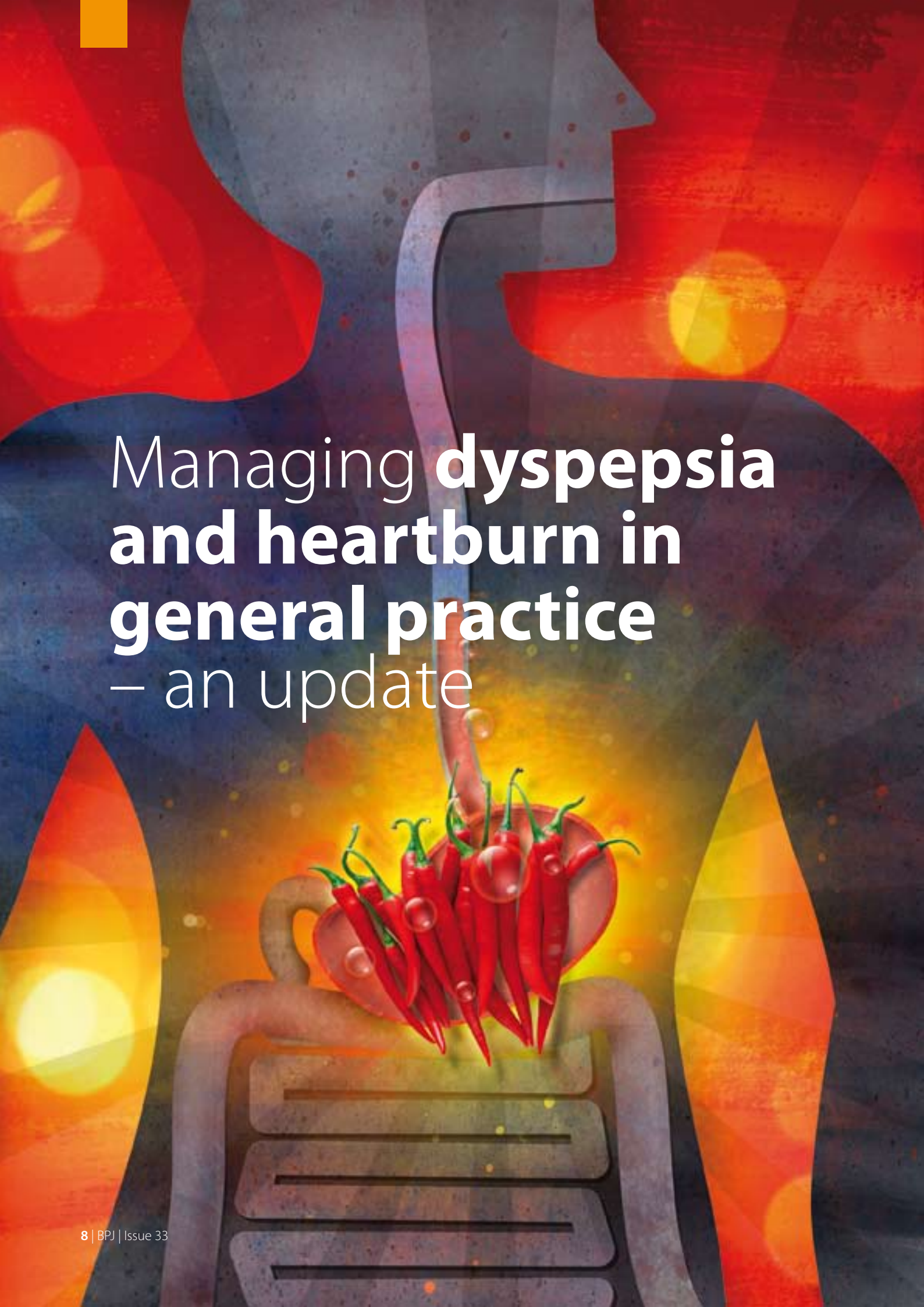
Managing **dyspepsia and heartburn in general practice** – an update



In response to many requests, we have updated our 2007 article on managing heartburn, undifferentiated dyspepsia and functional dyspepsia in general practice (BPJ 4, April 2007).

Defining dyspepsia and heartburn

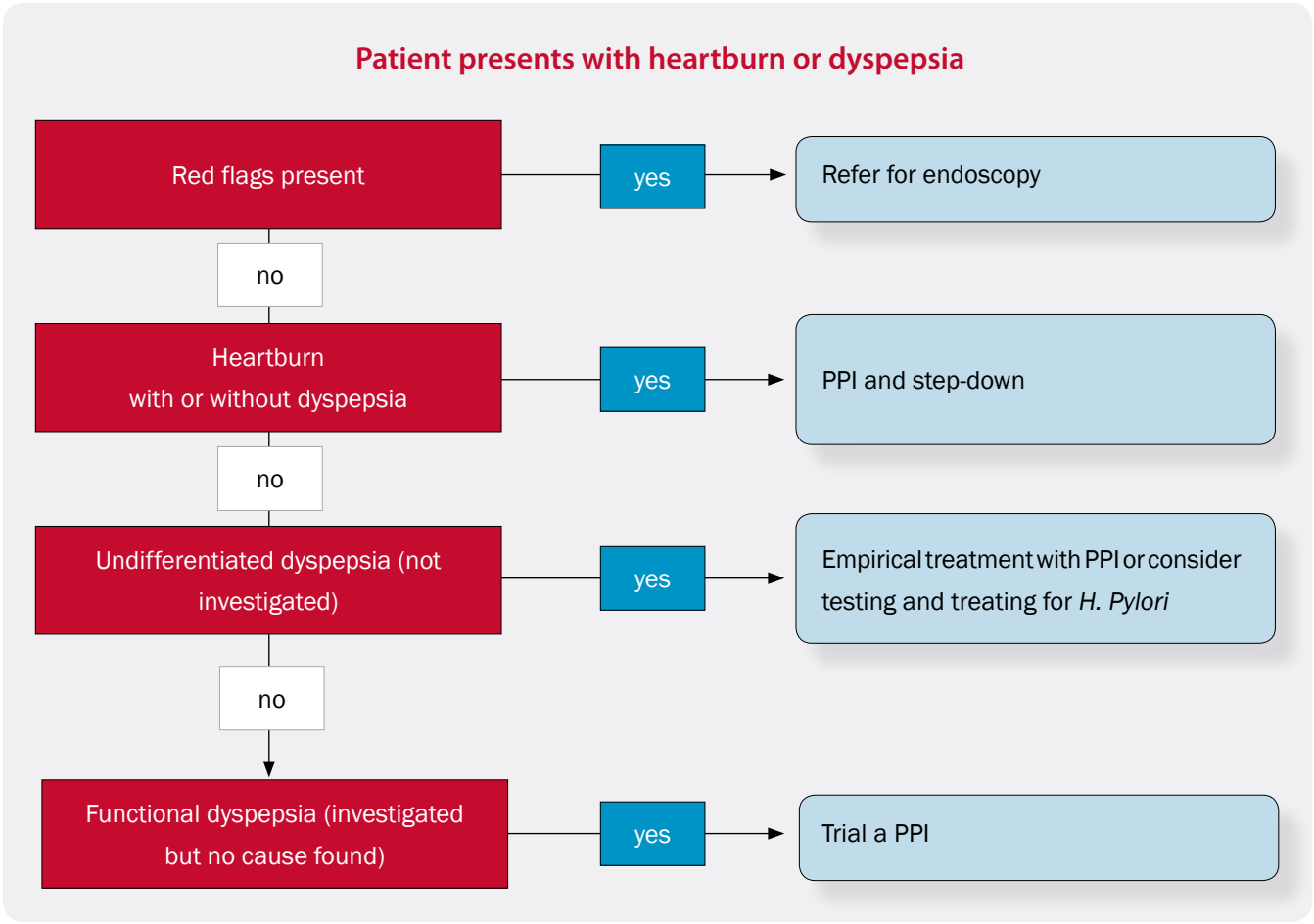
Dyspepsia is not a diagnosis but rather a description of symptoms that may indicate disease of the upper gastrointestinal tract. However, in the majority of cases there is no clear pathological cause and many people manage the symptoms themselves without consulting their GP.

Dyspepsia is pain or discomfort in the upper abdomen which is usually described as a burning sensation, heaviness or an ache. Associated symptoms include a feeling of fullness, early satiety after meals, anorexia, bloating, belching, nausea and vomiting. The symptoms of dyspepsia may be episodic, recurrent or chronic. Symptoms are often associated with eating, but this is not always the case.[1]

Undifferentiated dyspepsia is dyspepsia that has not been investigated. In a person at low risk of underlying pathology (Page 10), symptomatic management is appropriate, without the need for further investigation.

Functional or non-ulcer dyspepsia is dyspepsia, which has been investigated and no underlying pathology found.

Heartburn is described as a burning sensation rising from the epigastrium toward the neck. Heartburn, with or without associated dyspepsia, is most commonly associated with gastro-oesophageal reflux disease (GORD). Heartburn is often included within the description of "dyspepsia".

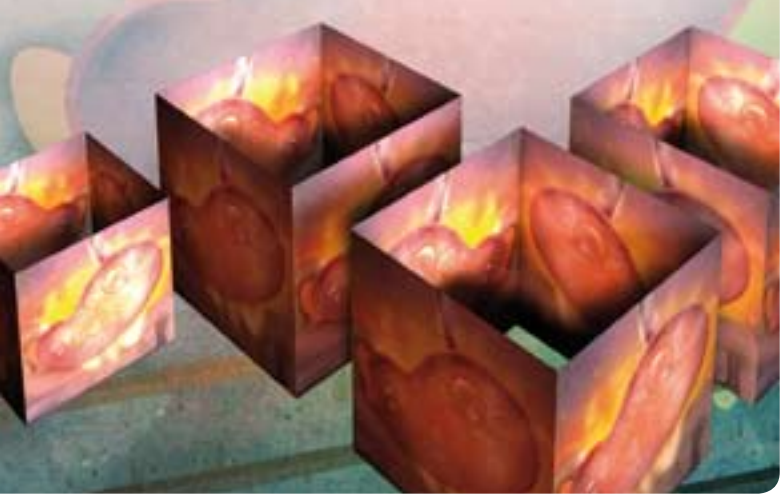


Red flags for people presenting with dyspepsia [1, 3]

The following factors increase the likelihood of significant organic disease:

- Age 50 years or older at first presentation (the incidence of gastric cancer increases with age)
- Age 40 years or older at first presentation for people of Māori, Pacific or Asian descent (gastric cancer tends to occur a decade earlier in these groups)
- Family history of gastric cancer with age of onset < 50 years
- Severe or persistent dyspepsia
- Previous peptic ulcer disease, particularly if complicated
- Ingestion of NSAIDs, including aspirin (check over-the-counter use)*
- Signs and symptoms of chronic gastrointestinal bleeding
- Iron deficiency anaemia
- Difficulty in swallowing
- Persistent or protracted vomiting
- Palpable abdominal mass
- Coughing spells or nocturnal aspiration
- Unexplained weight loss

* If a person taking NSAIDs has no other alarm features and symptoms are mild, initial management is to stop the NSAID and then re-assess symptoms



First check for red flags of significant organic disease

A number of features in the initial history or examination of people with dyspepsia or heartburn increases the likelihood of significant organic disease (see box "Red flags for people presenting with dyspepsia"). The presence of red flags indicates the need for referral for further investigation with endoscopy. If there is evidence of gastrointestinal bleeding or severe dysphagia, referral should be immediate.

Questioning of the patient may also reveal possible causes or precipitating factors for their symptoms including dietary habits (e.g. excessive caffeine or high fat), NSAID or aspirin use, use of other medicines, (e.g. calcium channel blockers, bisphosphonates, oral corticosteroids), past history of peptic ulcer or reflux disease or a family history of gastric cancer. It is also important to consider non-upper gastrointestinal tract causes of the symptoms such as cardiac, pancreatic, hepatobiliary, irritable bowel syndrome and musculoskeletal causes.[2]

N.B. When possible (i.e. with less urgent referral), acid suppressing medicines (H2 antagonists or proton pump inhibitors) should be stopped for at least two weeks prior to endoscopy as they may mask signs of organic disease. Antacids may be continued for symptom control.[3]

Best Practice Tip: Over-the-counter medicines

Treatments for dyspepsia such as antacids, ranitidine and omeprazole are available for purchase over-the-counter (OTC) from pharmacies. Pharmacists should check for alarm features and advise patients to seek medical attention if indicated. Lifestyle advice is also important. GPs should check what OTC medicines a patient has used, as this may give an indication of the severity and duration of the dyspepsia.

Heartburn with or without dyspepsia is usually caused by GORD and step-down PPI treatment is indicated

In the absence of red flags, the presence of heartburn is the single most important feature determining management.

Heartburn, with or without dyspepsia, is usually related to lower oesophageal dysfunction and the presence of GORD. There is some evidence that obesity is a risk factor for the development of GORD.[1] It is important that heartburn is differentiated from other causes of similar symptoms such as cardiac disease.

Simple lifestyle modifications may resolve mild symptoms of GORD, but acid suppressing treatment, using a step-down approach, is required if symptoms persist.

Barrett's oesophagus

Barrett's oesophagus is a complication of chronic GORD. It is a diagnosis made after endoscopy where normal cells lining the oesophagus (columnar epithelium) are found to be replaced by cells that usually line the gastric and intestinal mucosa (squamous epithelium). Patients diagnosed with Barrett's oesophagus are usually treated with long-term, high dose PPIs. They require surveillance with periodic gastroscopy as they are at increased risk of developing adenocarcinoma of the oesophagus even with PPI treatment.

Lifestyle modifications for managing GORD

Offer simple lifestyle advice including; healthy eating, weight reduction, smoking cessation and limiting alcohol intake.

Patients can be advised to avoid or minimise factors that seem to worsen their symptoms, such as bending over, eating shortly before going to bed and ingesting specific foods and beverages like alcohol, chocolate, spicy food and food with a high fat content. Some people may find that slightly raising the height of the head of the bed, while sleeping, may lessen symptoms.

Step-down acid suppressing treatment for managing GORD

The following step-down treatment regimen is appropriate for most patients. Patients should spend four to eight weeks at each step:[3]

Step One: Begin with a full dose PPI, e.g. omeprazole 20 mg daily

Step Two: Halve the dose of the PPI

Step Three: Change to a H2-antagonist, e.g. ranitidine 150 – 300 mg, twice daily

Step Four: Change to antacids or alginates as required

If there is no response to the full dose PPI after eight weeks, the dose can be doubled, e.g. to omeprazole 40 mg daily, and the response reviewed after six months. If response to treatment is still inadequate or if symptoms recur within one month of stopping, referral for endoscopy should be considered.[3] Although GORD is the most likely diagnosis in patients with predominant heartburn and reflux symptoms, these symptoms do not preclude the possibility of peptic ulcer disease, especially in patients who are infected with *Helicobacter pylori*.[4]

Best Practice Tip: It is generally recommended that PPIs (particularly omeprazole) are taken in the morning, 30 minutes before food, for optimal acid suppression. There is a theoretical basis for this but for many people, the timing in association with food is not important. However, when assessing response to a PPI or before considering a dose increase, it is worthwhile checking to see if the medicine is being taken as recommended.

Dyspepsia and heartburn in pregnancy

The most common cause of dyspepsia and heartburn in pregnancy is GORD.[1] Dyspepsia does not usually cause complications in pregnancy and is likely to resolve after the woman has given birth. Assessment to exclude a more serious cause includes enquiring about alarm features and a past history of GORD or peptic ulcer disease. Lifestyle, eating habits and current use of over-the-counter medicines such as antacids should also be checked.

Lifestyle advice is the usual first-line management, especially in the first trimester. If lifestyle advice does not adequately control symptoms, antacids or alginates can be tried if symptoms are relatively mild. Alginates, e.g. gaviscon, are particularly useful if heartburn symptoms are predominant. If symptoms are more severe, or persist despite treatment with an antacid or alginate, consider prescribing an acid-suppressing medicine such as ranitidine or omeprazole. Both of these medicines are considered to be relatively safe in pregnancy but omeprazole is more effective and a recent study has shown no association with major birth defects when administered in early (first trimester) pregnancy.[8] As with any medicine used in pregnancy, especially in the first trimester, treatment should be with the minimum effective dose for the shortest possible time.

Dyspepsia without heartburn

Who gets dyspepsia?

Dyspepsia can occur at any age but in older people it is more likely to be associated with organic diseases such as peptic ulcer disease or gastric cancer. NSAIDs, including aspirin, are a major cause of dyspepsia and peptic ulcers and these medicines are more frequently prescribed in people over 65, who in turn are more susceptible to complications.

There are no accurate figures linking the prevalence of dyspepsia with ethnicity in New Zealand. However, *H. pylori* infection which is associated with peptic ulceration is more common among Māori and Pacific peoples.

Initial management of undifferentiated dyspepsia without heartburn

In dyspepsia without heartburn that has not been investigated (undifferentiated dyspepsia), first rule out the possibility of serious disease, based on the presence of red flags. Review lifestyle factors and use of medicines that may be exacerbating symptoms. Patients can then be managed by either empiric treatment (usually with a PPI) or testing for *H.pylori*.

For most people, empiric treatment is appropriate. A suggested approach is as follows:[1]

- An antacid (or alginate) can be used for immediate relief of symptoms
- Prescribe a full dose PPI, e.g. omeprazole 20 mg, for one month
- If there is no response to the PPI, test and treat for *H.pylori*
- If there is no response to a PPI or H.pylori treatment, trial an H2-antagonist or a prokinetic (e.g. domperidone, metoclopramide) for one month. Referral can be considered at this point.
- If there is no response to the above steps refer for further investigation with endoscopy

- If symptoms recur, restart treatment with a PPI at the lowest effective dose and advise intermittent or as required treatment. Review maintenance treatment annually.[2]

Consider testing for *H.pylori* only after treatment failure

The pros and cons of a test and treat strategy (testing for *H.pylori* and then treating if positive) are widely debated and the decision to test for *H.pylori* is partly influenced by the likelihood of finding the infection.[2] The New Zealand Guidelines state that testing is recommended when there is a prevalence rate of greater than 30%.[3] As a guide, prevalence rates in the South Island are less than 30% but tend to be greater than 30% in adult Māori, Pacific and Asian people, people in lower socioeconomic areas and adult populations in Auckland.[3]

However, *H.pylori* infection rates are generally declining and a one month trial of a PPI is a reasonable approach for most patients with undifferentiated dyspepsia.

- An empiric trial of a PPI will treat the most common causes of dyspepsia, including GORD and peptic ulcer disease without the expense of *H.pylori* testing
- In populations with intermediate *H.pylori* prevalence (30 – 60%), empiric treatment and testing and treating are equally cost effective, but empiric treatment avoids the use of antibiotics and the possibility of resistance and adverse effects[2]
- A meta-analysis of randomised controlled trials that compared empiric PPI treatment with test and treat found no difference in treatment costs or symptoms when patients were followed up for one year[5]

Recommended test for *H. pylori* when indicated

If testing for *H. pylori* is indicated, the best test to use is dependent on the clinical setting. There are three tests, apart from performing endoscopy, to check for *H. pylori* infection. The most accurate test, in all clinical scenarios, is the Carbon-13 urea breath test. This test will determine if the patient has an active infection. However, this test is expensive and is not generally available. The faecal antigen test can also determine if active infection is present, but false-negative results are possible, which will limit interpretation when a diagnosis is required. Serology, using a blood sample, will show exposure to the infection, but this does not always mean that active infection is still present.

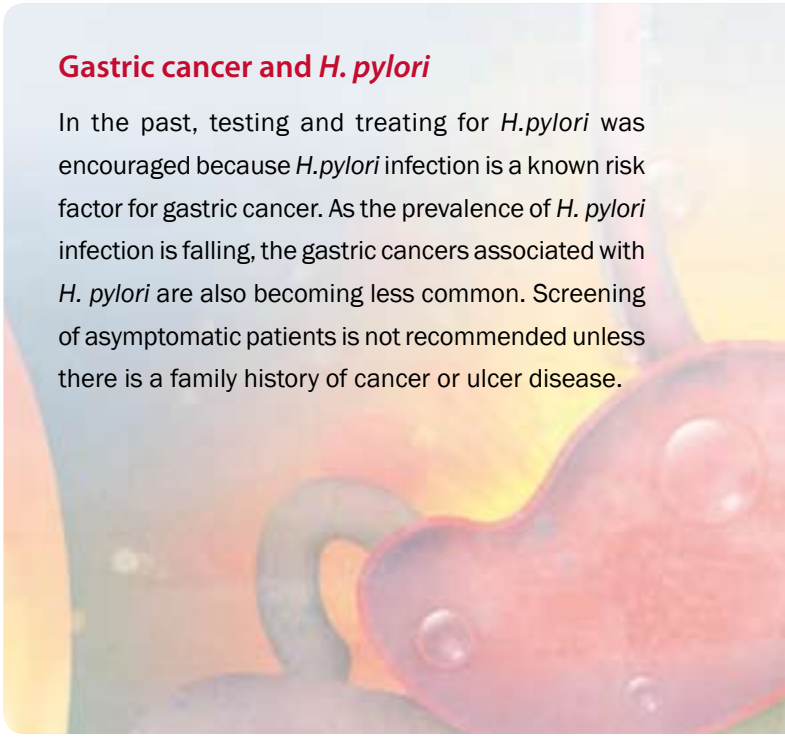
From a general practice perspective, serology is easy to obtain and is a reasonable approach for testing for *H. pylori*. A faecal antigen test is recommended to detect loss of infection after treatment.

Recommended treatment for *H.pylori*

For *H.pylori* eradication a seven day course of omeprazole 20 mg, clarithromycin 500 mg and amoxicillin 1 g (or metronidazole 400 mg, if allergic to penicillin), all taken twice daily is recommended. Note that the combination pack (Losec HP7 OAC) is no longer subsidised but triple therapy is subsidised if all three medicines are co-prescribed.

Gastric cancer and *H. pylori*

In the past, testing and treating for *H.pylori* was encouraged because *H.pylori* infection is a known risk factor for gastric cancer. As the prevalence of *H. pylori* infection is falling, the gastric cancers associated with *H. pylori* are also becoming less common. Screening of asymptomatic patients is not recommended unless there is a family history of cancer or ulcer disease.



Safety and long-term effects of PPIs

Many people have now been taking a PPI for several years and there have been a number of studies investigating long-term safety. Most studies are observational which cannot establish causality. There is no proven link with an increased risk of gastric cancer or nutritional deficiencies. From a general safety standpoint, PPIs should be used at the lowest effective dose for the shortest possible time and regularly reviewed.

Fractures of the hip, wrist, and spine

The data is conflicting as to whether PPI use is associated with an increased risk of bone fracture. There is a possible increased risk of fractures of the hip, wrist and spine.

In case controlled studies, long term PPI use has been associated with an increased risk of bone fracture, and this increased risk depends on the duration and dose of chronic use of the PPI. Use of a PPI for five years or more can increase the risk of osteoporotic fractures by 1.62-fold (95% CI: 1.02-2.58).[9] Other studies have shown that use of a PPI for seven years or more increases the risk of osteoporotic hip fractures by 4.55-fold (95% CI: 1.68-12.29).[9] PPI use for six to 12 months has been reported to be associated with an increased risk of osteoporotic hip and spine fractures.[9] If there is concern regarding the risk of bone fracture, such as for older adults who require long term PPI therapy, use the lowest effective PPI dose and ensure adequate dietary calcium intake.[10]

Vitamin B12 deficiency

Long-term use of PPIs does not lead to vitamin B12 deficiency except possibly in elderly people, or in people with Zollinger-Ellison Syndrome who are on high doses of a PPI for prolonged periods of time.[9] Routine testing for vitamin B12 is not advocated but may be advisable for such patients at increased risk.

Rare adverse reactions

PPIs are a relatively safe group of medicines and serious adverse events are rare. However, there have been case reports of interstitial nephritis with omeprazole, hepatitis with omeprazole and lansoprazole and visual disturbances with omeprazole and pantoprazole.[9]

Interstitial nephritis is characterised by acute renal failure, arthralgia, malaise and fever.

For further information see: **www.medsafe.govt.nz/profs/PUarticles/omeprazole.htm**

Interaction with clopidogrel

Omeprazole can be used to reduce the risk of gastrointestinal complications from antithrombotic treatment. However, omeprazole has been shown to decrease the formation of the active metabolite of clopidogrel and potentially reduce its anti-platelet effect. There is ongoing debate as to whether concomitant use of omeprazole and clopidogrel translates to adverse cardiovascular outcomes. Current advice from Medsafe is to avoid concomitant use. This advice may change as more evidence becomes available.

For further information see: **www.medsafe.govt.nz/profs/puarticles/clopidogrelandomeprazole.htm**

Functional dyspepsia is managed the same as undifferentiated dyspepsia

Defined pathology is unable to be identified in approximately half of the patients referred for endoscopy, and this is classified as functional dyspepsia. The cause of functional dyspepsia is not clearly understood and is likely to be multi-factorial. Some cases appear to be related to hyperacidity with associated heartburn and reflux symptoms, whereas others appear to be related to a disorder of gastrointestinal motility. Psychosocial and psychological factors may be involved but it is not known how significant these factors are on a population basis.

A PPI is considered first line treatment for functional dyspepsia, with or without symptoms of hyperacidity. Management follows the same approach as for undifferentiated dyspepsia.

Functional dyspepsia in patients, that have not responded to a PPI or prokinetic and are *H.pylori* negative (or have had the infection eradicated), is often challenging to treat.[2] There is some evidence that an antidepressant may be effective in reducing symptoms,[6] but it is not known if this is actually due to improved control of underlying depression. Either a tricyclic antidepressant (TCA) or a selective serotonin re-uptake inhibitor (SSRI) may be trialled.[7]

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