



Royal College of  
Obstetricians &  
Gynaecologists

# The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum

Green-top Guideline No. 69  
June 2016



# The Management of Nausea and Vomiting of Pregnancy and Hyperemesis Gravidarum

This is the first edition of this guideline.

## Executive summary of recommendations

### *Diagnosis of nausea and vomiting of pregnancy (NVP) and hyperemesis gravidarum (HG)*

How is NVP diagnosed?

**NVP should only be diagnosed when onset is in the first trimester of pregnancy and other causes of nausea and vomiting have been excluded.**

D

How is HG diagnosed?

**HG can be diagnosed when there is protracted NVP with the triad of more than 5% prepregnancy weight loss, dehydration and electrolyte imbalance.**

D

How can the severity of NVP be classified?

**An objective and validated index of nausea and vomiting such as the Pregnancy-Unique Quantification of Emesis (PUQE) score can be used to classify the severity of NVP.**

C

*What initial clinical assessment and baseline investigations should be done before deciding on treatment?*

**Clinicians should be aware of the features in history, examination and investigation that allow NVP and HG to be assessed and diagnosed and for their severity to be monitored.**

✓

What are the differential diagnoses?

**Other pathological causes should be excluded by clinical history, focused examination and investigations.**

✓

*What is the initial management of NVP and HG?*

How should the woman be managed?

**Women with mild NVP should be managed in the community with antiemetics.**

D

**Ambulatory daycare management should be used for suitable patients when community/primary care measures have failed and where the PUQE score is less than 13.**

C

**Inpatient management should be considered if there is at least one of the following:**

✓

- continued nausea and vomiting and inability to keep down oral antiemetics
- continued nausea and vomiting associated with ketonuria and/or weight loss (greater than 5% of body weight), despite oral antiemetics
- confirmed or suspected comorbidity (such as urinary tract infection and inability to tolerate oral antibiotics).

What therapeutic options are available for NVP and HG?

What is the safety and efficacy of pharmacological agents?

#### Antiemetics

**There are safety and efficacy data for first-line antiemetics such as antihistamines (H<sub>1</sub> receptor antagonists) and phenothiazines and they should be prescribed when required for NVP and HG (Appendix III).**

C

**Combinations of different drugs should be used in women who do not respond to a single antiemetic.**

✓

**For women with persistent or severe HG, the parenteral or rectal route may be necessary and more effective than an oral regimen.**

✓

**Women should be asked about previous adverse reactions to antiemetic therapies. Drug-induced extrapyramidal symptoms and oculogyric crises can occur with the use of phenothiazines and metoclopramide. If this occurs, there should be prompt cessation of the medications.**

B

**Clinicians should use antiemetics with which they are familiar and should use drugs from different classes if the first drug is not effective.**

B

**Metoclopramide is safe and effective, but because of the risk of extrapyramidal effects it should be used as second-line therapy.**

B

**There is evidence that ondansetron is safe and effective, but because data are limited it should be used as second-line therapy.**

C

#### Pyridoxine

**Pyridoxine is not recommended for NVP and HG.**

C

#### Corticosteroids

**Corticosteroids should be reserved for cases where standard therapies have failed.**

A

#### Diazepam

**Diazepam is not recommended for the management of NVP or HG.**

B

What is the best rehydration regimen for ambulatory daycare and inpatient management?

**Normal saline with additional potassium chloride in each bag, with administration guided by daily monitoring of electrolytes, is the most appropriate intravenous hydration.**

D

**Dextrose infusions are not appropriate unless the serum sodium levels are normal and thiamine has been administered.**

D

Which complementary therapies could be helpful?

Ginger

**Ginger may be used by women wishing to avoid antiemetic therapies in mild to moderate NVP.**

**A**

Acustimulations – acupressure and acupuncture

**Women may be reassured that acustimulations are safe in pregnancy. Acupressure may improve NVP.**

**B**

Hypnosis

**Hypnotic therapies should not be recommended to manage NVP and HG.**

**D**

### *Monitoring and adverse effects*

What complications or adverse effects can occur from NVP and HG and what are their preventive/management strategies?

**Urea and serum electrolyte levels should be checked daily in women requiring intravenous fluids.**

**Histamine H2 receptor antagonists or proton pump inhibitors may be used for women developing gastro-oesophageal reflux disease, oesophagitis or gastritis.**

**D**

**Thiamine supplementation (either oral or intravenous) should be given to all women admitted with prolonged vomiting, especially before administration of dextrose or parenteral nutrition.**

**D**

**Women admitted with HG should be offered thromboprophylaxis with low-molecular-weight heparin unless there are specific contraindications such as active bleeding. Thromboprophylaxis can be discontinued upon discharge.**

**C**

**Women with previous or current NVP or HG should consider avoiding iron-containing preparations if these exacerbate the symptoms.**

**D**

### *Further management*

What is the role of the multidisciplinary team?

**In women with severe NVP or HG, input may be required from other professionals, such as midwives, nurses, dieticians, pharmacists, endocrinologists, nutritionists and gastroenterologists, and a mental health team, including a psychiatrist.**

**D**

When should enteral and parenteral nutrition be considered and what are the risks to the mother and fetus?

**When all other medical therapies have failed, enteral or parenteral treatment should be considered with a multidisciplinary approach.**

**D**

When should termination of pregnancy be considered?

**All therapeutic measures should have been tried before offering termination of a wanted pregnancy.**

**D**

## *Discharge and follow-up*

What discharge and follow-up arrangements should be implemented?

**Women with NVP and HG should have an individualised management plan in place when they are discharged from hospital.**



**Women with severe NVP or HG who have continued symptoms into the late second or the third trimester should be offered serial scans to monitor fetal growth.**



*What is the effect of NVP and HG in the postnatal period?*

How should we advise about future pregnancies?

**Women with previous HG should be advised that there is a risk of recurrence in future pregnancies.**



**Early use of lifestyle/dietary modifications and antiemetics that were found to be useful in the index pregnancy is advisable to reduce the risk of NVP and HG in the current pregnancy.**



*What is the effect of NVP and HG on quality of life?*

**A woman's quality of life can be adversely affected by NVP and HG and practitioners should address the severity of a woman's symptoms in relation to her quality of life and social situation.**



**Practitioners should assess a woman's mental health status during the pregnancy and postnatally and refer for psychological support if necessary.**



**Women should be referred to sources of psychosocial support.**



**Practitioners should validate the woman's physical symptoms and psychological distress.**



**Women should be advised to rest as required to alleviate symptoms.**



## **1. Purpose and scope**

There is variation in the management of women who have nausea and vomiting of pregnancy (NVP) or hyperemesis gravidarum (HG) with an occasional lack of understanding of its severity and options for treatment and support.

The aim of this guideline is to provide evidence-based or best clinical practice information regarding the diagnosis and subsequent management of NVP and HG across community, ambulatory daycare and inpatient settings. It gives advice for multidisciplinary professionals involved in the care of women with these conditions, including how to counsel and support women before, during and after their pregnancies.

## **2. Introduction and background epidemiology**

NVP affects up to 80% of pregnant women<sup>1</sup> and is one of the most common indications for hospital admission among pregnant women, with typical stays of between 3 and 4 days.<sup>2-4</sup> For this guideline, NVP is defined as the symptom of nausea and/or vomiting during early pregnancy where there are no other causes. HG is the severe form of NVP, which affects about 0.3–3.6% of pregnant women.<sup>1,5-7</sup> Reported HG recurrence rates vary, from 15.2% in a Norwegian hospital registry study<sup>8</sup> to 81% if using self-reported diagnosis.<sup>9</sup>

The aetiological theories for NVP and HG range from the fetoprotective and genetic to the biochemical, immunological and biosocial.<sup>10,11</sup> They are primarily thought to be associated with rising levels of beta human chorionic gonadotrophin (hCG) hormone, and conditions with higher hCG levels, such as trophoblastic disease and multiple pregnancy, have been associated with increased severity of NVP.<sup>12,13</sup>

### 3. Identification and assessment of evidence

This guideline was developed in accordance with standard methodology for producing Royal College of Obstetricians and Gynaecologists (RCOG) Green-top Guidelines. Databases searched included the Cochrane Library, EMBASE and MEDLINE. The databases were searched using the relevant Medical Subject Headings (MeSH) terms, including all subheadings, and this was combined with a keyword search. Search terms included 'nausea and vomiting', 'vomiting', 'nausea', 'hyperemesis', 'morning sickness', 'antiemetic agent', 'fluids' and 'hydration'. The search was inclusive of all relevant articles published up to August 2015. The National Guideline Clearinghouse, National Institute for Health and Care Excellence (NICE) Evidence Search, Trip, Guidelines International Network and Geneva Foundation for Medical Education and Research website were also searched for relevant guidelines and reviews.

Where possible, recommendations are based on available evidence. Areas lacking evidence are highlighted and annotated as 'good practice points'. Further information about the assessment of evidence and the grading of recommendations may be found in Appendix I.

### 4. Diagnosis of NVP and HG

#### 4.1 How is NVP diagnosed?

**NVP should only be diagnosed when onset is in the first trimester of pregnancy and other causes of nausea and vomiting have been excluded.**

D

Onset of NVP is in the first trimester and if the initial onset is after 10<sup>+6</sup> weeks of gestation, other causes need to be considered. It typically starts between the fourth and seventh weeks of gestation, peaks in approximately the ninth week and resolves by the 20th week in 90% of women.<sup>14</sup>

Evidence level 2-

#### 4.2 How is HG diagnosed?

**HG can be diagnosed when there is protracted NVP with the triad of more than 5% prepregnancy weight loss, dehydration and electrolyte imbalance.**

D

HG is characterised by severe, protracted nausea and vomiting associated with weight loss of more than 5% of prepregnancy weight, dehydration and electrolyte imbalances.<sup>7</sup>

Evidence level 2-

#### 4.3 How can the severity of NVP be classified?

**An objective and validated index of nausea and vomiting such as the Pregnancy-Unique Quantification of Emesis (PUQE) score can be used to classify the severity of NVP.**

C

Objective, validated measures for the severity of nausea and vomiting include the Rhodes Index and the PUQE index. The Rhodes Index<sup>15,16</sup> was originally validated to measure nausea and vomiting in chemotherapy patients, including assessment of physical symptoms and the resulting stress, but has subsequently been used for NVP. A shorter disease-specific questionnaire (PUQE) was developed by the Motherisk Program,<sup>17</sup> an NVP helpline in Canada, which highly correlated with the Rhodes Index.<sup>18</sup> The PUQE was modified to include symptom profile over the previous

Evidence level 2+

24 hours including a wellbeing score that correlated with hydration status and, more recently, over a longer period of time.<sup>19,20</sup> The PUQE score can be used to determine whether the NVP is mild, moderate or severe (Appendix II) and can be used to track progress with treatment.

Evidence level 2+

## 5. What initial clinical assessment and baseline investigations should be done before deciding on treatment?

Clinicians should be aware of the features in history, examination and investigation that allow NVP and HG to be assessed and diagnosed and for their severity to be monitored.



**Table 1.** Features in the history, examination and investigations to monitor severity and other causes

<b>History</b>	<ul style="list-style-type: none"> <li>● Previous history of NVP/HG</li> <li>● Quantify severity using PUQE score: nausea, vomiting, hypersalivation, spitting, loss of weight, inability to tolerate food and fluids, effect on quality of life</li> <li>● History to exclude other causes:               <ul style="list-style-type: none"> <li>– abdominal pain</li> <li>– urinary symptoms</li> <li>– infection</li> <li>– drug history</li> <li>– chronic <i>Helicobacter pylori</i> infection</li> </ul> </li> </ul>
<b>Examination</b>	<ul style="list-style-type: none"> <li>● Temperature</li> <li>● Pulse</li> <li>● Blood pressure</li> <li>● Oxygen saturations</li> <li>● Respiratory rate</li> <li>● Abdominal examination</li> <li>● Weight</li> <li>● Signs of dehydration</li> <li>● Signs of muscle wasting</li> <li>● Other examination as guided by history</li> </ul>
<b>Investigation</b>	<ul style="list-style-type: none"> <li>● Urine dipstick:               <ul style="list-style-type: none"> <li>– quantify ketonuria as 1+ ketones or more</li> </ul> </li> <li>● MSU</li> <li>● Urea and electrolytes:               <ul style="list-style-type: none"> <li>– hypokalaemia/hyperkalaemia</li> <li>– hyponatraemia</li> <li>– dehydration</li> <li>– renal disease</li> </ul> </li> <li>● Full blood count:               <ul style="list-style-type: none"> <li>– infection</li> <li>– anaemia</li> <li>– haematocrit</li> </ul> </li> <li>● Blood glucose monitoring:               <ul style="list-style-type: none"> <li>– exclude diabetic ketoacidosis if diabetic</li> </ul> </li> <li>● Ultrasound scan:               <ul style="list-style-type: none"> <li>– confirm viable intrauterine pregnancy</li> <li>– exclude multiple pregnancy and trophoblastic disease</li> </ul> </li> <li>● In refractory cases or history of previous admissions, check:               <ul style="list-style-type: none"> <li>– TFTs: hypothyroid/hyperthyroid</li> <li>– LFTs: exclude other liver disease such as hepatitis or gallstones, monitor malnutrition</li> <li>– calcium and phosphate</li> <li>– amylase: exclude pancreatitis</li> <li>– ABG: exclude metabolic disturbances to monitor severity</li> </ul> </li> </ul>

**ABG** arterial blood gas; **LFTs** liver function tests; **MSU** midstream urine; **TFTs** thyroid function tests.

Reported HG recurrence rates vary, from 15.2% in a Norwegian hospital registry study<sup>8</sup> to 81% if using self-reported diagnosis.<sup>9</sup> However, the incidence of HG reduces in a second pregnancy if there is a change in paternity (10.9%) compared with no change (16%; adjusted OR 0.6, 95% CI 0.39–0.92).<sup>8,21</sup>

Evidence level 2+

NVP and HG are associated with hyponatraemia, hypokalaemia, low serum urea, raised haematocrit and ketonuria with a metabolic hypochloraemic alkalosis. If severe, a metabolic acidemia may develop. In two-thirds of patients with HG, there may be abnormal thyroid function tests (based on a structural similarity between thyroid-stimulating hormone [TSH] and hCG) with a biochemical thyrotoxicosis and raised free thyroxine levels with or without a suppressed thyroid stimulating hormone level. These patients rarely have thyroid antibodies and are euthyroid clinically. The biochemical thyrotoxicosis resolves as the HG improves<sup>22</sup> and treatment with antithyroid drugs is inappropriate.

Evidence level 2-

Liver function tests are abnormal in up to 40% of women with HG,<sup>23</sup> with the most likely abnormality being a rise in transaminases. Bilirubin levels can be slightly raised but without jaundice, and amylase levels can be mildly raised too. These abnormalities improve as the HG resolves.

Evidence level 3

An ultrasound scan should be scheduled to confirm viability and gestational age and to rule out multiple pregnancy or trophoblastic disease. Unless there are other medical reasons for an urgent scan, this can be scheduled for the next available appointment as long as the NVP has resolved with treatment.

### 5.1 What are the differential diagnoses?

**Other pathological causes should be excluded by clinical history, focused examination and investigations.**



Other pathological causes of nausea and vomiting include peptic ulcers, cholecystitis, gastroenteritis, hepatitis, pancreatitis, genitourinary conditions such as urinary tract infection or pyelonephritis, metabolic conditions, neurological conditions and drug-induced nausea and vomiting.<sup>24–26</sup>

Evidence level 3

Severe abdominal or epigastric pain is unusual in NVP and HG and may warrant further investigation of serum amylase levels and an abdominal ultrasound, and possibly oesophageal gastroduodenoscopy, which is considered safe in pregnancy.

Chronic infection with *Helicobacter pylori* can be associated with NVP and HG and testing for *H. pylori* antibodies may be considered.<sup>27,28</sup>

Evidence level 2+

## 6. What is the initial management of NVP and HG?

### 6.1 How should the woman be managed?

**Women with mild NVP should be managed in the community with antiemetics.**



**Ambulatory daycare management should be used for suitable patients when community/primary care measures have failed and where the PUQE score is less than 13.**





**Inpatient management should be considered if there is at least one of the following:**



- **continued nausea and vomiting and inability to keep down oral antiemetics**
- **continued nausea and vomiting associated with ketonuria and/or weight loss (greater than 5% of body weight), despite oral antiemetics**
- **confirmed or suspected comorbidity (such as urinary tract infection and inability to tolerate oral antibiotics).**

Since most women with NVP require only oral antiemetics, management in the community/primary care is appropriate to avoid unnecessary hospital admissions and disruption to the woman's life.<sup>29</sup> Women who have vomiting but are not dehydrated can be managed in the community with antiemetics, support, reassurance, oral hydration and dietary advice.

Evidence level 4

If women are unable to tolerate oral antiemetics or oral fluids then ambulatory daycare management, which provides parenteral fluids, parenteral vitamins (multi and B-complex)<sup>30</sup> and antiemetics, is appropriate if local resources allow. Various regimens have been shown to be effective.<sup>31</sup> A randomised controlled trial (RCT)<sup>32</sup> of 98 women showed that ambulatory daycare management involving intravenous fluids and stepwise increments in antiemetic therapy versus inpatient management was acceptable to women and resulted in reduced inpatient stay. In a study of 428 women<sup>31</sup> who had ambulatory daycare subcutaneous metoclopramide therapy (SMT), improvement in symptoms occurred in 89.3%. Those women who failed the SMT regimen (10.7%) had higher mean PUQE scores at the start of ambulatory daycare treatment than those for which it was successful ( $10 \pm 3$  versus  $7.6 \pm 2.8$  respectively,  $P < 0.001$ ). Moreover, they were more likely to have a PUQE score of 13 or higher, they had an earlier gestational age at the start of SMT ( $9.7 \pm 2.9$  weeks versus  $11.4 \pm 3.2$  weeks,  $P = 0.005$ ) and they were more likely to need intravenous hydration (91.3% versus 65.2%,  $P < 0.001$ ). In addition to the SMT regimen, women received adjuvant therapies at home such as intravenous hydration, subcutaneous ondansetron, histamine H2 receptor antagonists, and 2.1% received total parenteral nutrition. Ambulatory daycare management has been successfully and safely set up in units and is associated with high patient satisfaction.<sup>33</sup>

Evidence level 2+

Women who have recurrent NVP/HG despite adequate ambulatory daycare treatment should be managed as inpatients due to the associated complications, in particular electrolyte imbalance and nutritional deficiencies.

## 6.2 What therapeutic options are available for NVP and HG?

### 6.2.1 What is the safety and efficacy of pharmacological agents?

#### *Antiemetics*

**There are safety and efficacy data for first-line antiemetics such as antihistamines (H<sub>1</sub> receptor antagonists) and phenothiazines and they should be prescribed when required for NVP and HG (Appendix III).**



**Combinations of different drugs should be used in women who do not respond to a single antiemetic.**



**For women with persistent or severe HG, the parenteral or rectal route may be necessary and more effective than an oral regimen.**



**Women should be asked about previous adverse reactions to antiemetic therapies. Drug-induced extrapyramidal symptoms and oculogyric crises can occur with the use of phenothiazines and metoclopramide. If this occurs, there should be prompt cessation of the medications.**



**Clinicians should use antiemetics with which they are familiar and should use drugs from different classes if the first drug is not effective.**

**B**

**Metoclopramide is safe and effective, but because of the risk of extrapyramidal effects it should be used as second-line therapy.**

**B**

**There is evidence that ondansetron is safe and effective, but because data are limited it should be used as second-line therapy.**

**C**

A Cochrane review<sup>5</sup> and other systematic reviews and meta-analyses<sup>34–36</sup> and birth registry data<sup>36</sup> have reported on the safety and efficacy of many antiemetics for use in NVP and HG, with no increased risk of teratogenesis or other adverse pregnancy outcomes. These drugs include: antihistamines (histamine H1 receptor antagonists) such as promethazine, cyclizine, cinnarizine, doxylamine<sup>37</sup> and dimenhydrinate; phenothiazines including prochlorperazine, chlorpromazine and perphenazine; and dopamine antagonists including metoclopramide<sup>38</sup> and domperidone.

Evidence level 2++

Because different drug classes may have different mechanisms of action and therefore synergistic effects, combinations of drugs from different classes should be used in women who do not respond to a single antiemetic. Furthermore, persistent vomiting may mean that oral doses of antiemetics are not absorbed and therefore the intravenous, rectal, subcutaneous or intramuscular routes may be necessary and more effective.

Due to the risk of extrapyramidal effects with metoclopramide it should be used as second-line therapy. A review of metoclopramide,<sup>39</sup> conducted by the European Medicines Agency's Committee for Medicinal Products for Human Use, has confirmed the risks of short-term extrapyramidal disorders and tardive dyskinesia, particularly in young people. The review recommends metoclopramide should only be prescribed for short-term use (maximum dose of 30 mg in 24 hours or 0.5 mg/kg body weight in 24 hours [whichever is lowest] and maximum duration of 5 days) and that intravenous doses should be administered by slow bolus injection over at least 3 minutes to help minimise these risks. Dystonic reactions have been shown to be significantly less common in nonpregnant patients receiving a slow infusion as opposed to a bolus injection of 10 mg of metoclopramide.<sup>40</sup>

Evidence level 2++

Studies on the safety of ondansetron are mixed. A large retrospective analysis<sup>41</sup> of data from the Danish birth registry of 608 385 pregnancies found no increased risk of major birth defect, stillbirth, preterm labour or small-for-gestational age. However, a case-control study<sup>42</sup> with 4524 cases and 5859 controls found a two-fold increased risk of cleft palate (adjusted OR 2.37, 95% CI 1.18–4.76), although the authors suggest that this association may be due to chance due to the large number of variables investigated. Data from the Swedish Medical and Birth Register<sup>43</sup> demonstrated a small increased risk of cardiovascular defects and cardiac septal defects (OR 1.62, 95% CI 1.04–2.14, and risk ratio 2.05, 95% CI 1.19–3.28, respectively). For these reasons, the use of ondansetron should be limited to patients who are not adequately managed on the aforementioned antiemetics and preferably used after the first trimester of pregnancy.

Three small randomised studies<sup>44–46</sup> have shown ondansetron to be superior to doxylamine and pyridoxine in reducing nausea and vomiting,<sup>44</sup> equally effective but with fewer adverse effects than metoclopramide<sup>45</sup> and more effective at reducing severe vomiting than metoclopramide.<sup>46</sup>

Evidence level 2+

Suggested antiemetics for UK use are given in Appendix III.

## ***Pyridoxine***

**Pyridoxine is not recommended for NVP and HG.**

**C**

There is no association between the degree of NVP at 12 weeks and vitamin B6 levels measured at 15 weeks.<sup>47</sup> A Cochrane review<sup>5</sup> concluded that there is a lack of consistent evidence that pyridoxine is an effective therapy for NVP. Furthermore, a placebo-controlled trial<sup>48</sup> of its use in HG did not demonstrate any improvement in nausea, vomiting or rehospitalisation in 46 women given 20 mg orally three times a day in addition to intravenous fluids, intravenous metoclopramide three times a day and oral thiamine compared to the control group given placebo in addition to standard therapy. A matched nonrandomised study<sup>49</sup> demonstrated that the combination of doxylamine and pyridoxine was significantly more effective than pyridoxine alone.

Evidence level 2++

## ***Corticosteroids***

**Corticosteroids should be reserved for cases where standard therapies have failed.**

**A**

Corticosteroids have resulted in dramatic and rapid improvement in case series of women with refractory HG.<sup>50</sup> The results of randomised studies are conflicting<sup>51</sup> and the largest study failed to show improvement in the primary outcome of rehospitalisation (however, both groups also received metoclopramide and promethazine).<sup>52,53</sup> Case selection and route and dose of corticosteroid administration may explain the different results, with beneficial results being described in more severe cases of HG. A prospective double-blind study<sup>54</sup> of 40 women admitted to intensive care with severe HG demonstrated that daily intravenous hydrocortisone 300 mg was superior to intravenous metoclopramide in reducing vomiting and recurrence.

Evidence level 1+

Corticosteroids should not be used until conventional treatment with intravenous fluid replacement and regular antiemetics has failed. The suggested dose is intravenous hydrocortisone 100 mg twice daily, and once clinical improvement occurs convert to oral prednisolone 40–50 mg daily, with the dose gradually tapered until the lowest maintenance dose that controls the symptoms is reached. In most cases prednisolone needs to be continued until the gestational age at which HG would have typically resolved and in some extreme cases this occurs at delivery.<sup>29</sup>

Evidence level 4

## ***Diazepam***

**Diazepam is not recommended for the management of NVP or HG.**

**B**

A randomised trial<sup>55</sup> investigated 50 women with HG; they were treated with infusions of saline, glucose, vitamins and randomly allocated diazepam. While the addition of diazepam to the treatment regimen reduced nausea, there was no difference in vomiting between those treated with or without diazepam.

Evidence level 1-

### **6.2.2 What is the best rehydration regimen for ambulatory daycare and inpatient management?**

**Normal saline with additional potassium chloride in each bag, with administration guided by daily monitoring of electrolytes, is the most appropriate intravenous hydration.**

**D**

**Dextrose infusions are not appropriate unless the serum sodium levels are normal and thiamine has been administered.**

**D**

The most important intervention is likely to be appropriate intravenous fluid and electrolyte replacement. There is no evidence to determine which fluid regimen is most appropriate but given that most women admitted to hospital with HG are hyponatraemic, hypochloreaemic, hypokalaemic and ketotic, it seems appropriate to use normal saline and potassium chloride. General adult fluid management guidance can be found in NICE clinical guideline 174.<sup>56</sup> Dextrose-containing solutions can precipitate Wernicke's encephalopathy in thiamine-deficient states (see section 7.1); hence, each day intravenous dextrose is administered, high (e.g. 100 mg) doses of parenteral thiamine should be given to prevent Wernicke's encephalopathy.

Evidence level 3

Appendix IV provides a summary treatment algorithm for NVP and HG.

### 6.2.3 Which complementary therapies could be helpful?

#### *Ginger*

**Ginger may be used by women wishing to avoid antiemetic therapies in mild to moderate NVP.**

**A**

Three systematic reviews<sup>57-59</sup> have addressed the effectiveness of ginger for NVP. One found four RCTs that met the criteria and all found that oral ginger was more effective than placebo in reducing nausea and vomiting.<sup>57</sup> The second included a total of ten RCTs, comparing ginger with placebo (five studies), with vitamin B6 (four studies), and one with dimenhydrinate. Ginger was superior to placebo and equal to vitamin B6 and dimenhydrinate at improving nausea and vomiting.<sup>58</sup> The third analysed six studies and 508 subjects randomised to ginger or placebo and concluded that ginger was effective.<sup>59</sup> Ginger was superior to placebo but less effective than metoclopramide in a randomised trial including 102 patients with NVP.<sup>60</sup> Another group investigated the effect of ginger biscuits and found them to be better than placebo at reducing nausea.<sup>61</sup> No studies have addressed the effect of ginger in HG under the current definition.

Evidence level 1++

No increased risk of major malformations has been reported with use of ginger;<sup>62,63</sup> however, one review<sup>64</sup> highlighted potential maternal adverse effects, including an anticoagulant effect, stomach irritation and a potential interaction with beta blockers and benzodiazepines.

Evidence level 2+

#### *Acustimulations – acupressure and acupuncture*

**Women may be reassured that acustimulations are safe in pregnancy. Acupressure may improve NVP.**

**B**

Acupuncture is safe in pregnancy.<sup>65</sup> A systematic review<sup>66</sup> has addressed the efficacy in NVP of acustimulations (i.e. acupuncture, acupressure and electrical stimulation) at the pericardium 6 (PC6; Nei Guan) point. PC6 is located about 2.5 finger breadths up from the wrist crease on the inside of the forearm, between the tendons of palmaris longus and flexor carpi radialis. The review included 14 studies, and meta-analysis demonstrated acupressure applied by finger pressure or wristband and electrical stimulation both reduced NVP, but acupuncture methods did not. There was a placebo effect observed for improvement in nausea (three trials) and vomiting (five trials) when compared with controls. There is less evidence for a beneficial effect on vomiting.<sup>67</sup> A later systematic review<sup>68</sup> found six RCTs including 399 patients examining the effect of acupressure. Five studies reported positive results and, of these, two (102 patients) were in women with HG.

Evidence level 1+

## Hypnosis

**Hypnotic therapies should not be recommended to manage NVP and HG.**

**D**

A review<sup>69</sup> of six studies reporting hypnosis for HG, mainly small case series, concluded that the evidence was not sufficient to establish whether hypnosis (trance induction) is an effective treatment.

Evidence level 3

## 7. Monitoring and adverse effects

*7.1 What complications or adverse effects can occur from NVP and HG and what are their preventive/management strategies?*

**Urea and serum electrolyte levels should be checked daily in women requiring intravenous fluids.**



**Histamine H2 receptor antagonists or proton pump inhibitors may be used for women developing gastro-oesophageal reflux disease, oesophagitis or gastritis.**

**D**

**Thiamine supplementation (either oral or intravenous) should be given to all women admitted with prolonged vomiting, especially before administration of dextrose or parenteral nutrition.**

**D**

**Women admitted with HG should be offered thromboprophylaxis with low-molecular-weight heparin unless there are specific contraindications such as active bleeding. Thromboprophylaxis can be discontinued upon discharge.**

**C**

**Women with previous or current NVP or HG should consider avoiding iron-containing preparations if these exacerbate the symptoms.**

**D**

In women requiring intravenous fluids, daily monitoring of fluid and serum electrolyte levels is important to prevent and treat hyponatraemia and hypokalaemia.<sup>29,70</sup>

Evidence level 4

Recurrent intractable vomiting may lead to gastro-oesophageal reflux disease, oesophagitis or gastritis. Oesophageal gastroduodenoscopy is safe in pregnancy<sup>71</sup> and indicated if there is haematemesis or severe epigastric pain. A therapeutic trial with a proton pump inhibitor is appropriate for treatment and prevention and is safe in pregnancy.<sup>72</sup>

Evidence level 1+

A systematic review<sup>73</sup> concluded that safety data for histamine H2 receptor antagonists were generally reassuring but further studies are needed.

Evidence level 2+

Wernicke's encephalopathy due to vitamin B1 (thiamine) deficiency classically presents with blurred vision, unsteadiness and confusion/memory problems/drowsiness and on examination there is usually nystagmus, ophthalmoplegia, hyporeflexia or areflexia, gait and/or finger–nose ataxia. In HG, the presentation tends to be episodic and of slow onset. Wernicke's encephalopathy is a potentially fatal but reversible medical emergency. In the context of HG, it is totally preventable and studies<sup>74,75</sup> have stressed the association between Wernicke's encephalopathy and administration of intravenous dextrose and parenteral nutrition. One of these studies<sup>74</sup> reported that complete remission occurred in only 29% and permanent residual impairment was common. The overall pregnancy loss rate including intrauterine deaths and terminations was 48%.<sup>74</sup> Therefore thiamine supplementation is recommended for all women with protracted vomiting.

Evidence level 3

A retrospective study<sup>76</sup> found that the odds ratio for venous thromboembolism with HG was 2.5 (95% CI 2–3.2). A Canadian study<sup>77</sup> using hospital discharge data found an adjusted odds ratio for deep vein thrombosis of 4.4 (95% CI 2.4–8.4) in women with HG. However, since women with HG are only at markedly increased risk while persistently vomiting, thromboprophylaxis can be discontinued at discharge or when the HG resolves.<sup>78</sup>

Evidence level 2+

Oral iron can cause nausea and vomiting. In a Canadian prospective cohort study,<sup>79</sup> two-thirds of 97 women who discontinued iron supplements reported improvement in their severity of NVP.

Evidence level 2-

## 8. Further management

### 8.1 What is the role of the multidisciplinary team?

**In women with severe NVP or HG, input may be required from other professionals, such as midwives, nurses, dieticians, pharmacists, endocrinologists, nutritionists and gastroenterologists, and a mental health team, including a psychiatrist.**

D

There are many facets to severe NVP and HG and a holistic approach to assessment and treatment should be adopted.

Dietetic advice can be very helpful to treat or avoid potentially serious complications. Women requiring enteral or parenteral feeding require input from a gastroenterologist and a nutritionist.<sup>80</sup> Advice from other specialists such as a pharmacist and endocrinologist may often be required.

Evidence level 4

Involvement of a mental health team in the woman's care may improve quality of life and the ability to cope with pregnancy.<sup>81</sup> Emotional support and psychological or psychiatric care may be required<sup>27</sup> with targeted interventions specifically designed to treat mental health issues in HG, which are a result of HG rather than a cause.<sup>82–85</sup>

Evidence level 2-

### 8.2 When should enteral and parenteral nutrition be considered and what are the risks to the mother and fetus?

**When all other medical therapies have failed, enteral or parenteral treatment should be considered with a multidisciplinary approach.**

D

There are no defined criteria for parenteral or enteral feeding. Their effectiveness is not well established. Anecdotally, they can be successful and are often employed as a last resort when all other medical therapy has failed and the only other practical option is termination of the pregnancy.<sup>86,87</sup> Close monitoring of metabolic and electrolyte balance, related complications and nutritional requirements are needed so a multidisciplinary approach can be employed.

Evidence level 2-

Enteral feeding options to consider include nasogastric, nasoduodenal or nasojejunal tubes, or percutaneous endoscopic gastrostomy or jejunostomy feeding. Parenteral feeding with a peripherally inserted central catheter (PICC line) is often better tolerated than enteral feeding; however, it carries a higher risk of infection and vascular perforation.<sup>80</sup>

Evidence level 2+

There may be resistance to enteral feeding from the patient for cosmetic and psychological reasons or for fear of discomfort; however, it is more effective and safer than parenteral feeding.<sup>88</sup>

Evidence level 3



In some women, intragastric feeding by nasogastric or percutaneous endoscopic gastrostomy tube increases the risk of nausea and vomiting. It may be tolerated in the short term but not in protracted HG.<sup>89</sup>

Evidence level 3

In nasojejunal feeding, the tube is inserted endoscopically to the jejunum and feeding can be administered by a continuous infusion. One study<sup>89</sup> showed that although the majority of women improved greatly within 48 hours, ongoing vomiting and retching can dislodge gastric and postpyloric feeding tubes.

Feeding via a percutaneous endoscopic gastrojejunostomy, placed under general anaesthetic in the second trimester,<sup>90</sup> has been shown to be an effective, safe and well-tolerated treatment of HG. In the majority of women, the tube is removed after delivery. The risk of early dislodgement is minimised compared with nasoenteric placement.<sup>90</sup> Potential complications of percutaneous endoscopic jejunostomy include tube dislodgement, obstruction or migration, cutaneous or intra-abdominal abscesses, fistula formation, pneumatosis, occlusion and intestinal ischaemia.

Evidence level 2+

Total parenteral nutrition is a complex high-risk intervention; however, it may be useful in refractory cases to ensure sufficient calorie intake. It should only be used as a last resort when all other treatments have failed as it is inconvenient, expensive and can be associated with serious complications such as thrombosis, metabolic disturbances and infection.<sup>27,91</sup> A single nonrandomised study<sup>92</sup> has shown that total parenteral nutrition was associated with a decreased risk of perinatal morbidity. A strict protocol with careful monitoring is essential when undertaking total parenteral nutrition.<sup>93</sup>

### 8.3 *When should termination of pregnancy be considered?*

**All therapeutic measures should have been tried before offering termination of a wanted pregnancy.**

D

The Hyperemesis Education and Research (HER) Foundation in the USA reports that 10% of pregnancies complicated by HG end in termination in women who would not otherwise have chosen this.<sup>94</sup> Pregnancy Sickness Support in the UK found that many of these women have not been offered the full range of treatments available and fewer than 10% had been offered steroids.<sup>95</sup>

Evidence level 4

Treatment options of antiemetics, corticosteroids, enteral and parenteral feeding, and correction of electrolyte or metabolic disturbances should be considered before deciding that the only option is termination of the pregnancy.<sup>96,97</sup> A psychiatric opinion should also be sought, and the decision for termination needs to be multidisciplinary, with documentation of therapeutic failure if this is the reason for the termination. Women should be offered counselling before and after a decision of pregnancy termination is made.

Evidence level 2-

In a survey<sup>97</sup> of 808 women who terminated their pregnancies secondary to HG, 123 (15.2%) had at least one termination due to HG, and 49 (6.1%) had multiple terminations. Prominent reasons given for the terminations were inability to care for the family and self (66.7%), fear that they or their baby could die (51.2%), or that the baby would be abnormal (22%). In the same survey, women who terminated a pregnancy were more likely to report a negative attitude from their caregiver. Initiation of a prompt and responsive treatment plan may reduce this.<sup>86</sup> Occasionally, HG or its treatment may lead to life-threatening illness and termination of the pregnancy is seen as the only option.

Evidence level 4

## 9. Discharge and follow-up

### 9.1 What discharge and follow-up arrangements should be implemented?

**Women with NVP and HG should have an individualised management plan in place when they are discharged from hospital.**



**Women with severe NVP or HG who have continued symptoms into the late second or the third trimester should be offered serial scans to monitor fetal growth.**



At the time of discharge, it is essential that women are advised to continue with their antiemetics where appropriate and that they know how to access further care if their symptoms and/or signs recur (e.g. persistent vomiting, dehydration or ketonuria). Earlier treatment may reduce the need for hospital admission. Rehydration and a review of antiemetic treatment should ideally be undertaken in an ambulatory daycare setting.<sup>98</sup> Better communication and advice about the safety of antiemetics may enable general practitioners to adequately support women with HG.<sup>95,98</sup>

Evidence level 2-

For some women, checking for ketonuria may identify a problem before vomiting is severe, allowing earlier access for rehydration,<sup>33</sup> but level of ketones should not be relied upon over and above clinical symptoms.<sup>99</sup>

Evidence level 2+

Advice about patient support groups (e.g. Pregnancy Sickness Support) should be provided as many women and their partners find this form of support helpful.<sup>100-102</sup>

A follow-up appointment for antenatal care is important in women suffering from HG. Psychological and social support should be organised depending upon the clinical and social circumstances.

An observational study<sup>21</sup> has shown that women with HG and low pregnancy weight gain (less than 7 kg during pregnancy) are at an increased risk of preterm delivery (adjusted relative risk 3.0, 95% CI 1.9-4.3) and low birthweight (less than 2500 g; adjusted relative risk 2.8, 95% CI 1.7-4.3).

An Indian study<sup>76</sup> demonstrated that excessive vomiting in pregnancy (defined as vomiting that lasted beyond 5 months) was significantly (OR 4.48, 95% CI 1.10-18.28) associated with underweight children (in those aged less than 3 years) compared with vomiting lasting less than 5 months. When women with severe HG are considered, it has been shown that those requiring repeated admissions have an 18% incidence of small-for-gestational-age babies and significantly lower birthweights than babies of women with HG and single admissions.<sup>103</sup>

Evidence level 2+

## 10. What is the effect of NVP and HG in the postnatal period?

### 10.1 How should we advise about future pregnancies?

**Women with previous HG should be advised that there is a risk of recurrence in future pregnancies.**



**Early use of lifestyle/dietary modifications and antiemetics that were found to be useful in the index pregnancy is advisable to reduce the risk of NVP and HG in the current pregnancy.**



Reported HG recurrence rates vary, from 15.2% in a Norwegian hospital registry study<sup>8</sup> to 81% if using self-reported diagnosis.<sup>9</sup>

Evidence level 3



A Canadian study<sup>104</sup> comparing women with NVP (PUQE score of 13 or above) who took pre-emptive antiemetics before pregnancy or before the onset of symptoms with those who did not, reported lower recurrence rate of HG in the group that took pre-emptive antiemetics. There was also a significant improvement in the PUQE score of NVP severity compared with the previous pregnancy in the pre-emptive group. Women who have experienced severe NVP in a previous pregnancy may benefit from initiating dietary and lifestyle changes and commencing antiemetics before or immediately at the start of symptoms in a subsequent pregnancy.<sup>104</sup>

Evidence level 2+

A small randomised study<sup>105</sup> in women with previous NVP demonstrated that pre-emptive treatment with antiemetics resulted in fewer women with moderate to severe NVP.

## 11. What is the effect of NVP and HG on quality of life?

**A woman's quality of life can be adversely affected by NVP and HG and practitioners should address the severity of a woman's symptoms in relation to her quality of life and social situation.**

C

**Practitioners should assess a woman's mental health status during the pregnancy and postnatally and refer for psychological support if necessary.**

D

**Women should be referred to sources of psychosocial support.**

D

**Practitioners should validate the woman's physical symptoms and psychological distress.**

C

**Women should be advised to rest as required to alleviate symptoms.**

D

NVP has been reported to reduce quality of life, impairing a woman's ability to function on a day-to-day basis, and negatively affects relationships with her partner and family.<sup>81,104,106-117</sup> Women with HG are three to six times more likely than women with NVP to have low quality of life.<sup>22</sup> Persistent nausea is the symptom that most adversely affects quality of life.<sup>112,118</sup> Furthermore, causes of stress as a consequence of NVP include lack of understanding and support, inability to eat healthily, grief for loss of normal pregnancy, absence from work, financial pressures, isolation, inability to care for family, others' belief that it is psychosomatic and reluctance of doctors to treat the condition.<sup>24,106,119</sup> Perceived stress positively correlated with NVP and negatively correlated with social support in a cross-sectional study of 243 women.<sup>120</sup> It has been recommended that social support is necessary as an adjunct to treatment and the circle of support should be expanded to include family, friends and healthcare professionals.<sup>121</sup> A cohort study<sup>106</sup> of 648 women found that having support from at least three other persons was protective for NVP.

Evidence level 2-

Clinical assessment should be considered for depression and postnatal depression with appropriate referral. Depression and poor psychological health were found to be associated with NVP and HG in numerous studies,<sup>82,83,106,107,122-129</sup> but resulted from the disease and were not the cause of HG or NVP. A prospective case-control study<sup>83</sup> of 32 women compared with 41 matched controls found that, compared with controls, women with HG had significantly higher levels of somatisation, depression, anxiety and overall psychological distress even when HG had resolved to mild NVP.

A cohort study<sup>106</sup> of 648 women found that symptoms of major depression are associated with moderate and severe NVP but prior history of depression is not a determinant.<sup>106,130</sup>

Measures that address NVP, poor social support and depression are warranted throughout pregnancy.<sup>106</sup> A prospective cohort study<sup>109</sup> of 367 women suggests that practitioners could improve their management of NVP by addressing symptoms and life situation.

The theory of psychogenic aetiology proposed by Fairweather<sup>131</sup> has been severely criticised for poor methodology and bias.<sup>77,132,133</sup> Studies have failed to find a convincing association between a prior history of psychological poor health and risk of suffering from HG,<sup>83,124,126,129,134–136</sup> and poor mental health is a result of the suffering caused by HG rather than being causal.<sup>82,108,122,129,130,136–138</sup>

Evidence level 2+

Poor psychological health of women with HG is considered as the demoralisation of suffering from a prolonged, severe chronic illness and in this regard it is similar to mental health problems suffered in other chronic illnesses.<sup>139</sup>

The erroneous belief in the psychogenic aetiology of HG is still prevalent among healthcare professionals<sup>101,138–142</sup> and poor attitudes towards women contribute to a worse experience for NVP and HG sufferers.<sup>101,121,139,142</sup> A qualitative study of 19 women<sup>142</sup> and an online survey of 114 women<sup>140,143</sup> found that they struggled to obtain treatment for HG, were dissatisfied with communication during their appointments and found healthcare professionals dismissive and unsympathetic. A cohort study<sup>139</sup> of 808 women demonstrated that women who felt that their healthcare professional was unsympathetic reported more depression and anxiety. A review paper<sup>137</sup> recommends an integrated approach which addresses both physical and psychological suffering in HG.

Evidence level 4

Fatigue is associated with NVP in several studies.<sup>112,116,134,140</sup> Rest, particularly napping, is reported by women to relieve symptoms.<sup>115,118,144</sup> A survey<sup>143</sup> of 114 women conducted by a volunteer from Pregnancy Sickness Support found that rest was noted by the majority of respondents with HG as being the only effective management strategy aside from antiemetics. Any kind of sensory stimulation can trigger symptoms, so complete removal from sources of stimulation may be necessary.<sup>143,144</sup>

Evidence level 2-

## 12. Recommendations for future research

- Aetiology of NVP and HG.
- NVP and HG in relation to pregnancy, birth, and long-term outcomes in mother and baby.
- Safety of medication used in NVP and HG.

## 13. Auditable topics

- Women with mild NVP should be managed in the community with antiemetics (100%).
- Metoclopramide should not be used as a first-line antiemetic (100%).
- Urea and serum electrolyte levels should be checked daily in women with HG requiring intravenous fluids (100%).
- Thiamine supplementation should be given to all women admitted with prolonged vomiting (100%).
- Women with HG who are admitted to hospital should receive thromboprophylaxis with low-molecular-weight heparin, unless there are contraindications (100%).
- Women with severe NVP or HG who have symptoms extending into the late second trimester or beyond should have ultrasound scans to assess fetal growth (100%).

## 14. Useful links and support groups

- Hyperemesis Education and Research (HER) Foundation [<http://www.helper.org>].
- Motherisk [<http://www.motherisk.org/women/index.jsp>].
- Pregnancy Sickness Support [<http://www.pregnancysicknesssupport.org.uk>].
- UK Teratology Information Service (UKTIS):
  - For patients: bumps (best use of medicines in pregnancy). *Treating nausea and vomiting in pregnancy* [<http://www.medicinesinpregnancy.org/Medicine--pregnancy/NV/>].
  - For professionals: UKTIS. *Treatment of nausea and vomiting in pregnancy* [<http://www.medicinesinpregnancy.org/bumps/monographs/TREATMENT-OF-NAUSEA-AND-VOMITING-IN-PREGNANCY/>].

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## Appendix I: Explanation of guidelines and evidence levels

Clinical guidelines are: ‘systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions’. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No. 1 *Development of RCOG Green-top Guidelines* (available on the RCOG website at <http://www.rcog.org.uk/green-top-development>). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme.

Classification of evidence levels	Grades of recommendations
1++ High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias	<b>A</b> At least one meta-analysis, systematic review or randomised controlled trial rated as 1++, and directly applicable to the target population; or A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results
1+ Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias	<b>B</b> A body of evidence including studies rated as 2++ directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
1- Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias	<b>C</b> A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
2++ High-quality systematic reviews of case-control or cohort studies or high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal	<b>D</b> Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+
2+ Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal	
2- Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal	
3 Non-analytical studies, e.g. case reports, case series	
4 Expert opinion	
	<b>Good practice point</b>
	 Recommended best practice based on the clinical experience of the guideline development group

## Appendix II: Pregnancy-Unique Quantification of Emesis (PUQE) index<sup>20</sup>

Total score is sum of replies to each of the three questions. PUQE-24 score: Mild ≤ 6; Moderate = 7–12; Severe = 13–15.

Motherisk PUQE-24 scoring system					
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)	2–3 hours (3)	4–6 hours (4)	More than 6 hours (5)
In the last 24 hours have you vomited or thrown up?	7 or more times (5)	5–6 times (4)	3–4 times (3)	1–2 times (2)	I did not throw up (1)
In the last 24 hours how many times have you had retching or dry heaves without bringing anything up?	No time (1)	1–2 times (2)	3–4 times (3)	5–6 times (4)	7 or more times (5)

PUQE-24 score: Mild ≤ 6; Moderate = 7–12; Severe = 13–15.

How many hours have you slept out of 24 hours? \_\_\_\_\_ Why? \_\_\_\_\_

On a scale of 0 to 10, how would you rate your wellbeing? \_\_\_\_\_  
*0 (worst possible) → 10 (the best you felt before pregnancy)*

Can you tell me what causes you to feel that way? \_\_\_\_\_

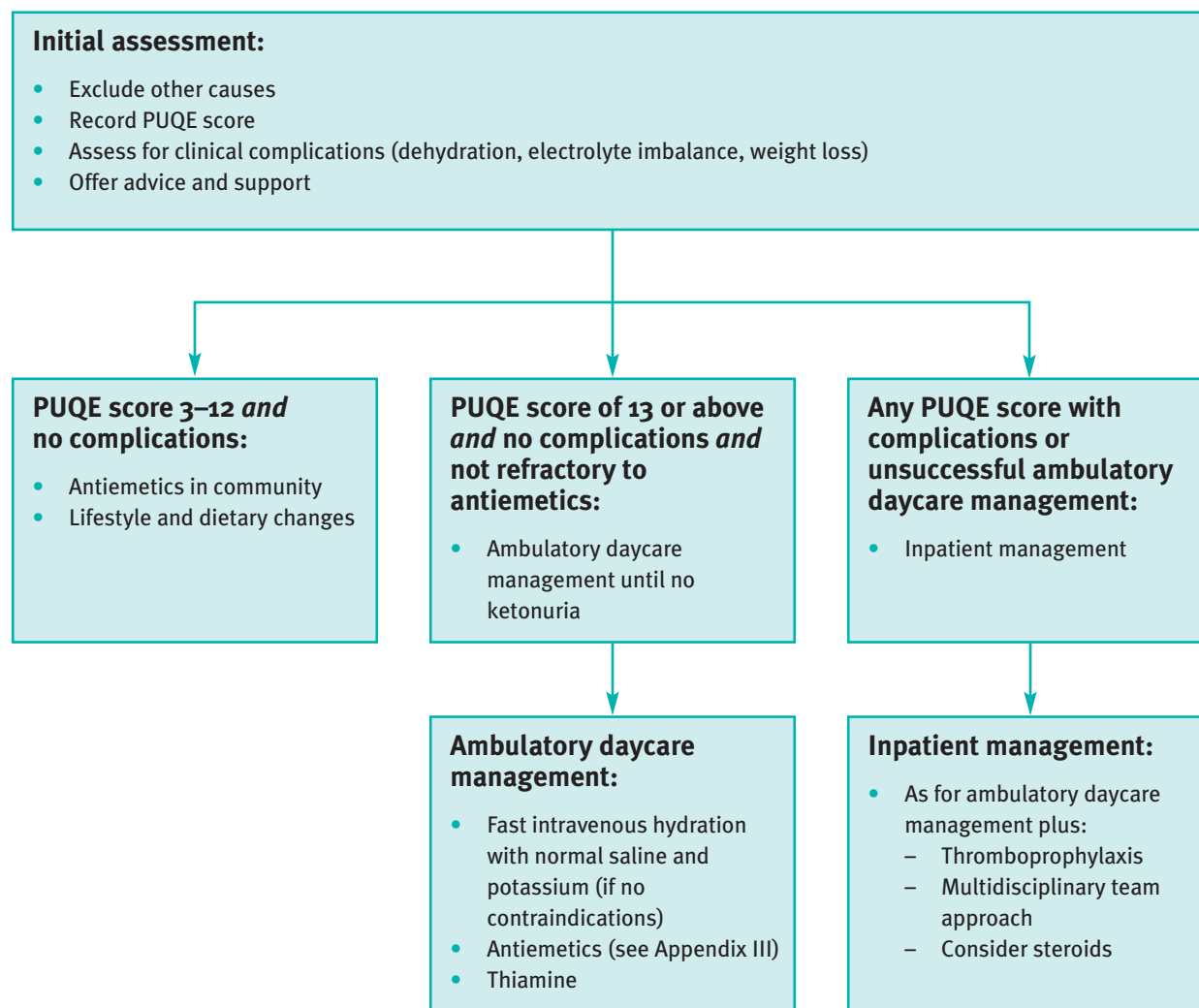


### Appendix III: Recommended antiemetic therapies and dosages

<b>First line</b>	<ul style="list-style-type: none"><li>• Cyclizine 50 mg PO, IM or IV 8 hourly</li><li>• Prochlorperazine 5–10 mg 6–8 hourly PO; 12.5 mg 8 hourly IM/IV; 25 mg PR daily</li><li>• Promethazine 12.5–25 mg 4–8 hourly PO, IM, IV or PR</li><li>• Chlorpromazine 10–25 mg 4–6 hourly PO, IV or IM; or 50–100 mg 6–8 hourly PR</li></ul>
<b>Second line</b>	<ul style="list-style-type: none"><li>• Metoclopramide 5–10 mg 8 hourly PO, IV or IM (maximum 5 days' duration)</li><li>• Domperidone 10 mg 8 hourly PO; 30–60 mg 8 hourly PR</li><li>• Ondansetron 4–8 mg 6–8 hourly PO; 8 mg over 15 minutes 12 hourly IV</li></ul>
<b>Third line</b>	<ul style="list-style-type: none"><li>• Corticosteroids: hydrocortisone 100 mg twice daily IV and once clinical improvement occurs, convert to prednisolone 40–50 mg daily PO, with the dose gradually tapered until the lowest maintenance dose that controls the symptoms is reached</li></ul>

**IM** intramuscular; **IV** intravenous; **PO** by mouth; **PR** by rectum.

## Appendix IV: Treatment algorithm for NVP and HG



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*All RCOG guidance developers are asked to declare any conflicts of interest. A statement summarising any  
conflicts of interest for this guideline is available from: [https://www.rcog.org.uk/en/guidelines-research-services/  
guidelines/gtg69/](https://www.rcog.org.uk/en/guidelines-research-services/guidelines/gtg69/).*

The final version is the responsibility of the Guidelines Committee of the RCOG.

The review process will commence in 2019, unless otherwise indicated.

#### DISCLAIMER

The Royal College of Obstetricians and Gynaecologists produces guidelines as an educational aid to good clinical practice. They present recognised methods and techniques of clinical practice, based on published evidence, for consideration by obstetricians and gynaecologists and other relevant health professionals. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor or other attendant in the light of clinical data presented by the patient and the diagnostic and treatment options available.

This means that RCOG Guidelines are unlike protocols or guidelines issued by employers, as they are not intended to be prescriptive directions defining a single course of management. Departure from the local prescriptive protocols or guidelines should be fully documented in the patient's case notes at the time the relevant decision is taken.