Testing for *Helicobacter pylori* in primary care: trouble in store?

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Abstract

Study objective—To assess the role of testing for *Helicobacter pylori* in the management of dyspeptic patients in primary care.

Design—Selective review of literature frequently quoted to support use of *H pylori* testing.

Main results—Testing for *H pylori* and referral of only positive cases for endoscopy aims to reduce the number of “unnecessary” endoscopies. Patients with negative results may receive short-term reassurance and subsequently place fewer demands on health services. However, studies to date have only assessed this practice in secondary care settings. Given the relatively high prevalence of both dyspepsia and *H pylori* infection, the transfer of this practice to primary care may lead to a paradoxical increase in endoscopy referrals. Identification of *H pylori* and prescribing of eradication treatment also aims to reduce endoscopy referrals. No primary care trials have yet assessed this approach. Given that fewer than one in four of dyspeptic patients have peptic ulceration, a high proportion may fail to respond to eradication treatment and subsequently require referral for endoscopy. The longer term clinical and psychosocial sequelae of treating or labelling patients with an infection associated with gastric cancer remain unknown.

Conclusions—Given uncertainty concerning the possible adverse effects of *H pylori* testing in primary care, we suggest a moratorium on its use in this setting until results from relevant clinical trials become available.

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pathology.⁵⁻⁸ Investigation, usually with upper gastrointestinal endoscopy, is required to establish a definitive diagnosis. This creates a problem: only endoscopy can ensure a definite diagnosis but referral of all dyspeptic patients would increase pressures on already stretched endoscopy services.

The discovery of *Helicobacter pylori* in 1983,^{9 10} and growing knowledge about its associations with upper gastrointestinal pathology are driving major changes in the management of dyspepsia.¹¹ *H pylori* eradication therapy cures and prevents recurrence of peptic ulcer disease but the utility of eradication in the management of dyspepsia from other causes remains unproved.¹²⁻¹⁴

Despite this, and other gaps in the evidence base, recent consensus guidelines recommend that *H pylori* testing becomes an integral component in the management of dyspeptic patients in primary care.^{15 16} A number of local guidelines also support this position (telephone survey of North West medical advisers, 1995).

We present a commentary on evidence frequently quoted to support the adoption of two commonly promoted practices (see fig 1) that use *H pylori* testing in primary care: (1) *H pylori* testing with endoscopy for those who test positive and reassurance or symptomatic treatment for negative cases; (2) *H pylori* testing and eradication therapy in positive cases with endoscopy reserved for symptomatic non-responders, and reassurance or symptomatic treatment for negative cases.

Both strategies set an age related threshold for referral for endoscopy, usually 45 years, to minimise the likelihood of failing to detect gastric malignancy, which is uncommon below this age.^{17 18}

Means of detecting *H pylori* in primary care

H pylori infection can be diagnosed by invasive and non-invasive methods. Invasive methods (histology, culture, and testing for Campylobacter-like organisms) require biopsy specimens to be taken at endoscopy and their use in primary care is therefore less appropriate.

Two non-invasive methods generally advocated for use in primary care are urea breath testing and serology. Breath tests detect labelled carbon dioxide hydrolysed from 13C- or 14C-labelled urea by the *H pylori* urease enzyme. Although highly sensitive and specific, this method has two main drawbacks, patients usually have to fast before examination; and the capital equipment costs are high.¹⁹

Serological testing for IgG and IgA antibodies to *H pylori* is highly sensitive and specific²⁰⁻²³

The management of dyspepsia places a major clinical and economic burden on the health service.^{1 2} General practitioners are under increasing pressure to contain increases in endoscopy referrals and prescribing of acid suppressing drugs.

Most people who experience dyspepsia do not seek medical attention as the majority of episodes are self limiting and treated by over the counter medication. Nevertheless, approximately one quarter of people with dyspeptic symptoms consult their general practitioner,³ accounting for up to 4% of all consultations.⁴

Dyspepsia may signify the onset of major upper gastrointestinal disease but clinical identification of the underlying cause is problematic as symptoms poorly predict underlying

Figure 1 Strategies proposed for the treatment of young patients with dyspepsia in primary care.

and is the only test unlikely to give false negative results in patients recently treated with antibiotics, bismuth compounds or proton pump inhibitors (PPIs).¹³ However, serology may be less sensitive in older patients with *H pylori* infection.²⁴

Serology testing seems to be the most attractive option for the initial detection of *H pylori* in primary care; it currently costs approximately one third of the price of urea breath testing and whole blood desk top kits can produce results in minutes in the surgery. When combinations of invasive and 13C urea breath tests are used as gold standards, their sensitivity (88–89%) and specificity (91%) are comparable with laboratory-based serological assays.^{24–25} Other researchers have found the test to be of lower accuracy,²⁶ perhaps indicating that the accuracy of serology kits varies in different populations.²⁷ Interpretation of results may also be hampered by interobserver error.²⁸ Urea breath testing is more appropriate in confirming eradication as serology tests can remain positive for up to six months after eradication.²⁹

H pylori testing and selection for endoscopy

The rationale behind this strategy is to maximise detection of peptic ulceration while reducing the number of “unnecessary” (that is, normal or negative) endoscopies.

Approximately 90% of peptic ulcers are associated with *H pylori* infection.¹⁴ Observational studies suggest that selecting only *H pylori* seropositive patients for endoscopy could result in the detection of almost all peptic ulcers while achieving reductions of 23–39% in endoscopy workload.^{30–37} However, cost savings may take between 5 and 18 years to accrue, largely depending on costs of acid suppressing medication and prevalence of infection.³⁸

While improving the diagnostic yield of peptic ulceration, this approach may underestimate the impact of negative endoscopy results,

associated with reduced general practitioner consultation and prescribing rates.^{39–41} A negative *H pylori* test may also confer some reassurance and result in similar benefits within the year after testing.³⁷ However, dyspepsia is a chronic, fluctuating syndrome with intermittent periods of breakthrough symptoms,⁴² and extended follow up is required to demonstrate the sustainability of such benefits. Presumed savings made by identifying and thus not investigating seronegative patients may diminish in the longer term should reassurance from a negative *H pylori* test prove insufficient, or dyspeptic symptoms unrelated to *H pylori* infection (for example, gastro-oesophageal reflux disease) recur.

All studies published to date tested for *H pylori* in patients already referred for endoscopy. It is not possible to ascertain the proportions of new and prevalent cases, although it may be reasonable to assume that the latter group predominates and that results from these studies cannot be generalised to new dyspeptic patients presenting in primary care.

Given the high background levels of *H pylori* seropositivity in the population,⁴³ a substantial proportion of dyspeptic patients with no evidence of peptic ulceration will test positive. Guidelines to general practitioners could make it explicit that *H pylori* testing should only take place after the decision to refer for endoscopy.¹⁵ However, experience suggests that availability of investigations, especially near patient tests, in primary care leads to an expansion of their original indications.^{44–45} Thus, if seropositivity is accepted as a criterion for investigation, and the threshold for use of *H pylori* testing is lowered, a paradoxical increase in endoscopy referrals may occur. Over-reliance on *H pylori* testing as a criterion for referral may also distract general practitioners from considering other risk factors in the pathogenesis of peptic ulceration, for example, smoking and alcohol intake.

Identification of *H pylori* and eradication therapy before endoscopy

The rationale behind this approach is that eradication therapy should cure and therefore avoid the need for endoscopy referral in most patients with peptic ulcer disease.^{46–48} Costs of maintenance acid suppressing drugs would be reduced for patients with peptic ulcer disease and, possibly, a proportion of patients with non-ulcer dyspepsia who respond to either true therapeutic or placebo effects.

Decision analyses suggests testing and eradication may be of equal or greater cost effectiveness compared with conventional management.^{47–49–50} However, conclusions are particularly sensitive to costs used, for example, of endoscopy or acid suppressing agents, with *H pylori* detection and investigation becoming more cost effective as endoscopy charges and drug costs increase.

On current evidence, less than one in four *H pylori* positive dyspeptic patients have peptic ulcer disease and can be expected to benefit from eradication therapy.^{30–34–51} This proportion may be less in dyspeptic patients presenting for

the first time in primary care.⁵² Treating all seropositive patients would therefore result in the majority of cases, most of whom would have non-ulcer dyspepsia, receiving an unproved treatment. Symptoms may recur or persist in many of these patients and up to one quarter of those with peptic ulcers not initially responding to eradication therapy (because of antibiotic resistance or poor compliance). General practitioners, unable to discriminate on clinical grounds between unresponsive peptic ulceration and non-ulcer dyspepsia, would have to decide whether to refer for endoscopy or start longer term treatment with acid suppressing drugs. Urea breath testing could determine whether eradication had occurred but sufficient clinical uncertainty might persist in the minds of both general practitioners and patients to prompt an endoscopy referral. If urea breath testing indicated the presence of active *H pylori* infection, consideration would have to be given to non-compliance or antibiotic resistance, and investigation of antibiotic resistance would necessitate endoscopy.

Therefore, the cost effectiveness of this approach in primary care could be undermined if a large number of symptomatic non-responders are referred for endoscopy or require further courses of acid suppressing drugs. Further disadvantages of this practice lie in its potential to induce antibiotic resistance through the widespread use of eradication therapy. The prevalence of *H pylori* resistance to metronidazole, commonly incorporated in eradication regimens, is around 40% in the UK.⁵³ However, metronidazole resistance does not necessarily prevent eradication and use of metronidazole for other indications will probably, at present, play a more significant part in inducing resistance. Side effects of current eradication regimens are frequent but perceived as severe enough by less than 10% of patients to warrant withdrawing from treatment.⁵⁴⁻⁵⁶ However, insufficient counselling of patients before beginning eradication treatment may also undermine effectiveness.

Trouble in store? Psychosocial sequelae of *H pylori* testing

H pylori has been defined as a category one (definite) carcinogen by the WHO/IARC.⁵⁷ An association with gastric cancer has been determined with a relative risk of between 2 and 9,⁵⁸⁻⁶² although the absolute risk to people with evidence of infection is probably small. A precise aetiological role of *H pylori* in the development of gastric cancer has not yet clearly been established.⁶³ Conflicting evidence of an association with ischaemic heart disease also exists.^{64 65} Until the long term results of intervention studies are known, the identification and eradication of *H pylori* remains unproved in the prevention of gastric cancer, or even ischaemic heart disease.¹³

Such knowledge places clinicians and patients in a difficult and uncertain position and there is pressure to prescribe eradication therapy if *H pylori* has been identified.⁶⁶ Infection with *H pylori* has not been shown to influence consulting rates in dyspeptic patients⁶⁷ but

KEY POINTS

- General practitioners are under increasing pressure to contain the prescribing and referral costs of treating dyspepsia.
- The availability of non-invasive tests for the detection of *H pylori* is driving major changes in the treatment of dyspepsia by general practitioners.
- Practices based upon *H pylori* detection in primary care may paradoxically increase prescribing costs and endoscopy referrals.
- Patient labelling from knowledge of *H pylori* status can also change consulting behaviour.
- A moratorium on testing in primary care may be necessary until results from relevant trials are available.

knowledge of *H pylori* status may modify both patient and doctor behaviour in unforeseen ways. The process of screening or disease labelling after a positive result may have psychosocial costs,^{68 69} including subsequent changes in health seeking behaviour.^{70 71}

Doctors and patients may perceive the relative risk of gastric cancer in *H pylori* infected people as being sufficiently high to warrant action. Individual perceptions of risk,⁷² coupled with the widespread uptake of serological testing, could have important effects on both patient and doctor behaviour, for example, by increasing consultation rates and lowering thresholds for further investigation. Severity or frequency of dyspeptic symptoms correlate poorly with decisions to consult: health beliefs and knowledge play more significant parts, especially if symptoms are perceived to be associated with cancer or ischaemic heart disease.⁷³ Alternatively, providing patients with a negative result, or eradicating *H pylori* in those with positive results, may yield improved psychosocial outcomes. No trial has yet assessed the psychological consequences of *H pylori* serological testing and treatment.

Information given to patients before and after testing is also likely to influence subsequent consulting behaviour. At present, few general practitioners report discussing the likelihood of gastric cancer with patients after a positive *H pylori* test.⁷⁴ Patient labelling could be avoided by prescribing eradication treatment to dyspeptic patients empirically without ascertaining *H pylori* status but the cost effectiveness and acceptability of this approach remain uncertain.

Conclusion

Testing for *H pylori* is being incorporated into routine clinical practice in primary care.^{75 76} Furthermore, media coverage of *H pylori* and promotion of screening by commercial health agencies may fuel public pressure for routine testing. Yet widespread serological testing in primary care could have substantial long term psychosocial and resource implications.

Use of *H. pylori* testing and eradication therapy could yet be proved to deliver significant advantages over conventional management of dyspepsia in primary care.¹⁴ Understandably, general practitioners are keen to adopt methods perceived as more cost effective in treating a common and costly symptom.⁷⁷ However, evidence from secondary care based studies is being inappropriately applied to primary care settings despite important differences in the prevalence of disease in these populations.¹¹ Interpretation of these studies is further limited by non-randomised or retrospective designs and comparatively short follow up periods that may fail to detect longer term adverse effects related to patient labelling.

There is a need for scepticism in the face of premature claims of cost effectiveness to prevent unnecessary medicalisation of patients' lives as well as to guide further research. Similar experiences have occurred in the past when, for example, it was argued that use of cholesterol lowering drugs in the primary prevention of ischaemic heart disease threatened "to turn a large percentage of the healthy population into patients, at a substantial potential cost to the NHS".⁷⁸ Given the uncertainty concerning the benefits and risks of *H. pylori* testing in primary care, we suggest a moratorium on its use in this setting until results from relevant clinical trials are available.

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