

Gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management

Clinical guideline

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Your responsibility

The recommendations in this guideline represent the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, professionals and practitioners are expected to take this guideline fully into account, alongside the individual needs, preferences and values of their patients or the people using their service. It is not mandatory to apply the recommendations, and the guideline does not override the responsibility to make decisions appropriate to the circumstances of the individual, in consultation with them and their families and carers or guardian.

Local commissioners and providers of healthcare have a responsibility to enable the guideline to be applied when individual professionals and people using services wish to use it. They should do so in the context of local and national priorities for funding and developing services, and in light of their duties to have due regard to the need to eliminate unlawful discrimination, to advance equality of opportunity and to reduce health inequalities. Nothing in this guideline should be interpreted in a way that would be inconsistent with complying with those duties.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

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This guideline replaces CG17.

This guideline is the basis of QS96.

Overview

This guideline covers investigating and managing gastro-oesophageal reflux disease (GORD) and dyspepsia in people aged 18 and over. It aims to improve the treatment of GORD and dyspepsia by making detailed recommendations on *Helicobacter pylori* eradication, and specifying when to consider laparoscopic fundoplication and referral to specialist services.

Fluoroquinolone antibiotics: In October 2019 we made changes to recommendations on eradicating *H pylori* and updated footnotes in this guideline to reflect new restrictions and precautions for the use of fluoroquinolone antibiotics because of rare reports of disabling and potentially long-lasting or irreversible side effects (see [Drug Safety Update](#) for details).

Who is it for?

- Healthcare professionals
- Commissioners and providers
- Adults with GORD or dyspepsia and their families

Introduction

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 guideline CG17) 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 guideline CG17 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](#).

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 the NICE guideline on [acute upper gastrointestinal bleeding](#).)

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

- 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 gastro-oesophageal reflux disease (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 the NICE guideline on [Barrett's oesophagus: ablative therapy](#))
 - 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 the NICE guideline on [suspected cancer: recognition and referral](#), 'unexplained' is defined as 'symptoms or signs that have not led to a diagnosis being made by the healthcare professional in primary care after initial assessment (including history, examination and any primary care investigations)'.

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.

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

People have the right to be involved in discussions and make informed decisions about their care, as described in [your care](#).

[Making decisions using NICE guidelines](#) explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off-label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.

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 the NICE guideline on [acute upper gastrointestinal bleeding](#).)
- 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 the NICE guideline on [suspected cancer: recognition and referral](#).

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 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]
- 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, consider a COX-2 selective NSAID instead of a standard NSAID. In either case, prescribe with a PPI. [2004, amended 2014]
- 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 course of treatment with:

- a PPI (see table 3 in [appendix A](#)) and
- bismuth and
- metronidazole and
- tetracycline. [new 2014, amended 2019]

1.9.7 Discuss treatment adherence with the person and emphasise its importance. For more information about supporting adherence, see the NICE guideline on [medicines adherence](#). [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 course of treatment with:

- a PPI (see table 3 in [appendix A](#)) and
- amoxicillin and
- tetracycline (or, if a tetracycline cannot be used, levofloxacin). [new 2014, amended 2019]

1.9.10 Offer people who are allergic to penicillin^[4] (and who have not had previous exposure to a fluoroquinolone antibiotic) a 7-day, twice-daily course of treatment with:

- a PPI (see table 3 in [appendix A](#)) and
- metronidazole and
- levofloxacin^[5]. [new 2014, amended 2019]

1.9.11 Offer people who are allergic to penicillin^[4] and who have had previous exposure to a fluoroquinolone antibiotic a 7-day course of:

- a PPI (see table 3 in [appendix A](#)) and
- bismuth and
- metronidazole and
- tetracycline. [new 2014, amended 2019]

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 the NICE guideline on [Barrett's oesophagus: ablative therapy](#))
- 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]

^[2] For more information about alarm signs please see the NICE guideline on [suspected cancer: recognition and referral](#).

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

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

^[5] See [MHRA advice](#) for restrictions and precautions for using fluoroquinolone antibiotics due to very rare reports of disabling and potentially long-lasting or irreversible side effects affecting musculoskeletal and nervous systems. Warnings include: stopping treatment at first signs of a serious adverse reaction (such as tendonitis), prescribing with special caution in people over 60 years and avoiding coadministration with a corticosteroid (March 2019).

^[6] In the NICE guideline on [suspected cancer: recognition and referral](#), '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)'

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.

Finding more information and resources

You can see everything NICE says on gastro-oesophageal reflux disease and dyspepsia in adults: investigation and management in our interactive flowchart on [dyspepsia and gastro-oesophageal reflux disease](#).

To find out what NICE has said on topics related to this guideline, see our web page on [gastro-oesophageal reflux, including Barrett's oesophagus](#).

For full details of the evidence and the guideline committee's discussions, see the [full version of the guideline](#). You can also find information about [how the guideline was developed](#), including details of the committee.

NICE has produced [tools and resources](#) to help you put this guideline into practice. For general help and advice on putting NICE guidelines into practice, see [resources to help you put guidance into practice](#).

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)

Proton pump inhibitor	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 gastro-oesophageal reflux disease (GORD), which is 40 mg, but considered to be dose-equivalent to other PPI. 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)

Proton pump inhibitor	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
¹ Change from the 2004 dose, specifically for severe oesophagitis, agreed by the GDG during the update of CG17. ² Off-label dose for gastro-oesophageal reflux disease.			

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

Proton pump inhibitor	Dose
Esomeprazole	20 mg
Lansoprazole	30 mg
Omeprazole	20–40 mg
Pantoprazole	40 mg
Rabeprazole	20 mg

Update information

October 2019: Changes have been made to recommendations 1.9.6, 1.9.9, 1.9.10 and 1.9.11 to reflect new restrictions and precautions for the use of fluoroquinolone antibiotics. These recommendations are labelled [new 2014, amended 2019].

November 2014: recommendation 1.7.7 has been amended to clarify the type of NSAID to be used and that a proton-pump inhibitor should also be prescribed.

September 2014: This guideline updates and replaces NICE guideline CG17 (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.

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Accreditation

