

Randomised trial of endoscopy with testing for *Helicobacter pylori* compared with non-invasive *H pylori* testing alone in the management of dyspepsia

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Abstract

Objective To compare the efficacy of non-invasive testing for *Helicobacter pylori* with that of endoscopy (plus *H pylori* testing) in the management of patients referred for endoscopic investigation of upper gastrointestinal symptoms.

Design Randomised controlled trial with follow up at 12 months.

Setting Hospital gastroenterology unit.

Participants 708 patients aged under 55 referred for endoscopic investigation of dyspepsia, randomised to non-invasive breath test for *H pylori* or endoscopy plus *H pylori* testing.

Main outcome measure Glasgow dyspepsia severity score at one year. Use of medical resources, patient oriented outcomes, and safety were also assessed.

Results In 586 patients followed up at 12 months the mean change in dyspepsia score was 4.8 in the non-invasive *H pylori* test group and 4.6 in the endoscopy group (95% confidence interval for difference -0.7 to 0.5, P=0.69). Only 8.2% of patients followed up who were randomised to breath test alone were referred for subsequent endoscopy. The use of non-endoscopic resources was similar in the two groups. Reassurance value, concern about missed pathology, overall patient satisfaction, and quality of life were similar in the two groups. The patients found the non-invasive breath test procedure less uncomfortable and distressing than endoscopy with or without sedation. No potentially serious pathology requiring treatment other than eradication of *H pylori* was missed.

Conclusion In this patient group, non-invasive testing for *H pylori* is as effective and safe as endoscopy and less uncomfortable and distressing for the patient. Non-invasive *H pylori* testing should be the preferred mode of investigation.

Introduction

Over the past 40 years, endoscopy has been used with increasing frequency in the investigation of upper gastrointestinal symptoms. More than 1% of the population of the United Kingdom undergo gastroscopy each year.¹ Despite this widespread use of the

procedure, a recent qualitative systematic review concluded that “the preponderance of available data does not support the effectiveness of endoscopy in the management of dyspepsia.”²

One of the main reasons for performing endoscopy in patients with dyspepsia is to detect underlying ulcer disease. However, non-invasive testing for *Helicobacter pylori* has been shown to be a useful predictor of endoscopic diagnosis in patients with dyspepsia. In patients without *H pylori* infection, ulcer disease is extremely rare and endoscopic examination is usually normal or shows evidence of oesophagitis.³⁻⁵ In dyspeptic patients with *H pylori* infection, endoscopy shows underlying ulcer disease in 10-50%.^{3 5 6}

Considerable interest exists in using non-invasive *H pylori* testing in place of endoscopy to determine the management of patients presenting with upper gastrointestinal symptoms. Patients with a negative *H pylori* test could be reassured that they do not have underlying ulcer disease and could be treated symptomatically, as would occur after an endoscopic examination showing no abnormality or evidence of oesophagitis. Patients with a positive *H pylori* test could all be given treatment to eradicate *H pylori*, which would cure the subgroup with underlying ulcer disease. Such a strategy involves treating dyspeptic patients positive for *H pylori* without actual ulcer disease. However, recent meta-analyses indicate that such treatment is superior to placebo in resolving symptoms in *H pylori* positive non-ulcer dyspepsia and is as effective as any other available treatment for the condition.⁷⁻⁹ In addition, other indications support eradication of the infection in non-ulcer dyspepsia—for example, removal of the increased risk of developing actual ulcer disease,¹⁰⁻¹² removal of an important risk factor for gastric cancer and lymphoma,^{13 14} and removal of concern about a potential adverse interaction between the infection and subsequent long term use of proton pump inhibitor treatment.¹⁵

Non-endoscopic management would be inappropriate for certain groups of patients, including those with symptoms suggestive of underlying malignancy and those taking non-steroidal anti-inflammatory drugs, who may develop ulcer disease in the absence of *H pylori* infection. Non-endoscopic management might

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also be inappropriate in older patients because of the higher incidence of malignancy in this age group.

We present the results of a randomised trial comparing non-invasive testing for *H pylori* with endoscopy in the management of patients referred for endoscopic investigation of upper gastrointestinal symptoms.

Methods

The ethics committees of the West Glasgow University NHS Trust and the local primary care trust approved the study. We recruited participants from patients referred by their general practitioners to the hospital for endoscopic investigation of upper gastrointestinal symptoms. Exclusion criteria were age over 55, the use of non-steroidal anti-inflammatory drugs (excluding low dose aspirin), and the presence of sinister symptoms. We selected patients by examining all referral letters to the hospital's gastroenterology outpatient clinics and open access endoscopy service. All patients whose referral letter indicated upper gastrointestinal symptoms and age under 55 years and made no comment about the presence of sinister symptoms or use of non-steroidal anti-inflammatory drugs were sent an appointment for our one stop clinic established specifically for the study. The appointment letter for the clinic informed patients that they might be invited to participate in a study comparing endoscopy with a non-invasive breath test. They were also told to stop any antisecretory drugs two weeks before the clinic appointment.

Baseline assessment

At their single visit to the clinic, the patients had a structured interview by either a consultant gastroenterologist or a specialist registrar in gastroenterology. Details recorded included the character of the patient's predominant symptom and any history of use of non-steroidal anti-inflammatory drugs or other drugs. Patients were specifically asked about the presence of any of the following sinister symptoms: dysphagia, recent weight loss of more than 3 kg, persistent vomiting, first degree relative with upper gastrointestinal malignancy, recent evidence of upper gastrointestinal bleeding, or history of gastric surgery. We assessed the severity of symptoms over the six months preceding the visit with a previously validated instrument, the Glasgow dyspepsia severity score.¹⁶ This score measures the frequency of upper gastrointestinal symptoms (0-5), their effect on normal activities (0-2), number of days of work missed because of symptoms (0-2), frequency of medical consultations (0-2), frequency of home visits (0-2), tests for dyspepsia (0-2), and use of over the counter (0-2) and prescribed (0-3) drugs. The total score ranges from 0 to 20, with higher scores indicating more severe dyspepsia.

We assessed quality of life with a 36 item medical outcomes study short form health survey (SF-36), which examines eight aspects of quality of life: general and mental health, physical function, social function, physical and emotional health, pain, and vitality.¹⁷ The scores for each of the eight aspects can range from 0 (worst) to 100 (best). We asked patients about their degree of worry about their condition and about their degree of concern that they might have a sinister

underlying disease. These were recorded on a 0-10 Likert-type scale. We also performed abdominal examination and recorded evidence of tenderness, organomegaly, or abdominal mass. The information obtained from the structured questions and examination was entered directly into a personal computer.

Intervention

We then invited all eligible patients to participate in the study by being randomised to endoscopy plus breath test for *H pylori* or breath test alone. We informed patients that recent studies indicated that the breath test may be as useful as endoscopy in determining appropriate management. We also informed them that they, or their general practitioner, would be free to request an early endoscopy if either felt that it was indicated.

After participants had given written, informed consent, we opened a sealed envelope that randomly allocated each patient to one or the other investigation strategy. The pharmacy department carried out the randomisation independently by using tables of random numbers to assign half the patients to each investigation strategy. Immediately after this, patients underwent either endoscopy plus the breath test or the breath test alone. Patients had their throat sprayed with lignocaine before endoscopy and were also offered intravenous sedation with midazolam. During the endoscopy, we took biopsies from both the antrum and body region for histology and urease slide test (CLO test; Delta West, Beatley, Australia). We performed the ¹⁴C-urea breath test as previously described,¹⁸ except that we used a citric acid drink in place of a fatty drink in order not to obscure the endoscopic view. The patients randomised to endoscopy also underwent the breath test, as this provided a quicker determination of their *H pylori* status than awaiting the result of the histology or urease test on their gastric biopsies. The breath test was analysed on site, and the result was available within 30 minutes.

The medical gastroenterologist saw patients again immediately after their tests and informed them of the findings. Patients who had received sedation for the endoscopy were seen one to two hours later. Patients who had undergone endoscopy were informed of the findings and of their *H pylori* status. If they were *H pylori* positive, we advised them to take eradication treatment irrespective of the presence or absence of ulcer disease. Patients who had only the breath test were informed of the result. If it was positive, we told them that they might have an underlying ulcer that would benefit from treatment of the infection and that studies in our population also indicated symptomatic benefit from treating the infection even in the absence of an ulcer.¹⁰ We reassured patients with a negative breath test result that they were very unlikely to have an ulcer and that their symptoms were likely to be due to gastro-oesophageal reflux disease or non-ulcer dyspepsia. All patients testing positive for *H pylori* were given a seven day course of *H pylori* eradication treatment consisting of omeprazole 20 mg twice daily, clarithromycin 250 mg three times daily, and amoxicillin 500 mg three times daily. Patients who were allergic to amoxicillin were given metronidazole 400 mg three times daily in its place. The clinic did not provide or recommend directly any other treatment. All patients were told to

see their general practitioner for further treatment if their symptoms persisted.

Before they left the clinic, we asked patients to score the degree of discomfort or distress caused by their diagnostic test on an 0-6 integer scale. In addition, we asked them if they would have the same test again happily, reluctantly, or never. We asked patients who had had an endoscopy whether they would have it again with or without sedation.

We then discharged the patients back to the care of their general practitioner. We sent a standardised letter to the general practitioner stating the results of the tests and whether or not *H pylori* eradication treatment had been prescribed. The letter also informed the general practitioner that open access breath testing was available to check whether the infection had been eradicated. We told the general practitioners that a negative breath test indicated that the symptoms were likely to be due to non-ulcer dyspepsia or gastro-oesophageal reflux disease.

Follow up

One year after randomisation, we asked the patients to attend an interview by non-medical, non-nursing staff for documentation of outcome. At that time, the Glasgow dyspepsia severity score and the SF-36 quality of life assessment were repeated. Details were also obtained from the patient about visits to the general practitioner or hospital for dyspepsia or other conditions, further investigations, and use of prescribed and over the counter drugs for dyspepsia or other conditions since randomisation. We used a computer based questionnaire to obtain this information. Most patients were able to interact directly with the computer, and assistance was provided as required. In addition, patients were asked about their concern regarding their condition, their concern about possible missed underlying disease, and their overall satisfaction with their initial investigation and management. These factors were assessed by asking the patient to place a mark on a Likert-type scale. The patients also had a ¹⁴C-urea breath test to re-check their *H pylori* status.

Power calculation

The planned study of 672 patients (436 positive for *H pylori*, 236 negative for *H pylori*) followed up at one year had 90% power to detect a difference in mean change in the Glasgow dyspepsia severity score of 1.03 in the *H pylori* positive subgroup and 1.41 in the *H pylori* negative subgroup at the 5% significance level overall (2.5% per subgroup). The expected proportion of 65% *H pylori* positive cases was based on an earlier study in our population with dyspepsia. The standard deviation of the change in dyspepsia score was assumed to be 3.5.

Statistical analysis

We compared the two treatment groups by using the two sample *t* test or the Mann-Whitney U test, as appropriate. We compared categorical data by using the χ^2 test, and we used analysis of variance to compare subgroups. We determined 95% confidence intervals where appropriate. We used the statistical package Minitab version 13 to make calculations, and made no correction in the subgroup analysis for multiple testing.

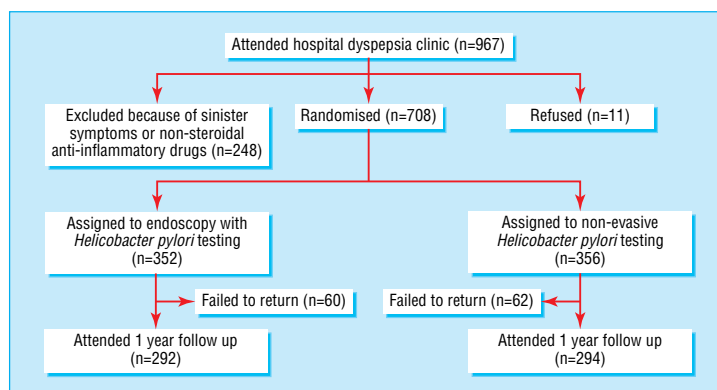


Fig 1 Flow chart of recruitment

Results

Over the two year recruitment period from October 1997 to October 1999, we saw 967 patients aged under 55 at the one stop dyspepsia clinic, which represented 81% of those who had been sent appointments. Of these 967 patients, 248 were not eligible for randomisation because of sinister symptoms or use of non-steroidal anti-inflammatory drugs and 11 refused randomisation (fig 1).

The predominant symptom was recorded in 705 of the 708 patients randomised and was epigastric pain or discomfort in 380 (54%), heartburn or acid reflux in 207 (29%), and a variety of other upper gastrointestinal symptoms in the remainder. The mean age of patients randomised was 36 (range 17-57) years, and 377 (53%) were men. The prevalence of *H pylori* infection was 50% (352/708).

In total, 352 patients were randomised to endoscopy with *H pylori* testing and 356 patients to non-invasive *H pylori* testing alone. The prevalence of *H pylori* infection was 51% (181/352) in the endoscopy plus breath test group and 48% (171/356) in the breath test alone group; the two groups were also similar in other respects (tables 1 and 2). Table 3 shows the endoscopic findings in the patients randomised to that investigation, subclassified according to predominant symptom and *H pylori* status.

One year after randomisation 292 (83%) of the 352 patients randomised to endoscopy and 294 (83%) of the 356 patients randomised to non-invasive *H pylori*

Table 1 Characteristics of the two groups at randomisation. Values are numbers (percentages) unless stated otherwise

	Endoscopy plus breath test (n=352)	Breath test alone (n=356)
Mean (SD; range) age in years	35.5 (9.4; 17-54)	36.6 (8.9; 18-57)
Male	190/352 (54)	187/356 (53)
Smokers	133/349 (38)	161/353 (46)
<i>Helicobacter pylori</i> positive	181/352 (51)	171/356 (48)
Mean (SD; range) Glasgow dyspepsia severity score	10.2 (2.1; 4-16)	10.3 (2.3; 4-16)
Median duration of dyspepsia (scored <0.5, 0.5-2, 2-5, 5-10, >10 years)	2-5 years	2-5 years
Proportion taking prescribed antisecretory drugs most days in previous six months	116/352 (33)	132/355 (37)
Heartburn or acid reflux as predominant symptom	87/352 (25)	120/353 (34)
Epigastric pain or discomfort as predominant symptom	199/352 (57)	181/353 (51)
Mean (SD; range) concern about condition (0-10 scale)	5.0 (2.2; 0-10)	5.2 (2.4; 0-10)
Mean (SD; range) concern about underlying serious disease (0-10 scale)	4.1 (2.4; 0-10)	4.4 (2.4; 0-10)

Table 2 Median (interquartile range) SF-36 quality of life scores

	At presentation		At one year		Improvement	
	Endoscopy plus breath test (n=349)	Breath test alone (n=352)	Endoscopy plus breath test (n=283)	Breath test alone (n=289)	Endoscopy plus breath test (n=283)	Breath test alone (n=289)
Physical functioning	95 (80 to 100)	90 (80 to 100)	95 (85 to 100)	95 (85 to 100)	0 (0 to 5)	0 (0 to 10)
Role functioning—physical	100 (50 to 100)	100 (50 to 100)	100 (75 to 100)	100 (75 to 100)	0 (0 to 25)	0 (0 to 25)
Bodily pain	61 (42 to 74)	56 (41 to 74)	72 (52 to 84)	72 (51 to 100)	9 (–10 to 26)	10 (0 to 28)
General health	65 (47 to 77)	62 (57 to 77)	72 (52 to 82)	72 (52 to 82)	2 (–5 to 12)	5 (–5 to 15)
Vitality	50 (40 to 70)	50 (35 to 65)	55 (40 to 70)	60 (40 to 75)	5 (–10 to 15)	5 (–5 to 20)
Social functioning	75 (62 to 100)	75 (50 to 100)	87 (62 to 100)	87 (62 to 100)	0 (0 to 25)	0 (0 to 25)
Role functioning—emotions	100 (33 to 100)	100 (33 to 100)	100 (33 to 100)	100 (33 to 100)	0 (0 to 33)	0 (0 to 33)
Mental health	68 (54 to 84)	68 (52 to 80)	72 (60 to 84)	76 (58 to 88)	0 (–8 to 16)	4 (–4 to 12)

testing could be reassessed (fig 1). The *H pylori* eradication rates at one year in the two groups were 79% (119/150) and 84% (118/141).

Primary outcome

The primary outcome measured was the Glasgow dyspepsia severity score. One year after randomisation, the mean change in score was similar in the endoscopy and non-invasive *H pylori* testing groups at 4.8 and 4.6 (95% confidence interval for difference –0.7 to 0.5, P=0.69). This represented a mean reduction in dyspepsia score since initial assessment of 46% in patients randomised to endoscopy and 45% in those randomised to the breath test. The mean scores at one year were similar at 5.4 and 5.6 in the two groups. The proportion of patients with complete resolution of dyspepsia (score <2) was similar in the two groups at 42/291 (14%) and 33/293 (11%) (–2% to 9% for difference, P=0.25).

The mean change in score in the *H pylori* positive patients was 5.4 in the endoscopy group and 5.0 in the breath test group (–1.2 to 0.5 for difference, P=0.38). In the *H pylori* negative patients the corresponding figures were 4.0 and 4.3 (–0.5 to 1.0, P=0.48).

Subsequent use of medical resources

The two groups were similar at one year with respect to proportions attending their general practitioner and hospital and use of prescribed and over the counter drugs over the 12 month period since randomisation (table 4). They were also similar with respect to repeat referral for further non-endoscopic investigations (table 4).

The subsequent use of endoscopy differed only slightly between the randomised groups. Of the 292 patients randomised to initial endoscopy and followed up, five (1.7%) were referred for a further endoscopy, compared with 24 (8.2%) of the 294 patients

randomised to initial non-invasive *H pylori* testing (95% confidence interval for difference 3% to 10%, P<0.001).

Patient oriented outcome

One year after randomisation, mean overall concern of patients about their disease and concern about missed pathology were similar in the two groups (table 4). The relative reassurance after non-invasive *H pylori* testing compared with endoscopy was unaffected by the magnitude of concern about serious disease at the time of randomisation (fig 2). Overall satisfaction with initial investigation and management (table 4) and SF-36 quality of life scores at one year after randomisation were similar in the two groups (table 2).

We also assessed the patients' experience of the two investigational procedures on an integer scale of 0 to 6, with 0 indicating no recollection, 1 no discomfort, and 6 severe distress. After the breath test, 96% of patients gave the test a score of 1, whereas only 13% of patients randomised to endoscopy had a score of 0 or 1 (95% confidence interval for difference 78% to 87%, P=0.000) (table 5). Of the patients randomised to endoscopy, 20% elected to have intravenous sedation with midazolam. Of those sedated, 32% could not remember the procedure, and the median score in the remainder was 2. The median score after the endoscopy without sedation was 4. After non-invasive *H pylori* testing, 341/342 (99.7%) said they would happily have it again compared with 38/66 (58%) after endoscopy with sedation and 79/256 (31%) after endoscopy without sedation. After endoscopy without

Table 3 Endoscopic diagnosis and relation to *Helicobacter pylori* status and predominant symptom in patients randomised to endoscopy plus *H pylori* testing. Values are numbers of patients

Diagnosis	<i>H pylori</i> positive (n=172)		<i>H pylori</i> negative (n=165)	
	Heartburn or acid reflux (n=37)	Other symptom (n=135)	Heartburn or acid reflux (n=49)	Other symptom (n=116)
Normal	24	94	38	95
Oesophagitis grade I	9	9	8	15
Oesophagitis grade II	1	2	2	1
Gastric ulcer (including prepyloric ulcer)	—	9	—	2
Duodenal ulcer	3	19	1	3
Gastric ulcer plus duodenal ulcer	—	1	—	—
Low grade MALToma	—	1	—	—

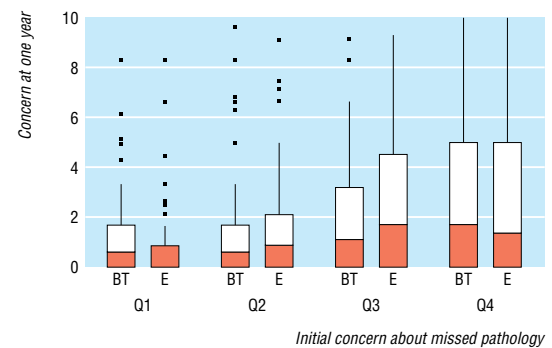


Fig 2 Box and whisker plots showing range, quarters, and median scores for concern about missed pathology at one year in the two groups, subdivided according to quarter (Q1-Q4) of concern at initial assessment. Points denote outliers. In some cases, minimum, Q1, and median are all 0. BT=non-invasive breath test for *Helicobacter pylori*; E=endoscopy plus *H pylori* testing

sedation, 66/253 (26%) said they would take sedation if they had to have the procedure again.

Safety

Table 3 shows the endoscopic diagnoses in the patients randomised to initial endoscopy. The only potentially serious abnormality detected was a low grade gastric MALToma (mucosal associated lymphoid tumour) identified in a routine biopsy from one of the *H pylori* positive patients. Further investigation indicated that this was confined to the gastric mucosa and needed no treatment other than the *H pylori* eradication treatment that had been given under the routine study protocol. The endoscopic diagnosis in the 24 patients randomised to non-invasive *H pylori* testing and then referred later for endoscopy showed no abnormality in 17 patients, oesophagitis grade I in three, oesophagitis grade II in two, and duodenal ulcer in one; the remaining patient could not tolerate the examination. There was no evidence of *H pylori* in the patient with the duodenal ulcer. Repeat endoscopic examination was normal in the five patients randomised initially to endoscopy and referred for further endoscopy.

Subgroup analysis

We analysed the results to see if the outcome of the two investigation strategies was affected by *H pylori* status and character of symptoms at presentation (table 6). The outcomes were similar in the two treatment strategies in patients who were *H pylori* negative compared with those who were positive and in patients with predominant heartburn or reflux symptoms compared with those with other predominant symptoms. Analysis of variance fitting treatment, *H pylori* status, and symptom at presentation as main effects showed no evidence of a significant treatment effect on Glasgow dyspepsia severity score ($P=0.95$), worry about condition ($P=0.55$), concern about missed pathology ($P=0.48$), or satisfaction ($P=0.89$).

Discussion

The use of simple non-invasive testing for *H pylori* in place of endoscopy in determining the management of

Table 4 Comparison of the two randomised groups over subsequent year. Values are numbers (percentages) unless stated otherwise

	Endoscopy plus breath test (n=292)	Breath test alone (n=294)
Mean (SD; range) Glasgow dyspepsia severity score	5.4 (3.4; 0-15)	5.6 (3.4; 0-15)
Frequency of:		
Visit to general practitioner for dyspepsia	98/292 (34)	108/293 (37)
Attendance at hospital outpatient clinic for dyspepsia	19/292 (7)	18/293 (6)
Endoscopy	4/292 (1)	24/294 (8)
Repeat breath test (in patients testing positive on entry)	27/292 (9) (26/156 (17))	19/294 (6) (18/142 (13))
Barium meal	5/292 (2)	1/294 (0.3)
Ultrasonography	3/292 (1)	10/294 (3)
Other gastrointestinal investigations	11/292 (4)	7/294 (2)
Drug usage (% treated) (median length of treatment):		
Proton pump inhibitor	69/291 (24) (24 weeks)	77/292 (26) (20 weeks)
H ₂ receptor antagonist	56/291 (19) (10 weeks)	68/293 (23) (20 weeks)
Antacids	82/291 (28) (18 weeks)	90/293 (31) (10 weeks)
Alginates	73/290 (25) (12 weeks)	82/291 (28) (6 weeks)
Patient oriented outcomes (0-10: 0=no concern, 10=extreme concern)		
Mean (SD; range) overall concern about symptoms	2.4 (2.6; 0-10)	2.4 (2.4; 0-10)
Mean (SD; range) concern about missed disease	1.7 (2.3; 0-10)	1.9 (2.5; 0-10)
Mean (SD; range) overall satisfaction with management	8.9 (1.6; 0.8-10)	8.9 (1.7; 0-10)

patients with uncomplicated dyspepsia has been the subject of debate for several years. This large prospective randomised study indicates that non-invasive *H pylori* testing is as effective and safe as endoscopy and is less uncomfortable and distressing for the patient.

The primary outcome was the Glasgow dyspepsia severity score. This was similar at one year in the two randomised groups, having fallen by 46% since entry in the endoscopy group and by 45% in the breath test alone group. A strength of the study was that it also assessed a wide range of other relevant outcomes, including subsequent use of medical resources, patient oriented outcomes, and safety.

Use of endoscopy

Subsequent use of endoscopy in patients randomised to non-invasive *H pylori* testing was low at 8.2% and only slightly higher than the 1.7% use of repeat endoscopy in patients randomised to initial endoscopy. The

Table 5 Discomfort score recorded after breath test alone, endoscopy with sedation, and endoscopy without sedation. Values are numbers (percentages)

	Cannot remember 0	No discomfort 1	2	3	4	5	Severe distress 6	Total (n=661) 7
Breath test alone	0	327 (95.6)	9 (2.6)	2 (0.6)	3 (0.9)	0	1 (0.3)	342
Endoscopy with sedation	20 (31.7)	14 (22.2)	12 (19.0)	4 (6.3)	4 (6.3)	6 (9.5)	3 (4.8)	63
Endoscopy without sedation	0	8 (3.1)	50 (19.5)	64 (25)	39 (15.2)	70 (27.3)	25 (9.8)	256

Table 6 Mean outcome scores (SD; range) at one year subdivided by *Helicobacter pylori* status and predominant symptom at initial presentation

	Positive for <i>H pylori</i>				Negative for <i>H pylori</i>			
	Heartburn or acid reflux		Other		Heartburn or acid reflux		Other	
	Endoscopy plus breath test (n=41)	Breath test alone (n=64)	Endoscopy plus breath test (n=95)	Breath test alone (n=87)	Endoscopy plus breath test (n=34)	Breath test alone (n=34)	Endoscopy plus breath test (n=121)	Breath test alone (n=105)
Glasgow dyspepsia severity score (0-20)	6.0 (2.8; 1-13)	6.4 (3.1; 1-15)	6.2 (3.4; 1-15)	5.7 (3.1; 0-14)	5.4 (3.2; 1-14)	6.1 (3.4; 1-14)	4.6 (3.6; 0-13)	4.8 (3.8; 1-16)
Worry about condition (0-10)	2.2 (2.2; 0-8)	2.4 (2.5; 0-9.5)	2.6 (2.5; 0-10)	2.8 (2.5; 0-10)	3.3 (2.9; 0-8.5)	2.7 (2.7; 0-8)	2.2 (2.6; 0-10)	1.8 (2.2; 0-9)
Concern about missed disease (0-10)	1.5 (1.9; 0-7.2)	1.9 (2.4; 0-9.3)	1.5 (2.1; 0-10)	2.1 (2.5; 0-10)	2.2 (2.7; 0-8.3)	1.9 (2.6; 0-10)	1.8 (0.4; 0-9.7)	1.6 (2.4; 0-10)
Overall satisfaction with management (0-10)	8.9 (1.6; 5-10)	8.8 (1.9; 1.7-10)	8.8 (1.7; 1.7-10)	8.5 (1.8; 5-10)	9.1 (1.1; 5-10)	9.3 (1.0; 5-10)	8.9 (1.7; 0.8-10.0)	9.4 (1.5; 0-10)

use of endoscopy over the 12 month follow up was thus reduced by 94% in patients randomised to non-invasive *H pylori* testing. This marked reduction in endoscopy was not accompanied by any subsequent increased use of other medical resources. Non-invasive *H pylori* testing is substantially cheaper than endoscopy, and its use will therefore reduce the overall cost of medical care.

Reassurance of patients and acceptability of procedure

Previous studies have shown that endoscopic examination is helpful, even if results are negative, as it reassures patients and reduces their overall concern.^{19, 20} Our study has shown that non-invasive *H pylori* testing is equivalent to endoscopy in this respect. It is often assumed that non-endoscopic investigation strategies will be inappropriate for patients who are particularly worried about an underlying serious disease at initial presentation. However, our study indicated that the most worried patients had equivalent reassurance from endoscopy and non-invasive breath test.

Another important consideration in deciding which investigation to use is the acceptability of the procedure itself to the patient. Patients found the breath test less uncomfortable and distressing than endoscopy. Endoscopy is now usually performed without sedation, and most patients found this procedure distressing and expressed unwillingness to undergo the experience again.

Safety

A concern about widespread implementation of non-invasive *H pylori* testing in place of endoscopy is that upper gastrointestinal malignancy may be missed in some patients. For that reason, we excluded patients with sinister symptoms and those aged 55 or over. A previous retrospective study in our catchment area²¹ and one from another region in the United Kingdom²² indicated that underlying malignancy in such patients presenting for endoscopy was extremely rare and when present was rarely curable. In this study, of the 352 patients who were randomised to initial endoscopy only one had a potentially serious condition. He had a normal endoscopy but was positive for *H pylori* and was found to have low grade MALToma in one of the gastric biopsies taken as part of the study protocol. This condition fully resolved with the standard *H pylori* eradication treatment that he had received as part of the study and before the histology became available. Consequently, this patient would not have been adversely affected by being randomised to non-invasive *H pylori* testing and eradication.

There is particular concern currently about the rising incidence of carcinoma at the gastro-oesophageal junction and of premalignant Barrett's oesophagus.²³ Our region has the highest reported incidence of this cancer in the world.²⁴ Despite this, not a single case of Barrett's oesophagus, severe oesophagitis (> grade II), or gastro-oesophageal junction malignancy occurred in our 352 patients recorded and randomised to endoscopy. Excluding patients with dysphagia and those aged over 55 seems to be an effective means of excluding potentially serious disease of the gastro-oesophageal junction.

Effect of predominant symptom

We included patients with the full spectrum of upper gastrointestinal symptoms, including patients whose symptoms indicated gastro-oesophageal reflux disease. Subanalysis of our results indicated that the two investigation strategies were equivalent in the patients with heartburn or reflux as well as in patients with more ulcer-like symptoms (table 6). The endoscopy, therefore, added no discernible value to the breath test in the management of either group of patients.

The prevalence of ulcers in the patients positive for *H pylori* with predominant heartburn or reflux symptoms was only 8%, which was significantly less than the 21% found in the *H pylori* positive patients with other upper gastrointestinal symptoms and little higher than the 4% seen in *H pylori* negative patients (table 3). The value of the test and eradicate *H pylori* strategy in the patients with heartburn or reflux was therefore relatively small, at least with respect to cure of underlying ulcers. It has recently been proposed that this strategy should be limited to patients with more ulcer-like symptoms, as this reduces the number of patients receiving *H pylori* treatment for each ulcer cured.²⁵ However, there are arguments both in favour of and against treating *H pylori* in patients with gastro-oesophageal reflux disease, and the subject remains very complex and controversial.²⁶ Empirical treatment without any investigation may be appropriate for patients with uncomplicated symptoms of heartburn or reflux.

Generalisability of findings

Are the results of our study generalisable to other regions and populations? The prevalence of infection with *H pylori* in our patients with dyspepsia was approximately 50%, which is similar to the mean value of 55.2% reported in a large meta-analysis of the prevalence of *H pylori* in patients with non-ulcer dyspepsia.²⁷ However, the prevalence of the infection varies considerably, depending largely on the socio-economic status and age of the group being studied.²⁸ Subanalysis indicated that the two strategies were of equivalent efficacy, irrespective of *H pylori* status at presentation. However, in populations with a very low prevalence of the infection and of *H pylori* related ulcer disease, both investigation strategies may be superfluous.

Previous studies

Only one previous study randomised patients with upper gastrointestinal symptoms to non-invasive *H pylori* testing or endoscopy.²⁹ That study, by Lassen et al, concluded that the test and eradicate *H pylori* strategy was as efficient and safe as prompt endoscopy. However, it did find that slightly fewer patients were very satisfied one year after non-invasive *H pylori* testing (56%) than after endoscopy (62%). In contrast, we found that satisfaction was similar after the two strategies, and this may be related to our specialist team providing the patients with a fuller description of the relative merits of the two modes of investigation.

One previous study compared the cost of management by non-invasive *H pylori* testing or by endoscopy by randomising general practices to the two investigation strategies.³⁰ The study included patients aged under 45 with ulcer-like symptoms for more than four weeks, without alarm symptoms, and in whom the gen-

eral practitioner considered further investigation appropriate. Over the 12 months after randomisation, the total cost of consultations, referrals, investigations, and treatment was on average £404.31 in the endoscopy group compared with only £205.67 in the non-invasive *H pylori* testing group.

Two smaller studies have compared *H pylori* testing with endoscopy in subgroups of patients with dyspepsia referred for endoscopy. Heaney et al randomised 500 patients aged under 45 referred to secondary care with ulcer-like dyspepsia and who had a positive *H pylori* breath test to either *H pylori* eradication or endoscopy and eradication of the infection in only those with ulcers.⁶ Over the one year follow up, the first group had superior relief of symptoms and a reduction of 75% in the use of endoscopy. A further study by Asante et al studied 154 patients aged under 45 with upper gastrointestinal symptoms, including heartburn or reflux symptoms, who were referred for open access endoscopy and found to have a negative result on serological testing for *H pylori*.⁴ The patients were randomised to endoscopy or no endoscopy and followed up for two years. No differences were found between the two investigation strategies with respect to resolution of dyspepsia, use of drugs, or visits to the general practitioner. Use of endoscopy was reduced by 83% over the two year follow up.

Conclusion

Our current study and the previous studies, therefore, all indicate that non-invasive testing for *H pylori* is as effective as endoscopy in managing patients with uncomplicated upper gastrointestinal symptoms. The non-endoscopic strategy has two potential benefits. The first is that patients find the procedure of non-invasive *H pylori* testing less uncomfortable and distressing than endoscopic examination. The second is that non-invasive *H pylori* testing is substantially cheaper than endoscopy. For these reasons, non-invasive *H pylori* testing seems to be the preferred investigation for patients with uncomplicated dyspepsia.

Finally, it should be emphasised that our study provides information on the relative merits of only two investigational strategies. It is likely that other approaches, such as empirical treatment without investigation or the use of other investigations, will be more appropriate for certain patients.

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What is already known on this topic

Endoscopy is a commonly used investigation for upper gastrointestinal symptoms, but its effectiveness has been questioned

Non-invasive testing for *Helicobacter pylori* has been shown to predict endoscopic diagnosis in patients with dyspepsia

What this study adds

In patients less than 55 years of age with uncomplicated dyspepsia, non-invasive testing for *H pylori* is as effective and as safe as endoscopy

Non-invasive *H pylori* testing is as reassuring to the patient as endoscopy and is less uncomfortable and distressing

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