

Dyspepsia and gastro-oesophageal reflux disease

Investigation and management of dyspepsia,
symptoms suggestive of gastro-oesophageal
reflux disease, or both

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NICE clinical guideline 184

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Introduction

This guideline updates and replaces 'Dyspepsia' (NICE clinical guideline 17). See [About this guideline](#) for details.

Dyspepsia describes a range of symptoms arising from the upper gastrointestinal (GI) tract, but it has no universally accepted definition. The British Society of Gastroenterology (BSG) defines dyspepsia as a group of symptoms that alert doctors to consider disease of the upper GI tract, and states that dyspepsia itself is not a diagnosis. These symptoms, which typically are present for 4 weeks or more, include upper abdominal pain or discomfort, heartburn, gastric reflux, nausea or vomiting. In this guideline, gastro-oesophageal reflux disease (GORD) refers to endoscopically determined oesophagitis or endoscopy-negative reflux disease.

Some of the costs associated with treating dyspepsia are decreasing, but the overall use of treatments is increasing. As a result, the management of dyspepsia continues to have potentially significant costs to the NHS.

The use of endoscopy has increased considerably over the past decade, as awareness of its value in investigating dyspepsia and GORD has grown.

The review of 'Dyspepsia: management of dyspepsia in adults in primary care' (NICE clinical guideline 17) highlighted some concerns about the drug regimens that were recommended in the guideline for *Helicobacter pylori* (hereafter referred to as *H pylori*) eradication, because some bacterial resistance has developed. Overall, the review process concluded that some guidance in this area should be updated and expanded to cover aspects of specialist hospital care.

NICE clinical guideline 17 covered the management of several underlying causes of dyspepsia in primary care, but there is a lack of comprehensive national guidance about managing GORD (in particular, surgical management) when pharmacological treatments fail. Because of this, and the possible role of GORD (with the subsequent development of Barrett's oesophagus) as a risk factor for cancer, the scope of the guideline update was extended to cover managing GORD in secondary care.

This guideline update covers adults (18 years and older) with symptoms of dyspepsia, symptoms suggestive of GORD, or both. It also covers endoscopic surveillance for adults with a diagnosis of Barrett's oesophagus, but it does not cover the management of Barrett's oesophagus. It is

important to note that children and young people (younger than 18 years) and people with a diagnosis of oesophagogastric cancer are not covered in this guideline update.

In this guideline, specialist care is defined as treatment decisions made by a consultant-led service in secondary or tertiary care.

Drug recommendations

The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's [Good practice in prescribing and managing medicines and devices](#) for further information. Where recommendations have been made for the use of drugs outside their licensed indications ('off-label use'), these drugs are marked with a footnote in the recommendations.

Specific dosage information on proton pump inhibitors (PPIs) is detailed in [appendix A](#).

Patient-centred care

This guideline offers best practice advice on the care of adults (18 years and older) with symptoms of dyspepsia or symptoms suggestive of GORD, or both.

Patients and healthcare professionals have rights and responsibilities as set out in the [NHS Constitution for England](#) – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. Healthcare professionals should follow the [Department of Health's advice on consent](#). If someone does not have capacity to make decisions, healthcare professionals should follow the [code of practice that accompanies the Mental Capacity Act](#) and the supplementary [code of practice on deprivation of liberty safeguards](#).

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in [Patient experience in adult NHS services](#).

Key priorities for implementation

The following recommendations have been identified as priorities for implementation. The full list of recommendations is in [section 1](#).

Referral guidance for endoscopy

- For people presenting with dyspepsia together with significant acute gastrointestinal bleeding, refer them immediately (on the same day) to a specialist. **[2004]** (Also see [Acute upper gastrointestinal bleeding](#) [NICE clinical guideline 141].)

Interventions for uninvestigated dyspepsia

- Leave a 2-week washout period after proton pump inhibitor (PPI) use before testing for *Helicobacter pylori* (hereafter referred to as *H pylori*) with a breath test or a stool antigen test. **[2004, amended 2014]**

Interventions for gastro-oesophageal reflux disease (GORD)

- Offer people a full-dose PPI (see table 2 in [appendix A](#)) for 8 weeks to heal severe oesophagitis, taking into account the person's preference and clinical circumstances (for example, underlying health conditions and possible interactions with other drugs). **[new 2014]**
- Offer a full-dose PPI (see table 2 in [appendix A](#)) long-term as maintenance treatment for people with severe oesophagitis, taking into account the person's preference and clinical circumstances (for example, tolerability of the PPI, underlying health conditions and possible interactions with other drugs), and the acquisition cost of the PPI. **[new 2014]**
- Do not routinely offer endoscopy to diagnose Barrett's oesophagus, but consider it if the person has GORD. Discuss the person's preferences and their individual risk factors (for example, long duration of symptoms, increased frequency of symptoms, previous oesophagitis, previous hiatus hernia, oesophageal stricture or oesophageal ulcers, or male gender). **[new 2014]**

Interventions for peptic ulcer disease

- Offer *H pylori* eradication therapy to people who have tested positive for *H pylori* and who have peptic ulcer disease. Also see [H pylori testing and eradication](#). **[2004]**
- For people using NSAIDs with diagnosed peptic ulcer, stop the use of NSAIDs where possible. Offer full-dose PPI (see table 1 in [appendix A](#)) or H₂RA therapy for 8 weeks and, if *H pylori* is present, subsequently offer eradication therapy. **[2004]**
- Offer people with peptic ulcer (gastric or duodenal) and *H pylori* retesting for *H pylori* 6 to 8 weeks after beginning treatment, depending on the size of the lesion. **[2004, amended 2014]**

Referral to a specialist service

- Consider referral to a specialist service for people:
 - of any age with gastro-oesophageal symptoms that are non-responsive to treatment or unexplained^[1]
 - with suspected GORD who are thinking about surgery
 - with *H pylori* that has not responded to second-line eradication therapy. **[new 2014]**

Surveillance for people with Barrett's oesophagus

- Consider surveillance to check progression to cancer for people who have a diagnosis of Barrett's oesophagus (confirmed by endoscopy and histopathology), taking into account:
 - the presence of dysplasia (also see [Barrett's oesophagus – ablative therapy](#) [NICE clinical guideline 106])
 - the person's individual preference
 - the person's risk factors (for example, male gender, older age and the length of the Barrett's oesophagus segment).

Emphasise that the harms of endoscopic surveillance may outweigh the benefits in people who are at low risk of progression to cancer (for example, people with stable non-dysplastic Barrett's oesophagus). **[new 2014]**

^[1] In Referral guidelines for suspected cancer (NICE clinical guideline 27), 'unexplained' is defined as 'a symptom(s) and/or sign(s) that has not led to a diagnosis being made by the primary care professional after initial assessment of the history, examination and primary care investigations (if any)'. (Please note that an update is in progress; publication expected May 2015. For more information see <http://www.nice.org.uk/Guidance/InDevelopment/GID-CGWAVE0618>.)

1 Recommendations

The following guidance is based on the best available evidence. The [full guideline](#) gives details of the methods and the evidence used to develop the guidance.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation). See [About this guideline](#) for details.

These recommendations apply to adults (aged 18 and over) with symptoms of dyspepsia, symptoms suggestive of gastro-oesophageal reflux disease (GORD), or both.

Terms used in this guideline

In this guideline, GORD refers to endoscopically determined oesophagitis or endoscopy-negative reflux disease.

1.1 The community pharmacist

- 1.1.1 Community pharmacists should offer initial and ongoing help for people with symptoms of dyspepsia. This includes advice about lifestyle changes, using over-the-counter medication, help with prescribed drugs and advice about when to consult a GP. **[2004]**
- 1.1.2 Community pharmacists should record adverse reactions to treatment and may participate in primary care medication review clinics. **[2004]**

1.2 Common elements of care

- 1.2.1 Offer simple lifestyle advice, including advice on healthy eating, weight reduction and smoking cessation. **[2004]**
- 1.2.2 Advise people to avoid known precipitants they associate with their dyspepsia where possible. These include smoking, alcohol, coffee, chocolate, fatty foods

and being overweight. Raising the head of the bed and having a main meal well before going to bed may help some people. **[2004]**

- 1.2.3 Provide people with access to educational materials to support the care they receive. **[2004]**
- 1.2.4 Recognise that psychological therapies, such as cognitive behavioural therapy and psychotherapy, may reduce dyspeptic symptoms in the short term in individual people. **[2004, amended 2014]**
- 1.2.5 Encourage people who need long-term management of dyspepsia symptoms to reduce their use of prescribed medication stepwise: by using the effective lowest dose, by trying 'as-needed' use when appropriate, and by returning to self-treatment with antacid and/or alginate therapy (unless there is an underlying condition or comedication that needs continuing treatment). **[2004, amended 2014]**

1.3 Referral guidance for endoscopy

- 1.3.1 For people presenting with dyspepsia together with significant acute gastrointestinal bleeding, refer them immediately (on the same day) to a specialist. **[2004]** (Also see [Acute upper gastrointestinal bleeding](#) [NICE clinical guideline 141].)
- 1.3.2 Review medications for possible causes of dyspepsia (for example, calcium antagonists, nitrates, theophyllines, bisphosphonates, corticosteroids and non-steroidal anti-inflammatory drugs [NSAIDs]). In people needing referral, suspend NSAID use. **[2004]**
- 1.3.3 Think about the possibility of cardiac or biliary disease as part of the differential diagnosis. **[2004, amended 2014]**
- 1.3.4 If people have had a previous endoscopy and do not have any new alarm signs^[2], consider continuing management according to previous endoscopic findings. **[2004]**

For more information about when to refer people to specialists when they present with symptoms that could be caused by cancer, see [Referral for suspected cancer](#) (NICE clinical guideline 27 [update in progress; publication expected May 2015: <http://www.nice.org.uk/Guidance/InDevelopment/GID-CGWAVE0618>]).

1.4 Interventions for uninvestigated dyspepsia

- 1.4.1 Be aware that dyspepsia in unselected people in primary care is defined broadly to include people with recurrent epigastric pain, heartburn or acid regurgitation, with or without bloating, nausea or vomiting. Also see [Common elements of care](#). **[2004, amended 2014]**
- 1.4.2 Leave a 2-week washout period after proton pump inhibitor (PPI) use before testing for *Helicobacter pylori* (hereafter referred to as *H pylori*) with a breath test or a stool antigen test. **[2004, amended 2014]**
- 1.4.3 Offer empirical full-dose PPI therapy (see table 1 in [appendix A](#)) for 4 weeks to people with dyspepsia. **[2004]**
- 1.4.4 Offer *H pylori* 'test and treat' to people with dyspepsia. **[2004]**
- 1.4.5 If symptoms return after initial care strategies, step down PPI therapy to the lowest dose needed to control symptoms. Discuss using the treatment on an 'as-needed' basis with people to manage their own symptoms. **[2004]**
- 1.4.6 Offer H₂ receptor antagonist (H₂RA) therapy if there is an inadequate response to a PPI. **[2004, amended 2014]**

1.5 Reviewing patient care

- 1.5.1 Offer people who need long-term management of dyspepsia symptoms an annual review of their condition, and encourage them to try stepping down or stopping treatment (unless there is an underlying condition or comedication that needs continuing treatment). **[2004, amended 2014]**

- 1.5.2 Advise people that it may be appropriate for them to return to self-treatment with antacid and/or alginate therapy (either prescribed or purchased over-the-counter and taken as needed). **[2004, amended 2014]**

1.6 Interventions for gastro-oesophageal reflux disease (GORD)

- 1.6.1 Manage uninvestigated 'reflux-like' symptoms as uninvestigated dyspepsia. **[2004, amended 2014]**
- 1.6.2 Offer people with GORD a full-dose PPI (see table 1 in [appendix A](#)) for 4 or 8 weeks. **[2004]**
- 1.6.3 If symptoms recur after initial treatment, offer a PPI at the lowest dose possible to control symptoms. **[2004, amended 2014]**
- 1.6.4 Discuss with people how they can manage their own symptoms by using the treatment when they need it. **[2004]**
- 1.6.5 Offer H₂RA therapy if there is an inadequate response to a PPI. **[2004, amended 2014]**
- 1.6.6 People who have had dilatation of an oesophageal stricture should remain on long-term full-dose PPI therapy (see table 1 in [appendix A](#)). **[2004]**
- 1.6.7 Offer people a full-dose PPI (see table 2 in [appendix A](#)) for 8 weeks to heal severe oesophagitis, taking into account the person's preference and clinical circumstances (for example, underlying health conditions and possible interactions with other drugs). **[new 2014]**
- 1.6.8 If initial treatment for healing severe oesophagitis fails, consider a high dose of the initial PPI, switching to another full-dose PPI (see table 2) or switching to another high-dose PPI (see table 2 in [appendix A](#)), taking into account the person's preference and clinical circumstances (for example, tolerability of the initial PPI, underlying health conditions and possible interactions with other drugs). **[new 2014]**

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- 1.6.9 Offer a full-dose PPI (see table 2 in [appendix A](#)) long-term as maintenance treatment for people with severe oesophagitis, taking into account the person's preference and clinical circumstances (for example, tolerability of the PPI, underlying health conditions and possible interactions with other drugs), and the acquisition cost of the PPI. **[new 2014]**
- 1.6.10 If the person's severe oesophagitis fails to respond to maintenance treatment, carry out a clinical review. Consider switching to another PPI at full dose or high dose (see table 2 in [appendix A](#)), taking into account the person's preference and clinical circumstances, and/or seeking specialist advice. **[new 2014]**
- 1.6.11 Do not routinely offer endoscopy to diagnose Barrett's oesophagus, but consider it if the person has GORD. Discuss the person's preferences and their individual risk factors (for example, long duration of symptoms, increased frequency of symptoms, previous oesophagitis, previous hiatus hernia, oesophageal stricture or oesophageal ulcers, or male gender). **[new 2014]**

1.7 Interventions for peptic ulcer disease

- 1.7.1 Offer *H pylori* eradication therapy to people who have tested positive for *H pylori* and who have peptic ulcer disease. Also see [H pylori testing and eradication](#). **[2004]**
- 1.7.2 For people using NSAIDs with diagnosed peptic ulcer, stop the use of NSAIDs where possible. Offer full-dose PPI (see table 1 in [appendix A](#)) or H₂RA therapy for 8 weeks and, if *H pylori* is present, subsequently offer eradication therapy. **[2004]**
- 1.7.3 Offer people with gastric ulcer and *H pylori* repeat endoscopy 6 to 8 weeks after beginning treatment, depending on the size of the lesion. **[2004, amended 2014]**
- 1.7.4 Offer people with peptic ulcer (gastric or duodenal) and *H pylori* retesting for *H pylori* 6 to 8 weeks after beginning treatment, depending on the size of the lesion. **[2004, amended 2014]**

- 1.7.5 Offer full-dose PPI (see table 1 in [appendix A](#)) or H₂RA therapy for 4 to 8 weeks to people who have tested negative for *H pylori* who are not taking NSAIDs. **[2004]**
- 1.7.6 For people continuing to take NSAIDs after a peptic ulcer has healed, discuss the potential harm from NSAID treatment. Review the need for NSAID use regularly (at least every 6 months) and offer a trial of use on a limited, 'as-needed' basis. Consider reducing the dose, substituting an NSAID with paracetamol, or using an alternative analgesic or low-dose ibuprofen (1.2 g daily). **[2004]**
- 1.7.7 In people at high risk (previous ulceration) and for whom NSAID continuation is necessary, offer gastric protection or consider substitution with a cyclooxygenase (COX)-2-selective NSAID. **[2004]**
- 1.7.8 In people with an unhealed ulcer, exclude non-adherence, malignancy, failure to detect *H pylori*, inadvertent NSAID use, other ulcer-inducing medication and rare causes such as Zollinger–Ellison syndrome or Crohn's disease. **[2004]**
- 1.7.9 If symptoms recur after initial treatment, offer a PPI to be taken at the lowest dose possible to control symptoms. Discuss using the treatment on an 'as-needed' basis with people to manage their own symptoms. **[2004, amended 2014]**
- 1.7.10 Offer H₂RA therapy if there is an inadequate response to a PPI. **[2004]**

1.8 Interventions for functional dyspepsia

- 1.8.1 Manage endoscopically determined functional dyspepsia using initial treatment for *H pylori* if present, followed by symptomatic management and periodic monitoring. **[2004]**
- 1.8.2 Offer eradication therapy to people testing positive for *H pylori*. **[2004]**
- 1.8.3 Do not routinely offer re-testing after eradication, although the information it provides may be valued by individual people. **[2004]**

- 1.8.4 If *H pylori* has been excluded and symptoms persist, offer either a low-dose PPI (see table 1 in [appendix A](#)) or an H₂RA for 4 weeks. **[2004, amended 2014]**
- 1.8.5 If symptoms continue or recur after initial treatment, offer a PPI or H₂RA to be taken at the lowest dose possible to control symptoms. **[2004, amended 2014]**
- 1.8.6 Discuss using PPI treatment on an 'as-needed' basis with people to manage their own symptoms. **[2004]**
- 1.8.7 Avoid long-term, frequent dose, continuous antacid therapy (it only relieves symptoms in the short term rather than preventing them). **[2004, amended 2014]**

1.9 *Helicobacter pylori* testing and eradication

Testing

- 1.9.1 Test for *H pylori* using a carbon-13 urea breath test or a stool antigen test, or laboratory-based serology where its performance has been locally validated. **[2004, amended 2014]**
- 1.9.2 Perform re-testing for *H pylori* using a carbon-13 urea breath test. (There is currently insufficient evidence to recommend the stool antigen test as a test of eradication^[3].) **[2004]**
- 1.9.3 Do not use office-based serological tests for *H pylori* because of their inadequate performance. **[2004, amended 2014]**

Eradication

First-line treatment

- 1.9.4 Offer people who test positive for *H pylori* a 7-day, twice-daily course of treatment with:
- a PPI (see table 3 in [appendix A](#)) and

- amoxicillin **and**
- either clarithromycin or metronidazole.

Choose the treatment regimen with the lowest acquisition cost, and take into account previous exposure to clarithromycin or metronidazole. **[new 2014]**

1.9.5 Offer people who are allergic to penicillin^[4] a 7-day, twice-daily course of treatment with:

- a PPI (see table 3 in [appendix A](#)) **and**
- clarithromycin **and**
- metronidazole. **[new 2014]**

1.9.6 Offer people who are allergic to penicillin^[4] and who have had previous exposure to clarithromycin a 7-day, twice-daily course of treatment with:

- a PPI (see table 3 in [appendix A](#)) **and**
- bismuth **and**
- metronidazole **and**
- tetracycline. **[new 2014]**

1.9.7 Discuss treatment adherence with the person and emphasise its importance. For more information about supporting adherence, see [Medicines adherence](#) (NICE clinical guideline 76). **[new 2014]**

Second-line treatment

1.9.8 Offer people who still have symptoms after first-line eradication treatment a 7-day, twice-daily course of treatment with:

- a PPI (see table 3 in [appendix A](#)) **and**
- amoxicillin **and**

- either clarithromycin or metronidazole (whichever was not used first-line). **[new 2014]**

1.9.9 Offer people who have had previous exposure to clarithromycin and metronidazole a 7-day, twice-daily course of treatment with:

- a PPI (see table 3 in [appendix A](#)) **and**
- amoxicillin **and**
- a quinolone or tetracycline (whichever has the lowest acquisition cost). **[new 2014]**

1.9.10 Offer people who are allergic to penicillin^[5] (and who have not had previous exposure to a quinolone) a 7-day, twice-daily course of treatment with:

- a PPI (see table 3 in [appendix A](#)) **and**
- metronidazole **and**
- levofloxacin. **[new 2014]**

1.9.11 Offer people who are allergic to penicillin^[5] and who have had previous exposure to a quinolone:

- a PPI (see table 3 in [appendix A](#)) **and**
- bismuth **and**
- metronidazole **and**
- tetracycline. **[new 2014]**

1.9.12 Seek advice from a gastroenterologist if eradication of *H pylori* is not successful with second-line treatment. **[new 2014]**

1.10 Laparoscopic fundoplication

1.10.1 Consider laparoscopic fundoplication for people who have:

- a confirmed diagnosis of acid reflux and adequate symptom control with acid suppression therapy, but who do not wish to continue with this therapy long term
- a confirmed diagnosis of acid reflux and symptoms that are responding to a PPI, but who cannot tolerate acid suppression therapy. **[new 2014]**

1.11 Referral to a specialist service

1.11.1 Consider referral to a specialist service for people:

- of any age with gastro-oesophageal symptoms that are non-responsive to treatment or unexplained^[6]
- with suspected GORD who are thinking about surgery
- with *H pylori* that has not responded to second-line eradication therapy. **[new 2014]**

1.12 Surveillance for people with Barrett's oesophagus

1.12.1 Consider surveillance to check progression to cancer for people who have a diagnosis of Barrett's oesophagus (confirmed by endoscopy and histopathology), taking into account:

- the presence of dysplasia (also see [Barrett's oesophagus – ablative therapy](#) [NICE clinical guideline 106])
- the person's individual preference
- the person's risk factors (for example, male gender, older age and the length of the Barrett's oesophagus segment).

Emphasise that the harms of endoscopic surveillance may outweigh the benefits in people who are at low risk of progression to cancer (for example, people with stable non-dysplastic Barrett's oesophagus). **[new 2014]**

^[6] For more information about alarm signs please see [Referral for suspected cancer](#) (NICE clinical guideline 27 [update in progress; publication expected May 2015. For more information see <http://www.nice.org.uk/Guidance/InDevelopment/GID-CGWAVE0618>]).

^[3] This refers to evidence reviewed in 2004.

^[4] For the assessment of allergy to beta-lactam antibiotics and referral to specialist care, please see [Drug allergy](#) (NICE clinical guideline 183).

^[5] For the assessment of allergy to beta-lactam antibiotics and referral to specialist care, please see [Drug allergy](#) (NICE clinical guideline 183).

^[6] In [Referral guidelines for suspected cancer](#) (NICE clinical guideline 27), 'unexplained' is defined as 'a symptom(s) and/or sign(s) that has not led to a diagnosis being made by the primary care professional after initial assessment of the history, examination and primary care investigations (if any)'. (Please note that an update is in progress; publication expected May 2015. For more information see <http://www.nice.org.uk/Guidance/InDevelopment/GID-CGWAVE0618>.)

2 Research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

2.1 Patient characteristics, risk factors and predictors that indicate endoscopy for excluding Barrett's oesophagus

In people who experience symptoms of gastro-oesophageal reflux disease (GORD) or symptoms suggestive of GORD, what patient characteristics, risk factors and predictors indicate when endoscopy is needed to exclude Barrett's oesophagus?

Why this is important

The aim is to identify adults with symptoms of GORD or symptoms suggestive of GORD who may benefit from having an endoscopy for the purpose of early identification of Barrett's oesophagus (or to exclude Barrett's oesophagus).

2.2 Laparoscopic fundoplication compared with medical management

What is the effectiveness of laparoscopic fundoplication compared with medical management in people with GORD that does not respond to optimal proton pump inhibitor (PPI) treatment?

Why this is important

Current evidence on the clinical and cost effectiveness of laparoscopic fundoplication compared with medical management involves people who had relatively good treatment control with PPIs at baseline. The driver was the desire to be free from medication rather than their GORD being non-responsive to PPIs.

2.3 Effective proton pump inhibitor dosage for severe erosive reflux disease

What is the clinical effectiveness of double-dose PPIs in people with severe erosive reflux disease (Los Angeles classification grade C/D or Savary–Miller grade 3/4):

- to reduce severe oesophagitis
- to control symptoms
- as maintenance therapy?

Why this is important

People with severe erosive reflux disease or severe oesophagitis (Los Angeles classification grade C/D or Savary–Miller grade 3/4) experience severe heartburn, and prolonged acid and pepsin exposure in the lower oesophagus, which can affect their day-to-day wellbeing. It would substantially improve people's quality of life if an optimal treatment regimen could be identified. Currently, there is a lack of evidence on the efficacy of 'double-dose' PPIs in treating severe erosive reflux disease.

2.4 Other specialist management

What specialist management is effective for people whose symptoms do not respond to PPIs despite optimum primary care, or for people whose symptoms return after surgery?

Why this is important

There is a small group of people whose symptoms do not resolve, despite medical management and/or surgery for reflux. The group should be divided into people with proven (by pH monitoring) GORD and people with symptoms but no diagnosed reflux. The first group should have a trial of a twice-daily, high-dose PPI versus a standard or full-dose PPI. The second group should have a trial of tricyclic antidepressants versus standard or full-dose PPI. The purpose of any treatment should focus on improving quality of life.

2.5 Specialist investigation

What specialist investigations should be conducted to exclude a diagnosis of functional dyspepsia in people with uninvestigated dyspepsia that does not respond to PPIs or H₂ receptor antagonists (H₂RAs) despite optimum primary care?

Why this is important

People with uninvestigated dyspepsia that fails to respond to PPIs or H₂RAs, despite optimum primary care, can have a poor quality of life. It is important to ensure that appropriate investigations are carried out to make the correct diagnosis or to correct misdiagnosis, so that the most appropriate treatment can be offered.

3 Other information

3.1 Scope and how this guideline was developed

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

How this guideline was developed

NICE commissioned the Internal Clinical Guidelines Programme to develop this guideline. The Centre established a Guideline Development Group (see [section 4](#)), which reviewed the evidence and developed the recommendations.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

3.2 Related NICE guidance

Further information is available on the [NICE website](#).

Published

General

- [Patient experience in adult NHS services](#). NICE clinical guidance 138 (2012).
- [Medicines adherence](#). NICE clinical guidance 76 (2009).

Condition-specific

- [Drug allergy](#). NICE clinical guideline 183 (2014).
- [Endoscopic radiofrequency ablation for gastro-oesophageal reflux disease](#). NICE interventional procedure guidance 461 (2013).
- [Laparoscopic insertion of a magnetic bead band for gastro-oesophageal reflux disease](#). NICE interventional procedure guidance 431 (2012).
- [Acute upper gastrointestinal bleeding](#). NICE clinical guideline 141 (2012).

- [Minimally invasive oesophagectomy](#). NICE interventional procedure guidance 407 (2011).
- [Endoluminal gastroplication for gastro-oesophageal reflux disease](#). NICE interventional procedure guidance 404 (2011).
- [Barrett's oesophagus – ablative therapy](#). NICE clinical guideline 106 (2010).
- [Chest pain of recent onset](#). NICE clinical guideline 95 (2010).
- [Endoscopic submucosal dissection of gastric lesions](#). NICE interventional procedure guidance 360 (2010).
- [Endoscopic mucosal resection and endoscopic submucosal dissection of non-ampullary duodenal lesions](#). NICE interventional procedure guidance 359 (2010).
- [Endoscopic submucosal dissection \(ESD\) of oesophageal dysplasia and neoplasia](#). NICE interventional procedure guidance 355 (2010).
- [Photodynamic therapy for Barrett's oesophagus](#). NICE interventional procedure guidance 350 (2010).
- [Epithelial radiofrequency ablation for Barrett's oesophagus](#). NICE interventional procedure guidance 344 (2010).
- [Photodynamic therapy for early oesophageal cancer](#). NICE interventional procedure guidance 200 (2006).
- [Catheterless oesophageal pH monitoring](#). NICE interventional procedure guidance 187 (2006).
- [Endoscopic injection of bulking agents for gastro-oesophageal reflux disease](#). NICE interventional procedure guidance 55 (2004).

Under development

NICE is developing the following guidance (details available from [the NICE website](#)):

- [GORD in children](#). NICE clinical guideline. Publication expected January 2015.
- [Suspected cancer](#) (update of CG27). NICE clinical guideline. Publication expected May 2015.

4 The Guideline Development Group, NICE Internal Clinical Guidelines Programme and NICE project team

4.1 Guideline Development Group

The Guideline Development Group members listed are those for the 2014 update. For the composition of (the) previous Guideline Development Group(s), see the [full guideline](#).

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Appendix A: Dosage information on proton pump inhibitors

In 2004, when the original guideline was developed (CG17), doses of proton pump inhibitors (PPIs) were based on the British National Formulary (BNF) at the time, as in table 1 below.

During the update of this guideline (2014), the Guideline Development Group (GDG) has further defined the PPI doses specifically for severe oesophagitis and *H pylori* eradication therapy, as in tables 2 and 3 below.

Table 1 PPI doses relating to evidence synthesis and recommendations in the original guideline (CG17; 2004)

PPI	Full/standard dose	Low dose (on-demand dose)	Double dose
Esomeprazole	20 mg ¹ once a day	Not available	40 mg ³ once a day
Lansoprazole	30 mg once a day	15 mg once a day	30 mg ² twice a day
Omeprazole	20 mg once a day	10 mg ² once a day	40 mg once a day
Pantoprazole	40 mg once a day	20 mg once a day	40 mg ² twice a day
Rabeprazole	20 mg once a day	10 mg once a day	20 mg ² twice a day

¹ Lower than the licensed starting dose for esomeprazole in GORD, which is 40 mg, but considered to be dose-equivalent to other PPIs. When undertaking meta-analysis of dose-related effects, NICE classed esomeprazole 20 mg as a full-dose equivalent to omeprazole 20 mg.

² Off-label dose for GORD.

³ 40 mg is recommended as a double dose of esomeprazole because the 20-mg dose is considered equivalent to omeprazole 20 mg.

Table 2 PPI doses for severe oesophagitis in this guideline update (2014)

PPI	Full/standard dose	Low dose (on-demand dose)	High/double dose
Esomeprazole	40 mg ¹ once a day	20 mg ¹ once a day	40 mg ¹ twice a day
Lansoprazole	30 mg once a day	15 mg once a day	30 mg ² twice a day

Omeprazole	40 mg ¹ once a day)	20 mg ¹ once a day)	40 mg ¹ twice a day
Pantoprazole	40 mg once a day	20 mg once a day	40 mg ² twice a day
Rabeprazole	20 mg once a day	10 mg once a day	20 mg ² twice a day
<p>¹ Change from the 2004 dose, specifically for severe oesophagitis, agreed by the GDG during the update of CG17.</p> <p>² Off-label dose for GORD.</p>			

Table 3 PPI doses for *H pylori* eradication therapy in this guideline update (2014)

PPI	Dose
Esomeprazole	20 mg
Lansoprazole	30 mg
Omeprazole	20–40 mg
Pantoprazole	40 mg
Rabeprazole	20 mg

About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions.

NICE guidelines are developed in accordance with a [scope](#) that defines what the guideline will and will not cover.

This guideline was developed by the NICE Internal Clinical Guidelines Programme. The Internal Clinical Guidelines Programme worked with a Guideline Development Group, comprising healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, which reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in [The guidelines manual](#).

NICE produces guidance, standards and information on commissioning and providing high-quality healthcare, social care, and public health services. We have agreements to provide certain NICE services to Wales, Scotland and Northern Ireland. Decisions on how NICE guidance and other products apply in those countries are made by ministers in the Welsh government, Scottish government, and Northern Ireland Executive. NICE guidance or other products may include references to organisations or people responsible for commissioning or providing care that may be relevant only to England.

Update information

This guideline updates and replaces NICE clinical guideline 17 (published in April 2004).

Recommendations are marked as **[new 2014]**, **[2014]**, **[2004]** or **[2004, amended 2014]**:

- **[new 2014]** indicates that the evidence has been reviewed and the recommendation has been added or updated
- **[2014]** indicates that the evidence has been reviewed but no change has been made to the recommended action
- **[2004]** indicates that the evidence has not been reviewed since 2004
- **[2004, amended 2014]** indicates that the evidence has not been reviewed since 2004, but changes have been made to the recommendation wording that change the meaning.

Recommendations from NICE clinical guideline 17 that have been amended

Recommendations are labelled **[2004, amended 2014]** if the evidence has not been reviewed since 2014 but changes have been made to the recommendation wording that change the meaning.

Recommendation in 2004 guideline	Recommendation in 2014 guideline	Reason for change
1.2.3 Consider the possibility of cardiac or biliary disease as part of the differential diagnosis.	1.3.3 Think about the possibility of cardiac or biliary disease as part of the differential diagnosis. [2004, amended 2014]	Changed to make recommendation active.

<p>1.3.6 Psychological therapies, such as cognitive behavioural therapy and psychotherapy, may reduce dyspeptic symptoms in the short term in individual patients. Given the intensive and relatively costly nature of such interventions, routine provision by primary care teams is not currently recommended.</p>	<p>1.2.4 Recognise that psychological therapies, such as cognitive behavioural therapy and psychotherapy, may reduce dyspeptic symptoms in the short term in individual people. [2004, amended 2014]</p>	<p>Changed to make recommendation active and to bring in line with The guidelines manual 2012 and editorial guidance.</p>
<p>1.3.7 Patients requiring long-term management of dyspepsia symptoms should be encouraged to reduce their use of prescribed medication stepwise: by using the effective lowest dose, by trying as-required use when appropriate, and by returning to self-treatment with antacid and/or alginate therapy.</p>	<p>1.2.5 Encourage people who need long-term management of dyspepsia symptoms to reduce their use of prescribed medication stepwise: by using the effective lowest dose, by trying 'as-needed' use when appropriate, and by returning to self-treatment with antacid and/or alginate therapy (unless there is an underlying condition or comedication that needs continuing treatment). [2004, amended 2014]</p>	<p>Changed to make this recommendation active and for clarity as this recommendation now only applies to people without an underlying condition or comedication that needs continuing treatment.</p>

<p>1.4.1 Dyspepsia in unselected patients in primary care is defined broadly to include patients with recurrent epigastric pain, heartburn, or acid regurgitation, with or without bloating, nausea or vomiting.</p> <p>Review common elements of care for managing dyspepsia (section 1.3).</p>	<p>1.4.1 Be aware that dyspepsia in unselected people in primary care is defined broadly to include people with recurrent epigastric pain, heartburn or acid regurgitation, with or without bloating, nausea or vomiting. Also see 'Common elements of care'. [2004, amended 2014]</p>	<p>Changed to make recommendation active and for clarity.</p>
<p>1.4.2 Initial therapeutic strategies for dyspepsia are empirical treatment with a PPI or testing for and treating <i>H pylori</i>. There is currently insufficient evidence to guide which should be offered first. A 2-week washout period following PPI use is necessary before testing for <i>H pylori</i> with a breath test or a stool antigen test.</p>	<p>1.4.2 Leave a 2-week washout period after proton pump inhibitor (PPI) use before testing for <i>Helicobacter pylori</i> (hereafter referred to as <i>H pylori</i>) with a breath test or a stool antigen test. [2004, amended 2014]</p>	<p>Changed to make recommendation active and for clarity.</p>

<p>1.4.6 Offer H₂RA or prokinetic therapy if there is an inadequate response to a PPI.</p>	<p>1.4.6 Offer H₂ receptor antagonist (H₂RA) therapy if there is an inadequate response to a PPI. [2004, amended 2014]</p>	<p>Reference to prokinetic therapy has been removed as the original guideline only reviewed the evidence for cisapride, not domperidone or metoclopramine. Cisapride has been suspended in the UK since the publication of CG17.</p>
<p>1.5.1 Offer people requiring long-term management of symptoms for dyspepsia an annual review of their condition, encouraging them to try stepping down or stopping treatment.</p>	<p>1.5.1 Offer people who need long-term management of dyspepsia symptoms an annual review of their condition, and encourage them to try stepping down or stopping treatment (unless there is an underlying condition or comedication that needs continuing treatment). [2004, amended 2014]</p>	<p>Changed for clarity.</p>
<p>1.5.2 A return to self-treatment with antacid and/or alginate therapy (either prescribed or purchased over-the-counter and taken as-required) may be appropriate.</p>	<p>1.5.2 Advise people that it may be appropriate for them to return to self-treatment with antacid and/or alginate therapy (either prescribed or purchased over-the-counter and taken as needed). [2004, amended 2014]</p>	<p>Changed to make recommendation active.</p>

<p>1.6.1 Gastro-oesophageal reflux disease (GORD) refers to endoscopically determined oesophagitis or endoscopy-negative reflux disease. Patients with uninvestigated 'reflux-like' symptoms should be managed as patients with uninvestigated dyspepsia.</p>	<p>1.6.1 Manage uninvestigated 'reflux-like' symptoms as uninvestigated dyspepsia. [2004, amended 2014]</p>	<p>Changed to make recommendation active.</p>
<p>1.6.3 If symptoms recur following initial treatment, offer a PPI at the lowest dose possible to control symptoms, with a limited number of repeat prescriptions.</p>	<p>1.6.3 If symptoms recur after initial treatment, offer a PPI at the lowest dose possible to control symptoms. [2004, amended 2014]</p>	<p>Removed 'with a limited number of repeat prescriptions' as the GDG felt this was included due to the costs of PPI at the time of original publication. Costs have since fallen and therefore limiting repeat prescriptions due to costs is not a factor in current practice.</p>
<p>1.6.5 Offer H₂RA or prokinetic therapy if there is an inadequate response to a PPI.</p>	<p>1.6.5 Offer H₂RA therapy if there is an inadequate response to a PPI. [2004, amended 2014]</p>	<p>Reference to prokinetic therapy has been removed as the original guideline only reviewed the evidence for cisapride, not domperidone or metoclopramine. Cisapride has been suspended in the UK since the publication of CG17.</p>

<p>1.7.3 Patients with gastric ulcer and <i>H pylori</i> should receive repeat endoscopy, retesting for <i>H pylori</i> 6–8 weeks after beginning treatment, depending on the size of the lesion.</p>	<p>1.7.3 Offer people with gastric ulcer and <i>H pylori</i> repeat endoscopy 6 to 8 weeks after beginning treatment, depending on the size of lesion. [2004, amended 2014]</p>	<p>The GDG felt the original recommendation needed to be split to reflect the different actions taken in each flowchart within the Full guideline. People with gastric ulcers needed an endoscopy and retesting, however just retesting for <i>H pylori</i> was necessary for people with duodenal ulcers.</p>
<p>1.7.3 Patients with gastric ulcer and <i>H pylori</i> should receive repeat endoscopy, retesting for <i>H pylori</i> 6–8 weeks after beginning treatment, depending on the size of the lesion.</p>	<p>1.7.4 Offer people with peptic ulcer (gastric or duodenal) and <i>H pylori</i> retesting for <i>H pylori</i> 6 to 8 weeks after beginning treatment, depending on the size of lesion. [2004, amended 2014]</p>	<p>The GDG felt the original recommendation needed to be split to reflect the different actions taken in each flowchart within the Full guideline. People with gastric ulcers needed an endoscopy and retesting, however just retesting for <i>H pylori</i> was necessary for people with duodenal ulcers.</p> <p>The GDG felt peptic ulcer was the more appropriate term to use and included gastric and duodenal for further clarification.</p>

<p>1.7.8 If symptoms recur following initial treatment, offer a PPI to be taken at the lowest dose possible to control symptoms, with a limited number of repeat prescriptions. Discuss using the treatment on an as-required basis with patients to manage their own symptoms.</p>	<p>1.7.9 If symptoms recur after initial treatment, offer a PPI to be taken at the lowest dose possible to control symptoms. Discuss using the treatment on an 'as-needed' basis with people to manage their own symptoms. [2004, amended 2014]</p>	<p>Removed 'with a limited number of repeat prescriptions' as the GDG felt this was included due to the costs of PPI at the time of original publication. Costs have since fallen and therefore limiting repeat prescriptions due to costs is not a factor in current practice.</p>
<p>1.8.4 If <i>H pylori</i> has been excluded or treated and symptoms persist, offer either a low-dose PPI or an H₂RA for 1 month.</p>	<p>1.8.4 If <i>H pylori</i> has been excluded and symptoms persist, offer either a low-dose PPI (see table 1 in appendix A) or an H₂RA for 4 weeks. [2004, amended 2014]</p>	<p>Treatment has been removed from this recommendation and this is now covered by recommendations on <i>H pylori</i> eradication.</p>
<p>1.8.5 If symptoms continue or recur following initial treatment offer a PPI or H₂RA to be taken at the lowest dose possible to control symptoms, with a limited number of repeat prescriptions.</p>	<p>1.8.5 If symptoms continue or recur after initial treatment offer a PPI or H₂RA to be taken at the lowest dose possible to control symptoms. [2004, amended 2014]</p>	<p>Removed 'with a limited number of repeat prescriptions' as the GDG felt this was included due to the costs of PPI at the time of original publication. Costs have since fallen and therefore limiting repeat prescriptions due to costs is not a factor in current practice.</p>

1.8.7 Long-term, frequent dose, continuous prescription of antacid therapy is inappropriate and only relieves symptoms in the short term rather than preventing them.	1.8.7 Avoid long-term, frequent dose, continuous antacid therapy (it only relieves symptoms in the short term rather than preventing them). [2004, amended 2014]	Changed to make recommendation active and for clarity
1.9.1 <i>H pylori</i> can be initially detected using a carbon-13 urea breath test or a stool antigen test, or laboratory-based serology where its performance has been locally validated.	1.9.1 Test for <i>H pylori</i> using a carbon-13 urea breath test or a stool antigen test, or laboratory-based serology where its performance has been locally validated. [2004, amended 2014]	Changed to make recommendation active.
1.9.3 Office-based serological tests for <i>H pylori</i> cannot be recommended because of their inadequate performance.	1.9.3 Do not use office-based serological tests for <i>H pylori</i> because of their inadequate performance. [2004, amended 2014]	Changed to make recommendation active.

Strength of recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also [Patient-centred care](#)).

Interventions that must (or must not) be used

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions that should (or should not) be used – a 'strong' recommendation

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer...') when we are confident that an intervention will not be of benefit for most patients.

Interventions that could be used

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Recommendation wording in guideline updates

NICE began using this approach to denote the strength of recommendations in guidelines that started development after publication of the 2009 version of [The guidelines manual](#) (January 2009). This does not apply to any recommendations ending **[2004]** (see [Update information](#) above for details about how recommendations are labelled). In particular, for recommendations labelled **[2004]** the word 'consider' may not necessarily be used to denote the strength of the recommendation.

Other versions of this guideline

The full guideline, [Dyspepsia and gastro-oesophageal reflux disease](#), contains details of the methods and evidence used to develop the guideline. It is published by the Internal Clinical Guidelines Programme.

The recommendations from this guideline have been incorporated into a [NICE Pathway](#).

We have produced [information for the public](#) about this guideline.

Implementation

[Implementation tools and resources](#) to help you put the guideline into practice are also available.

Your responsibility

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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