Note: This is a two-article spread with a shared commentary. Please scroll down for the second article.

Noninvasive *Helicobacter pylori* testing was as effective as endoscopy for managing dyspepsia

McColl KE, Murray LS, Gillen D, et al. **Randomised trial of endoscopy with testing for *Helicobacter pylori* compared with non-invasive *H. pylori* testing alone in the management of dyspepsia.** BMJ. 2002;324:999-1002.

QUESTION

In patients with upper gastrointestinal symptoms presenting for investigation of dyspepsia, is treatment based on a urea breath test for *Helicobacter pylori* alone as effective as endoscopy and urea breath testing?

DESIGN

Randomized {allocation concealed*}†, unblinded,* controlled trial with 1-year follow-up.

SETTING

A gastroenterology clinic in Glasgow, Scotland, UK.

PATIENTS

708 patients (mean age 37 y, 53% men) who were referred by their general practitioners for investigation of upper gastrointestinal symptoms. Exclusion criteria were age > 55 years, nonsteroidal anti-inflammatory drugs, or sinister symptoms. Follow-up was 83%.

INTERVENTION

Patients were allocated to endoscopy plus the noninvasive ^{14}C urea breath test (n = 352) or the breath test alone (n = 356) for determination of *H. pylori* status. Patients were informed of their status after the test, and patients with positive results were prescribed a 7-day course of *H. pylori* eradication treatment with omeprazole, 20 mg twice daily; clarithromycin, 250 mg 3 times daily; and amoxicillin, 500 mg (or metronidazole, 400 mg) 3 times daily.

MAIN OUTCOME MEASURES

Change from baseline on the Glasgow Dyspepsia Severity Score (GDSS). Secondary outcomes were use of medical resources, patient assessment of the procedures, and safety.

MAIN RESULTS

Analysis was by intention to treat. At 1 year, the mean change from baseline on the GDSS was similar between groups (P = 0.69) (Table). The study had 90% power to detect a difference in mean change on the GDSS of 1.03 and 1.41 between the groups that were positive and negative for *H. pylori*, respectively. The mean reduction in GDSS was 46% in the endoscopy group and 45% in the breath test–alone group. Groups did not differ for resolution of dyspepsia (14% vs 11%, P = 0.25). More patients who received the breath test alone were referred for further endoscopy than were those who received the breath test and endoscopy (8.2% vs 1.7%, P < 0.001). Groups did not differ for further nonendoscopic investigations.

CONCLUSION

In patients with upper gastrointestinal symptoms presenting for investigation of dyspepsia, a urea breath test for *Helicobacter pylori* was as effective as endoscopy plus breath test for managing dyspepsia.

Source of funding: NHS Executive Research and Development Technology Assessment Programme.

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*See Glossary.

†Information provided by author.

Noninvasive ^{14}C urea breath test vs endoscopy plus breath test for dyspepsia at 1 year‡

Outcome	Breath test (baseline)	Endoscopy plus breath (baseline)	Difference in mean change from baseline (95% CI)
Glasgow Dyspepsia Severity Score	5.6 (10.2)	5.4 (10.2)	0.2 (–0.7 to 0.5)

‡CI defined in Glossary.

COMMENTARY

Patients with dyspeptic symptoms should be managed with 2 goals in mind: early detection of malignant disease and cost-effective relief of symptoms. Patients < 55 years of age without "alarm features" (e.g., weight loss, dysphagia, and anemia) are at very low risk for malignancy and do not require endoscopic investigation. The question of management then turns on the relative costs and effectiveness of endoscopy, noninvasive tests, and eradication of *H. pylori* and empiric acid suppression a (1).

The trials by McColl and Chiba and their colleagues provide important information for physicians managing patients presenting with uninvestigated dyspepsia. The study by McColl and colleagues adds to 2 previous studies (2, 3) that confirm the cost-effectiveness of a secondary care–based *H. pylori* test-and-treat service compared with endoscopy-based management. All 3 trials of test-and-treat compared with endoscopy-based management showed equivalent effectiveness, but costs were reduced because fewer patients had endoscopy. The trial by McColl and colleagues showed a rate of endoscopy in the year of follow-up in the test-and-treat group of only 8%, whereas Heaney (2) and Lassen (3) showed rates nearer 30%. Patients positive for *H. pylori* in both groups of the trial by McColl and colleagues received eradication therapy. Thus, any differences caused by the eradication therapy itself were abolished. The trial can therefore be considered to address the question, "Is the cost of endoscopy warranted by the effect on symptoms, quality of life, and patient satisfaction of having the investigation?" The answer is "no."

The trial by Chiba and colleagues (CADET-*Hp*) takes the McColl and colleagues' trial 2 steps further. First, patient recruitment and the intervention took place in a primary care setting. Second, test-and-treat was compared with acid suppression alone. In contrast to the trial by McColl and colleagues, CADET-*Hp* was designed to examine the effect of eradication therapy on dyspeptic symptoms and found a substantial improvement in the proportion of patients with dyspeptic symptoms at the end of the trial. However, the difference in costs was small and not statistically significant.

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Helicobacter pylori eradication improved dyspepsia symptoms

Chiba N, Veldhuyzen van Zanten SJ, Sinclair P, et al. **Treating *Helicobacter pylori* infection in primary care patients with uninvestigated dyspepsia: the Canadian adult dyspepsia empiric treatment—*Helicobacter pylori* positive (CADET-*Hp*) randomised controlled trial.** BMJ. 2002;324:1012-6.

QUESTION

In patients with dyspepsia and a positive test result for *Helicobacter pylori*, is an *H. pylori* eradication strategy more effective than placebo for improving dyspepsia symptoms?

DESIGN

Randomized {allocation concealed*}†, blinded (clinicians, patients, data collectors, outcome assessors, {data analysts and manuscript writers}†),* placebo-controlled trial with 1-year follow-up.

SETTING

36 family practices in Canada.

PATIENTS

294 patients (mean age 49 y, 50% men) who were ≥ 18 years of age and had uninvestigated symptoms of dyspepsia for ≥ 3 months. Dyspepsia was defined as a complex of epigastric pain including heartburn, acid regurgitation, excessive burping or belching, increased abdominal bloating, nausea, abnormal or slow digestion, or early satiety. All patients had to have positive test results for *H. pylori* on the Helisal rapid blood test and the ^{13}C urea breath test. Exclusion criteria included gastroesophageal reflux disease, upper gastrointestinal investigation in the previous 6 months or ≥ 2 times in the past 10 years, eradication therapy for *H. pylori* in the past 6 months, previous gastric surgery, ulcer disease or endoscopic esophagitis, and the irritable bowel syndrome. Follow-up was 87%.

INTERVENTION

Patients were allocated to omeprazole, 20 mg; metronidazole, 500 mg; and clarithromycin, 250 mg (eradication) (n = 145), or omeprazole, 20 mg, and placebo metronidazole and placebo clarithromycin (placebo) (n = 149) twice daily for 7 days.

MAIN OUTCOME MEASURES

Global overall severity of dyspepsia symptoms assessed with a 7-point scale (1 = no problem, 7 = very severe problems). Treatment success was a score of 1 or 2. Secondary outcomes were proportion of asymptomatic patients and treatment success according to *H. pylori* status.

MAIN RESULTS

Analysis was by intention to treat, and an analysis of all evaluable patients was also done (n = 267). Patients in the eradication group had greater treatment response than did those in the placebo group (Table). More patients in the eradication group were completely asymptomatic (Table). Treatment was more successful in patients in whom *H. pylori* was eradicated than in those it was not (54% vs 39%, P = 0.02). Eradication treatment reduced societal costs, but the difference was not statistically significant (Cdn $53, 95% CI −86 to 180).

CONCLUSION

In patients with dyspepsia and a positive test result for *Helicobacter pylori*, an *H. pylori* eradication strategy was more effective than placebo for improving dyspepsia symptoms.

Source of funding: Astra-Zeneca Canada Inc.

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*See Glossary.

†Information provided by author.

***Helicobacter pylori* eradication vs placebo for uninvestigated dyspepsia at 1 year‡**

Outcomes	Eradication	Placebo	RBI (95% CI)	NNT (CI)
Treatment success	50%	36%	37% (5 to 80)	7 (4 to 63)
Completely asymptomatic	28%	15%	92% (21 to 205)	8 (5 to 24)

‡Abbreviations defined in Glossary; RBI, NNT, and CI calculated from data in article.

COMMENTARY *(continued from page 16)*

The reason for the difference in effects and costs between CADET-*Hp* and McColl and colleagues lies in the use of eradication therapy for *H. pylori*. In CADET-*Hp*, the control-group patients did not receive eradication therapy and were therefore at risk for recurrent peptic ulcers that had healed initially with omeprazole. Furthermore, patients with nonulcer dyspepsia may also benefit from *H. pylori* eradication. A Cochrane review of 9 placebo-controlled trials of *H. pylori* eradication therapy in patients without peptic ulcers or esophagitis at endoscopy found a number needed to treat of 15 (4).

The CADET-*Hp* trial does not show conclusively that *H. pylori* test-and-treat is more cost-effective in primary care than omeprazole alone, because it was only done in *H. pylori*–positive patients. The cost-effectiveness of this strategy needs to be tested by randomizing patients with dyspepsia, both positive and negative for *H. pylori*, before noninvasive testing for *H. pylori* to determine the effect of the management strategy on the whole group. It does, however, lend more support to the eradication of *H. pylori* in all patients known to be infected.

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