NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Dyspepsia and gastro-oesophageal reflux disease (GORD): investigation and management of dyspepsia, symptoms suggestive of GORD, or both

1.1 Short title

Dyspepsia and gastro-oesophageal reflux disease

2 The remit

This is an update of 'Dyspepsia' (NICE clinical guideline 17).

This update is being undertaken as part of the guideline review cycle.

3 Clinical need for the guideline

3.1 Epidemiology

a) 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, acid reflux, nausea, or vomiting.

b) The UK prevalence depends on the definition of dyspepsia used, and ranges from 12% to 41%. Using the broad BSG definition, it is estimated that annually around 40% of the adult population may have dyspepsia. Dyspepsia accounts for between 1.2% and 4% of

all consultations in primary care in the UK, half of which are for functional dyspepsia (previously known as non-ulcer dyspepsia).

c) The causes of dyspepsia include gastric and duodenal ulcers, gastro-oesophageal reflux disease (GORD), oesophagitis, and oesophageal or gastric cancers; however, the cause is often unknown (functional dyspepsia). In addition, certain foods and drugs (such as anti-inflammatory drugs) are believed to contribute to the symptoms and underlying causes of dyspepsia.

d) An endoscopy may be indicated for some people with dyspepsia in order to investigate the cause. Morbidity and mortality rates from diagnostic upper GI endoscopy are low.

e) *Helicobacter pylori* (*H pylori*) is widely present in the general population, often causing no harm, but it is strongly associated with gastric and duodenal ulcers. However, its role in functional dyspepsia and GORD is less clear. The prevalence of *H pylori* infection varies internationally, with over 80% of Japanese and South American people infected, compared with a rate of approximately 40% in the UK and 20% in Scandinavia.

f) Also, some evidence suggests that H pylori infection is associated with social deprivation (for example housing) and that its prevalence increases with age.

g) GORD is a chronic condition where excess acidic gastric juices from the stomach flow back up into the oesophagus. It can be severe or frequent enough to cause symptoms, damage the oesophagus (for example, oesophagitis), or both. It can lead to an abnormality of the cells in the lining of the oesophagus (Barrett's oesophagus), which is itself considered the most important risk factor for oesophageal adenocarcinoma, the incidence of which has increased considerably in the past decade.

h) There are several risk factors for GORD including hiatus hernia, certain foods, heavy alcohol use, smoking, and pregnancy, but there is also a genetic component. Some studies have shown a weak link between obesity and GORD. There is also some evidence to suggest that GORD is more likely to occur in socially disadvantaged people. Its prevalence increases with age. Functional heartburn is diagnosed when there are symptoms of reflux in the absence of pathology.

i) Hospital episode statistics data from 2010–11 showed that there were over 41,000 consultant episodes for people with dyspepsia (39% male and 61% female), over 35, 000 of people with GORD with oesophagitis (59% male and 41% female) and nearly 38,000 with GORD without oesophagitis (49% male and 51% female).

3.2 Current practice

a) Some of the costs associated with treating dyspepsia are decreasing, but the overall usage of treatments is increasing. As a result, the management of dyspepsia continues to have potentially significant costs to the NHS. The number of prescriptions of drugs for dyspepsia has greatly increased since the publication of the 2004 guideline. From 2005 to early 2010, prescribing of drugs for dyspepsia increased from 7.6 to 11.5 million items per quarter while costs have nearly halved from £122 to £62 million per quarter. A significant reduction in the costs of proton pump inhibitors (PPI) has contributed to this. In the same time period, PPI use increased by 79%, and now accounts for 86% of the £52.9 million quarterly cost of drugs for dyspepsia.

b) The use of endoscopy has increased considerably over the past decade, as awareness of its utility in diagnosing dyspepsia and GORD has grown.

c) The review of NICE clinical guideline 17 'Dyspepsia: managing dyspepsia in adults in primary care' (2004) highlighted some

concerns about the drug regimens currently recommended in the guideline for *H pylori* eradication, as some bacterial resistance had developed. There were also concerns that current guidance relating to PPIs is out of date. Overall, the review process concluded that the guideline should be updated, including an expansion to cover aspects of specialist hospital care.

d) The current guideline covers the management of several underlying causes of dyspepsia in primary care but there is currently a lack of comprehensive national guidance about the management of GORD (in particular, surgical management) when pharmacological treatments fail. Given this, and the possible role of GORD (with the subsequent development of Barrett's oesophagus) as a risk factor for cancer, an extension of the scope of the guideline to cover the management of GORD into secondary care is needed. This is in line with the broader aim of supporting Department of Health initiatives in the early detection of upper GI cancer.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, ‘Further information’).

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

Areas from the original guideline that will be updated

a) Adults (18 years and older) with symptoms of dyspepsia or symptoms suggestive of GORD, or both.

Areas not in the original guideline that will be included in the update

b) Adults taking prescribed drugs in whom preventative treatment to avoid gastro-oesophageal pathology may be necessary.

c) Adults with a diagnosis of Barrett's oesophagus.

d) No subgroups of people have been identified as needing specific consideration.

4.1.2 Groups that will not be covered

a) Children (younger than 18 years).

b) People with a diagnosis of oesophago-gastric cancer.

4.2 Healthcare setting

Areas not in the original guideline that will be included in the update (CG17 covered adults in a primary care setting only)

a) All settings where care is delivered for NHS patients.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

Areas from the original guideline that will be updated

a) Community management of dyspepsia symptoms – particularly the use of over-the-counter drugs, including PPIs, antacids, or alginates.

b) Effectiveness of lifestyle interventions (such as diet, alcohol intake, smoking).

c) Provision of patient information.

d) Investigation and diagnosis of the cause of dyspepsia and/or reflux symptoms using clinical reviews (signs and symptoms), trial of PPIs, *H pylori* test-and-treat, and/or endoscopy.

e) Investigations for the diagnosis of GORD and assessment of disease impact (such as oesophageal manometry, pH monitoring, and oesophageal impedance testing).

f) Type of *H pylori* test (breath, stool, laboratory-based serology).

g) Pharmacological management of dyspepsia and GORD and sequencing of these treatments including:

- PPIs
- H_2 receptor antagonists (as second-line and subsequent therapy)
- *H pylori* eradication regimens (when applicable).

Note that guideline recommendations will normally fall within licensed indications; exceptionally, and only if clearly supported by evidence, use outside a licensed indication may be recommended. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients.

h) Psychological interventions such as cognitive behavioural therapy (CBT) for functional dyspepsia.

i) Investigation to assess the response to treatment for dyspepsia, heartburn and/or reflux with endoscopy (including repeat endoscopy) or *H pylori* test (where *H pylori* was treated).

j) Step-down or stopping of prescription drug, possibly including move to self-treatment with antacids.

k) Criteria for referral to consultant-led medical or surgical services.

l) Diagnosis and management of functional heartburn (including the use of tricyclic anti-depressants for management).

m) Specialist medical management of refractory dyspepsia.

n) Specialist medical and surgical management of GORD, including total or partial fundoplication (open or laparoscopic).

Areas not in the original guideline that will be included in the update

o) Prophylactic treatment using PPIs or H pylori test-and-treat for the prevention of dyspepsia symptoms or pathological changes to the oesophagus in patients taking prescribed drugs that might precipitate these.

p) Surveillance of patients with Barrett's oesophagus (except patients with high-grade dysplasia).

4.3.2 Clinical issues that will not be covered

Areas from the original guideline that will not be updated

a) Alarm signs and systems for oesophagogastric cancer

Areas not covered by the original guideline or the update

b) Diagnosis and management of oesophagogastric cancer

c) Treatment of Barrett's oesophagus.

d) Heartburn in pregnancy.

e) Treatment of Zollinger–Ellison syndrome, achalasia, or hiatus hernia (the investigation and management of dyspepsia and reflux symptoms in patients with these conditions will be covered).

f) Emergency management of bleeding or perforated ulcers.

g) Emergency management of acute upper GI bleeding.

h) Management of dysphagia.

i) H_2 receptor antagonists as first-line therapy.

j) First-line *H pylori* eradication regimens that include H_2 receptor antagonists.

k) Surgical dilatation of strictures in patients with GORD.

l) Certain minimally invasive surgical techniques for GORD including:

- endoscopic gastroplication
- endoscopic radiofrequency ablation
- endoscopic augmentation of the lower oesophageal sphincter with hydrogel implants.

4.4 Main outcomes

General

a) Reduction in symptoms (severity/frequency).

b) Biopsy findings (pathology).

c) Endoscopic appearance of oesophagus.

d) Health-related quality of life (measured using EQ-5D and/or disease-specific tools, if available).

e) Reduction in medication requirement (frequency and dose).

f) Adverse effects of interventions (diagnostic or treatment).

g) Resource use and costs.

GORD-specific

h) Occurrence of Barrett's oesophagus and progression to adenocarcinoma.

i) Findings from oesophageal manometry, pH monitoring and impedance testing.

4.5 Review questions

a) What is the effectiveness of prophylactic treatment using PPIs or *H pylori* test-and-treat for the prevention of dyspepsia in those taking prescribed drugs that might cause dyspepsia symptoms (calcium antagonists, nitrates, theophyllines), or cause pathological changes in the oesophagus (bisphosphonates, corticosteroids, NSAIDs, aspirin, clopidogrel, dipyridamole, and selective serotonin reuptake inhibitors)?

b) What is the safety and effectiveness of pharmacist-advised PPIs, antacids, or alginates to reduce dyspepsia or symptoms suggestive of GORD?

c) What is the effectiveness of lifestyle interventions to reduce symptoms of dyspepsia or GORD, or both?

d) What information should be given to patients initially presenting to a GP with dyspepsia or heartburn?

e) In patients presenting with dyspepsia and/or heartburn symptoms without alarm signs or symptoms, what is the clinical utility of endoscopy compared with an empirical trial of PPI therapy or compared with *H pylori* test-and-treat?

f) What tests should be used in patients with suspected GORD who have normal findings on endoscopy and who have not responded to an empirical trial of PPI therapy (pH monitoring, oesophageal manometry or impedance, or a combination of these tests)?

g) What characteristics/symptoms of GORD indicate endoscopy in order to exclude Barrett's Oesophagus?

h) What is the diagnostic utility of tests to confirm *H pylori* infection?

i) In patients with symptoms of dyspepsia who are positive for *H pylori*, which regimens are the most clinically effective in eradicating *H pylori*?

j) Should all patients treated to eradicate *H pylori* be retested for *H pylori* to assess their *H pylori* status? Should only patients with continuing symptoms after *H pylori* eradication treatment be retested for *H pylori*?

k) What *H pylori* eradication regimens should be offered as second-line (or third-line) treatments when first-line treatments fail?

l) Should *H pylori* eradication treatment be used in patients with endoscopically confirmed GORD?

m) What is the comparative effectiveness of different PPIs for uninvestigated dyspepsia, gastric ulcer, duodenal ulcer, functional dyspepsia, and GORD?

n) What is the comparative effectiveness of different pharmacological treatments for the first-line treatment of uninvestigated dyspepsia, gastric ulcer, duodenal ulcer, functional dyspepsia, and GORD?

o) What pharmacological treatments should be offered as second-line (or third-line) treatments when first-line treatment fails in gastric ulcer, duodenal ulcer, functional dyspepsia, and GORD?

p) What other medical treatments are effective if all the above pharmacological treatments fail?

q) Are psychological interventions such as CBT effective in reducing symptoms in functional dyspepsia compared with no CBT?

r) Should a repeat endoscopy be performed on all patients treated for ulcer dyspepsia to assess the response to treatment or should a repeat endoscopy be performed only on those patients where treatment has failed? Does this depend on the location of the ulcer?

s) Should a repeat endoscopy be performed on all patients treated for GORD with oesophagitis to assess response to treatment or should

a repeat endoscopy be performed only on those patients where treatment has failed?

t) Are step-down regimens effective for patients being treated pharmacologically for dyspepsia or GORD?

u) What patient characteristics/criteria indicate referral of a patient with dyspepsia or GORD to a consultant-led medical or surgical service?

v) After what diagnostic tests can a diagnosis of functional heartburn be confirmed?

w) What is the effectiveness of tricyclic antidepressants in the management of functional heartburn?

x) What is the effectiveness of fundoplication compared with medical management in patients with GORD?

y) Should surveillance be used for patients with Barrett's Oesophagus to detect progression to cancer?

4.6 Economic aspects

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.7 Status

4.7.1 Scope

This is the consultation draft of the scope. The consultation dates are 24 February to 22 March 2012.

4.7.2 Timing

The development of the guideline recommendations will begin in May 2012.

5 Related NICE guidance

5.1 Published guidance

5.1.1 NICE guidance to be updated

This guideline will update and replace the following NICE guidance:

- Dyspepsia. NICE clinical guideline 17 (2004).

5.1.2 Other related NICE guidance

- Service user experience in adult mental health. NICE clinical guideline. NICE clinical guideline 136 (2011).
- 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. NICE clinical guideline 106 (2010).
- Epithelial radiofrequency ablation for Barrett's oesophagus. NICE interventional procedure guidance 344 (2010).
- Photodynamic therapy for Barrett's oesophagus. NICE interventional procedure guidance 350 (2010).
- Chest pain of recent onset. NICE clinical guideline 95 (2010).
- Endoscopic mucosal resection and endoscopic submucosal dissection of non-ampullary duodenal lesions. NICE interventional procedure guidance 359 (2010).
- Endoscopic submucosal dissection of gastric lesions. NICE interventional procedure guidance 360 (2010).
- Endoscopic submucosal dissection of oesophageal dysplasia and neoplasia. NICE interventional procedure guidance 355 (2010).
- Medicines adherence. NICE clinical guideline 76 (2009).

- Endoscopic radiofrequency ablation for gastro-oesophageal reflux disease. NICE interventional procedure guidance 292 (2009).
- Antenatal care. NICE clinical guideline 62 (2008).
- Endoscopic augmentation of the lower oesophageal sphincter using hydrogel implants for the treatment of gastro-oesophageal reflux disease. NICE interventional procedure guidance 222 (2007).
- Catheterless oeosophageal pH monitoring. NICE interventional procedure guidance 187 (2006).
- Photodynamic therapy for early oesophageal cancer. NICE interventional procedure guidance 200 (2006).
- Endoscopic injection of bulking agents for gastro-oesophageal reflux disease. NICE interventional procedure guidance 55 (2004).

5.2 Guidance under development

NICE is currently developing the following related guidance (details available from the NICE website):

- Patient experience in adult NHS services. NICE clinical guideline. Publication. Publication expected TBC.
- Acute upper GI bleeding. NICE clinical guideline. Publication expected June 2012.
- Laparoscopic insertion of a magnetic-bead band for gastro-oesophageal reflux disease. NICE interventional procedure. Publication expected July 2012.
- GORD in children. NICE clinical guideline. Publication expected TBC.
- Referral for suspected cancer (update of CG27). NICE clinical guideline. Publication expected TBC.

6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- 'How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS'

- 'The guidelines manual'.

Information on the progress of the guideline will also be available from the NICE website.