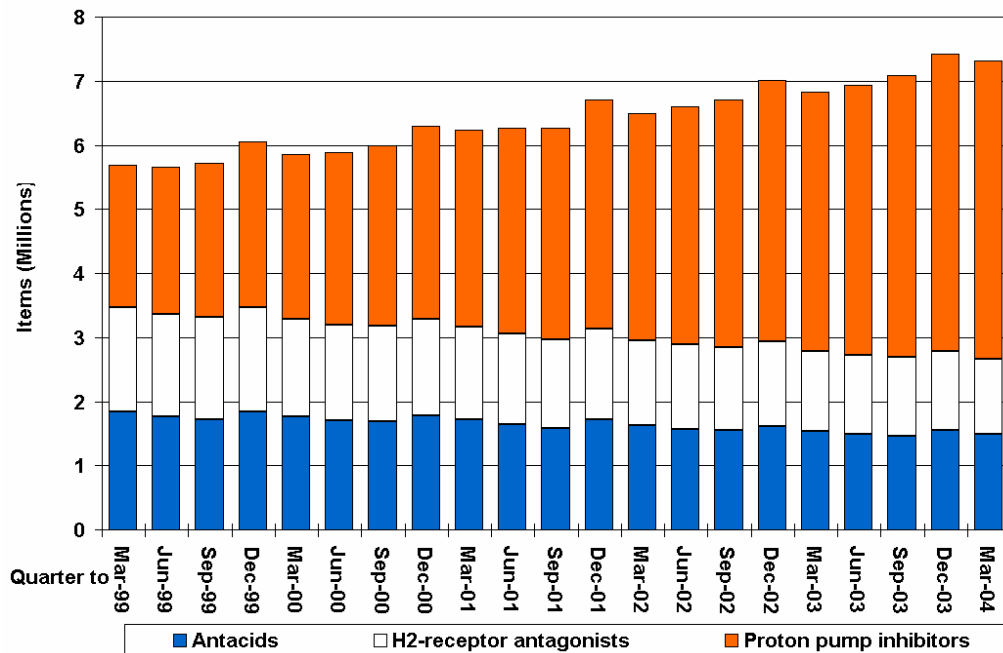


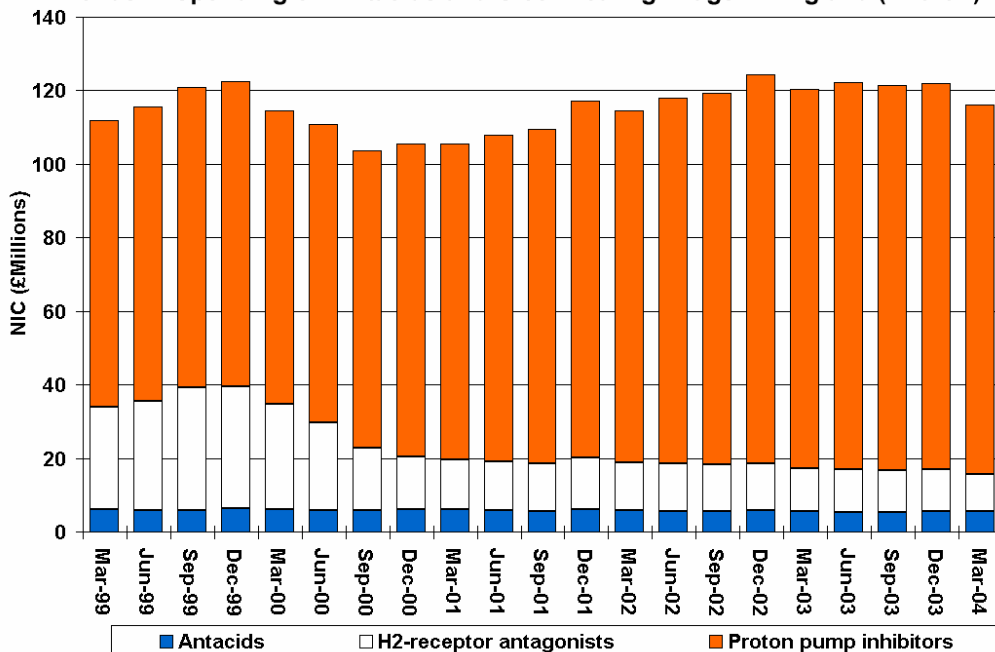
Drugs for Dyspepsia

In the UK one estimate is that around 40% of adults suffer from dyspepsia although only 5% consult their GP each year.¹ The most common causes of dyspepsia are gastro-oesophageal reflux disease (GORD), peptic ulcer disease (PUD) and non-ulcer dyspepsia (NUD). Prescribed drugs and endoscopies cost the NHS around £600 million annually and over-the-counter medication costs patients a further £100 million.¹ Use of proton pump inhibitors (PPIs) has increased over the last 5 years while prescribing of H₂-receptor antagonists (H₂RAs) and antacids has fallen (Chart 1). Overall, expenditure on drugs to treat dyspepsia has remained fairly constant (Chart 2).

Trends in the Prescribing of Antacids and Ulcer Healing Drugs in England (Chart 1)



Trends in Spending on Antacids and Ulcer Healing Drugs in England (Chart 2)



Specialist referral or endoscopic investigation (to be seen within 2 weeks) is indicated for patients of any age with dyspepsia who present with any of the following alarm symptoms: chronic gastrointestinal (GI) bleeding, progressive unintentional weight loss, progressive dysphagia, persistent vomiting; or who have iron deficiency anaemia, epigastric mass or suspicious barium meal.¹ Patients over 55 years with dyspepsia but no alarm symptoms do not require routine referral for endoscopy. However, they can be considered for endoscopy if symptoms persist despite *Helicobacter pylori* (*H. pylori*) testing and initial PPI therapy or where the risk of cancer is high.¹ Of those patients with symptoms severe enough to require endoscopy, 40% will have GORD, 40% will have NUD and 13% will have an ulcer.¹

Uninvestigated dyspepsia

Self-treatment with an antacid and/or alginate therapy is appropriate for most patients with uninvestigated dyspepsia. However, additional therapy may be required if symptoms persistently affect a patient's quality of life. Initially patients with dyspepsia should be offered *H. pylori* 'test and treat' or a treatment dose of a PPI for one month; available evidence is insufficient to advise which should be offered first.¹ A recent trial compared 'test and treat' to omeprazole treatment in 219 patients aged under 45 years presenting with dyspepsia without alarm symptoms. Patients received either omeprazole or eradication therapy after testing for *H. pylori*. The 'test and treat' strategy was more effective at improving symptoms and reducing referral rates for endoscopy than PPI therapy.²

Gastro-oesophageal reflux disease (GORD)

GORD includes both oesophagitis determined by endoscope and endoscopy negative reflux disease. Patients with severe GORD should be offered a treatment dose of a PPI for one or two months. If symptoms recur following initial treatment then a PPI should be 'stepped down' to the lowest dose at which symptoms are controlled.¹ After treatment with PPIs an increase in healing has been demonstrated compared with placebo or H₂RAs.³ There is no evidence that eradication of *H. pylori* is beneficial when symptoms of GORD recur.⁴

Lifestyle advice including avoidance of certain food or drink which exacerbates symptoms, losing weight if overweight, raising the head of the bed and stopping smoking should be offered to patients. There is limited evidence of success with these interventions in relieving GORD symptoms but they provide general health benefits.

Non-ulcer dyspepsia (NUD)

H. pylori is present in around half of patients with NUD and its eradication relieves the symptoms of NUD in 1 in 15 people treated. The benefits of routine treatment to eradicate *H. pylori* in patients with dyspepsia and normal endoscopy findings are unclear.⁵ If *H. pylori* has been excluded or treated and symptoms persist then a low dose PPI or H₂RA should be offered. Treatment with a H₂RA or PPI should be encouraged on an 'as needed' basis for patients to manage their symptoms, using the lowest dose possible to control symptoms. Long-term, frequent dose antacid therapy is inappropriate; it does not prevent symptoms and only provides short-term relief.¹

Peptic ulcer disease (PUD)

Nearly all patients who have PUD will test positive for *H. pylori*: eradication therapy should be offered to these patients to reduce ulcer recurrence and increase ulcer healing.¹ For patients taking NSAIDs, offer full dose PPI or H₂RA therapy for one month and if *H. pylori* is present subsequently try eradication therapy.¹ Where possible NSAIDs should be discontinued. Patients who are not receiving NSAIDs should be offered *H. pylori* eradication therapy first. A two-week wash out period following PPI use is necessary before testing for *H. pylori*. The gold standard for detecting *H. pylori* is a non-invasive carbon urea breath test. The breath test's specificity results in fewer patients being inappropriately treated with eradication therapy. Laboratory based serology testing should only be used if it has already been locally validated because it performs less well than the breath test or stool antigen testing. Near patient testing is not recommended due to the inadequate performance of these tests. Patients testing positive should be prescribed a 7-day course of a PPI, and either metronidazole and clarithromycin 250mg, or an amoxicillin and clarithromycin 500mg regimen.¹ Re-testing for *H. pylori* should always use a carbon urea breath test.

Reducing GI adverse events

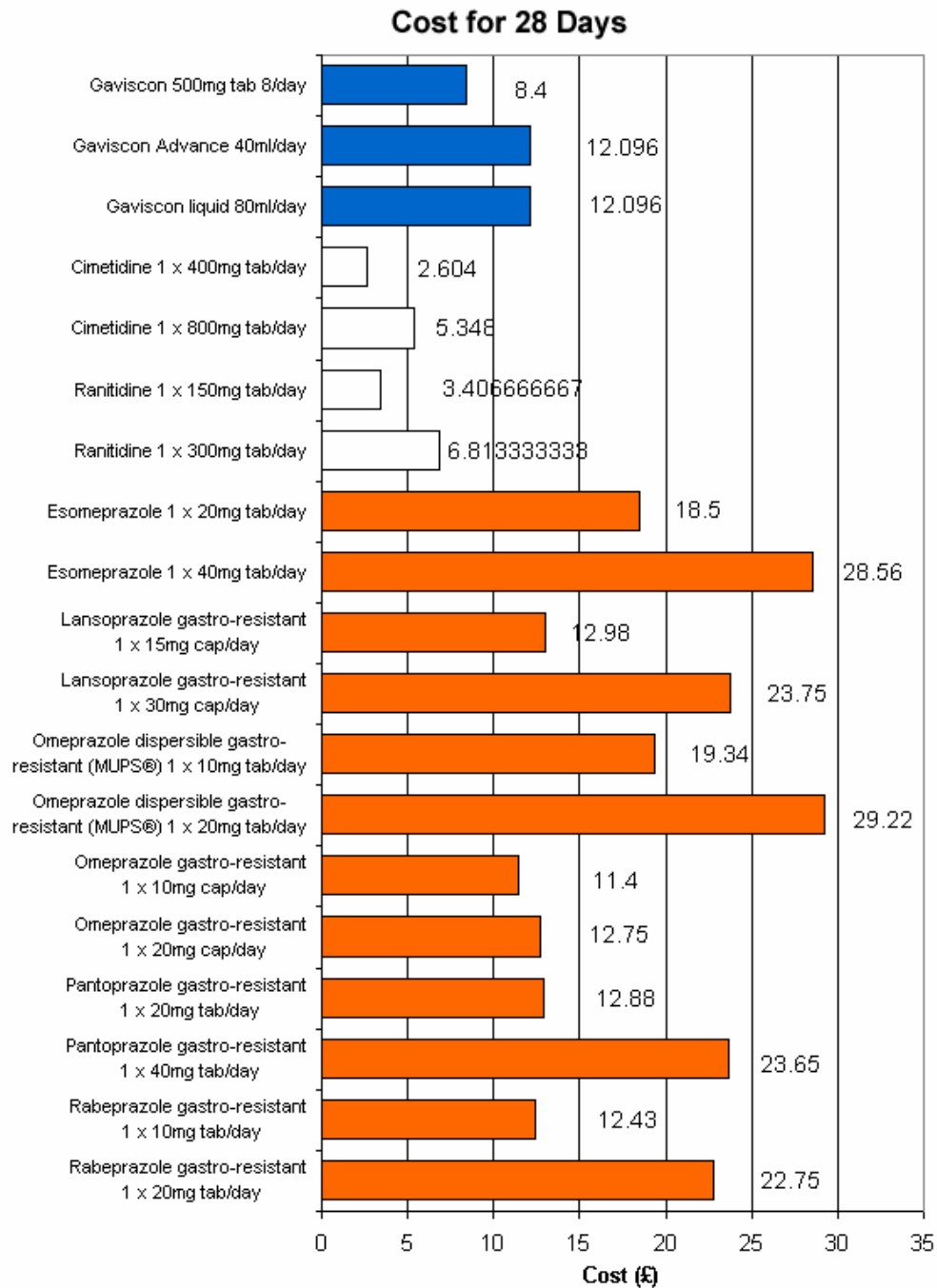
NSAIDs including Cox II selective drugs cause GI adverse effects and before prescribing the risks versus benefits should be assessed. Prescribing of NSAIDs has increased by 13% in the last 5 years. In the quarter to March 2004, there were over 5 million NSAID items at a cost of £60.8 million; 1.6 million of these items were for Cox II selective drugs, costing £37.9 million. Prescription items for Cox II selective inhibitors have grown by over 500% in the past 5 years while costs have risen almost 10-fold. Using Cox II selective inhibitors rather than a standard NSAID may reduce the risk of serious GI adverse events in high risk patients. However, a recent population based study has shown that a 41% rise in NSAID use, entirely due to increased use of Cox II selective inhibitors, was accompanied by a 10% increase in hospitalisation rates for upper GI haemorrhage.⁶ An observational study that investigated the burden of adverse drug reactions (ADR) as a cause of hospital admissions found NSAIDs were implicated in 30% of admissions due to an ADR (363 cases). Aspirin was the drug most often associated with adverse events. Other NSAIDs including rofecoxib and celecoxib also caused ADRs resulting in admission.⁷

The factors associated with a high risk of GI adverse events from NSAIDs include:

- age over 65 years
- use of other medicines known to increase the chance of upper GI adverse events
- serious co-morbidity
- prolonged use of maximum recommended doses of standard NSAIDs
- previous history of PUD/dyspepsia.⁸

Patients at high risk of GI adverse events who need to take an NSAID can be co-prescribed either a PPI or misoprostol, alternatively a Cox II selective NSAID can be prescribed. Compared with placebo, misoprostol significantly reduces NSAID associated gastric and duodenal ulcers found on endoscopy and reduces serious upper GI complications.⁹ PPIs are the treatment of choice for *H. pylori* positive patients who present with a bleeding ulcer and who need to continue NSAIDs. Eradicating *H. pylori* before commencing an NSAID is useful in patients at high risk of PUD or with a previous history of PUD.¹⁰

Evidence from observational studies suggests that the use of selective serotonin re-uptake inhibitors (SSRIs) increases the risk of developing GI bleeding to around three times the risk for patients not using SSRIs. However, the absolute risk is small, around 3 extra episodes of upper GI bleeding requiring hospitalisation per 1,000 patient-years of treatment. SSRIs appear to carry a higher risk of bleeding in patients aged over 80 years or those with a history of GI bleeding, therefore, it is prudent to avoid SSRIs in these groups of patients or in those also taking aspirin or another NSAID.¹¹



Prices based on Drug Tariff July 2004 or Chemist & Druggist July 2004

Prescribing data

PPIs accounted for 63% (4.6 million) of items for drugs to treat dyspepsia and 86% of cost (£100.3 million), quarter to March 2004. Just over half of these items were for lansoprazole (Table 1). This drug accounted for 54% of spending on PPIs. Omeprazole was the next most commonly prescribed PPI followed by rabeprazole. During the past 5 years prescribing of PPIs has more than doubled (Chart 1). However, the increase in spending over the same period is more modest at just 29%. This is largely due to increased prescribing of lansoprazole. The Drug Tariff prices of omeprazole gastro-resistant capsules were reduced considerably in December 2003 (see price chart).

Table 1: Changes in Prescribing of Proton Pump Inhibitors in the Last 3 Years

	Items (millions)		% Change	Net Ingredient Cost (£millions)		% Change
	Quarter to			Quarter to		
	March-02	March-04		March-02	March-04	
Lansoprazole	1.8	2.4	39%	39.3	53.8	37%
Omeprazole	1.1	1.2	6%	41.2	23.1	-44%
Rabeprazole	0.3	0.4	25%	7.5	9.1	21%
Pantoprazole	0.2	0.3	60%	3.5	5.3	54%
Esomeprazole	0.1	0.3	107%	3.7	8.1	122%

Prescribing of H₂RAs has fallen by almost 28% during the past 5 years, with spending showing a 63% decrease. They now account for 16% of all items for drugs to treat dyspepsia and 9% of cost. 77% of H₂RA prescribing in the quarter to March 2004 was for ranitidine (0.9 million items, £7.9 million). Cimetidine was the next most commonly prescribed at 16% of prescribing (0.2 million items) and 11% of cost (£1.1 million). Prescribing of drugs classified under the BNF section "Dyspepsia and GORD" is also decreasing (19% in the past 5 years). This group of drugs mainly consists of antacids and compound alginates. In the quarter to March 2004 there was a total of 1.5 million items, costing £5.5 million. Compound alginates accounted for 90% of items and cost. Prescribing of drugs in the BNF sub-section "Antacids and Simeticone" has almost halved in the past 5 years with only 150,000 items prescribed, quarter to March 2004.

SUMMARY

- Refer patients presenting with alarm symptoms immediately for further investigation. Patients aged over 55 years with dyspepsia but without alarm symptoms do not require routine initial referral for endoscopy.
- A full dose PPI should be initiated for one to two months in severe cases of GORD. If symptoms recur after initial therapy the PPI should be 'stepped down' to the lowest dose that controls symptoms.
- Treatment for non-ulcer dyspepsia should be on an 'as needed' basis at the lowest dose of a H₂RA or PPI at which symptoms are controlled.
- *H. pylori* positive patients with peptic ulcers should receive eradication therapy.

- Patients who are at high risk of GI adverse events and who need to continue taking an NSAID can receive either misoprostol or a PPI with a standard NSAID or alternatively a Cox II selective NSAID.
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	Quarter to June 04	
	National	
	Items/1000 PUs	NIC/1000 PUs
Antacids and simeticone	2.01	£5.77
Compound alginates, etc	18.64	£71.28
H2-receptor antagonists	16.43	£141.81
Proton pump inhibitors	68.93	£1,480.75

Prescribing and Spending on Drugs for Dyspepsia in England for Quarter to June 2004

