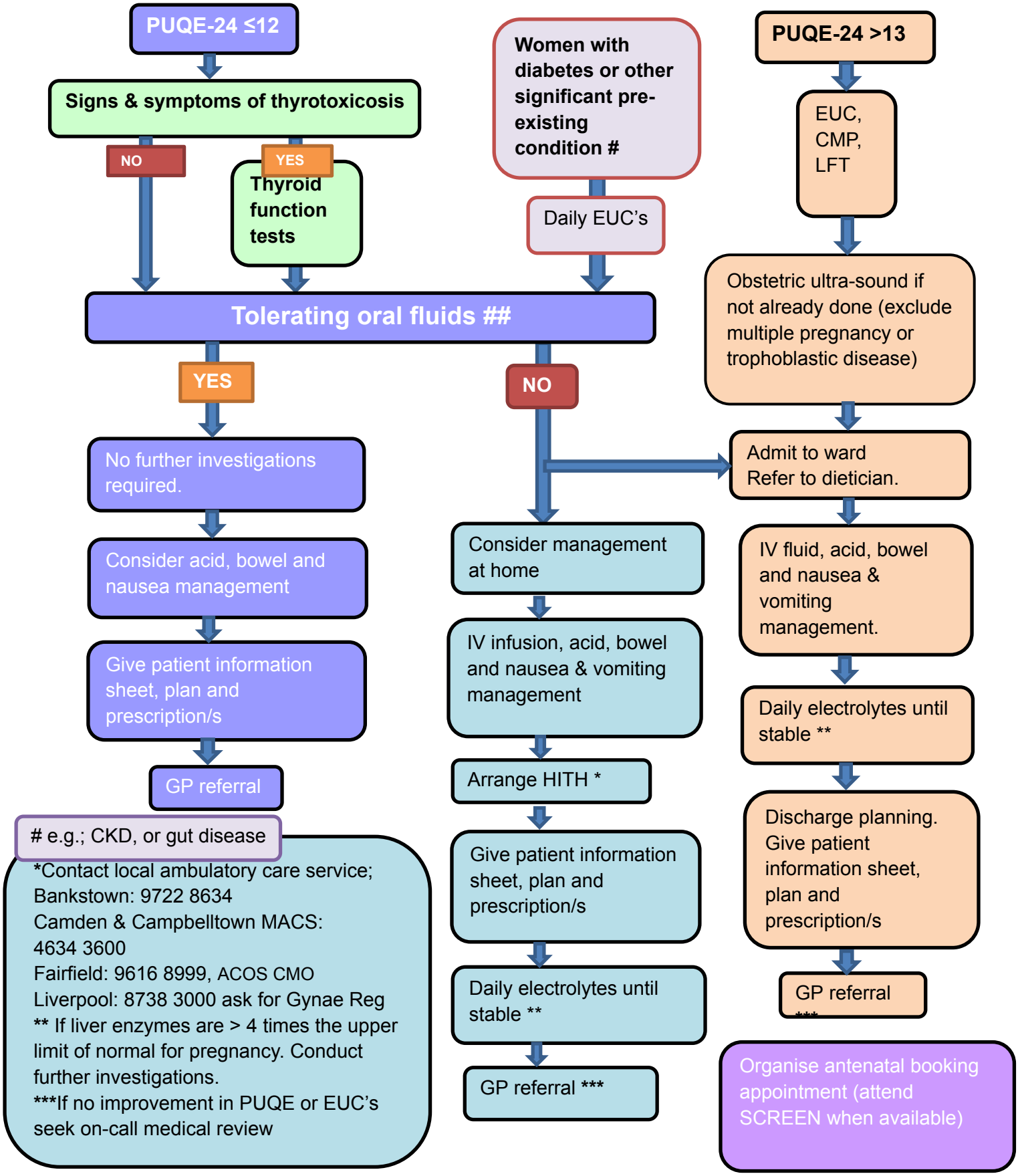
The following resources are available by following the link:

Fact Sheet	Sickness (nausea) and vomiting in pregnancy. • Includes 'My sickness in Pregnancy Plan (Nausea or vomiting)' • Available in English, Vietnamese, Cambodian and Arabic	Link

8. Attachments

Attachment 1: Management Flowchart for NVP & HG
Attachment 2: PUQE-24 assessment

Attachment 1: Management Flowchart for NVP & HG



Attachment 2: PUQE-24 assessment

Health
South Western Sydney
Local Health District

Nausea or Vomiting of Pregnancy and Hyperemesis Gravidarum: PUQE assessment.

Motherisk PUQE-24 scoring system:				
1. In the last 24 hours, for how long have you felt nauseated or sick to your stomach?				
Not at all (1)	1 hour or less (2)	2 to 3 hours (3)	4 to 6 hours (4)	More than 6 hours (5)
2. In the last 24 hours, have you vomited or thrown up?				
I did not throw up (1)	1 to 2 times (2)	3 to 4 times (3)	5 to 6 times (4)	7 or more times (5)
3. In the last 24 hours, how many times have you had retching or dry heaves without throwing up?				
None (1)	1 to 2 times (2)	3 to 4 times (3)	5 to 6 times (4)	7 or more times (5)
Total score (add scores in brackets)				
Mild 3 to 6: Moderate 7 to 12;			Admission not required. Consider repeat IV fluids manage at home. See NVP & HG guideline	
Severe 13 to 15.			Consider admission as per NVP & HG guideline.	