Reappraisal of non-invasive management strategies for uninvestigated dyspepsia: a cost-minimization analysis
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
Two approaches for the treatment of patients with uninvestigated dyspepsia were examined. These were Helicobacter pylori (H. pylori) test-and-treat versus empirical antisecretory (proton-pump inhibitor) therapy. The test-and-treat strategy included an enzyme-linked immunoabsorbent assay serological testing for H. pylori. Those patients who tested positive were treated with a 14-day course of proton-pump inhibitor-based triple therapy, while those who had negative serology were given standard-dose proton-pump inhibitor therapy for 4 weeks. All patients in the empirical antisecretory therapy group received a 4-week course of standard-dose proton-pump inhibitor therapy, without any diagnostic assessment.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The hypothetical study population comprised patients with uncomplicated dyspepsia of sufficient severity to justify an empirical course of antisecretory therapy. It was assumed that the patients had no prior evaluation for H. pylori or prior documentation of peptic ulcer disease.

Setting
The setting was primary care. The economic study used data from the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1985 and 2001. The dates relating to resource use were not reported. No price year was given.

Source of effectiveness data
The effectiveness evidence was derived from a review of published studies.

Modelling
A one-year symptom-driven decision analytical model was constructed to predict the natural history of peptic ulcer disease and its interaction with H. pylori. In addition, to assess the overall costs of the two treatment approaches in a hypothetical cohort of 1,000 patients with uninvestigated dyspepsia. Every 6 weeks, the patients were distributed among different health states. The model was validated using the authors’ epidemiological data. Specific details of the model were presented elsewhere (Fendrick, et al., see Other Publications of Related Interest).
Outcomes assessed in the review
The model parameters estimated in the analysis were the clinical probabilities of the following:

H. pylori prevalence;

the likelihood of active ulcer disease;

the fraction of ulcers due to H. pylori;

the success rate (including compliance) for H. pylori eradication;

the ulcer healing rate after antisecretory therapy;

the recurrent symptom rate with active ulcer, healed ulcer and no ulcer;

the ulcer recurrence rate with and without H. pylori infection; and

the sensitivity and specificity of the H. pylori serological test.

Study designs and other criteria for inclusion in the review
Some of the primary studies included in the review were randomised trials and population-based studies. A significant source of the epidemiological data was the authors' clinical study, as reported in Ladabaum et al. (see Other Publications of Related Interest).

Sources searched to identify primary studies
MEDLINE was searched for English language articles providing data that could be used as model inputs. The bibliographies of accepted articles were also reviewed. Current issues of the peer-reviewed general medicine, infectious disease, and gastroenterology literature were searched for additional data.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Thirty-nine primary studies were included in the review.

Methods of combining primary studies
The primary study estimates were combined using narrative methods.

Investigation of differences between primary studies
Not carried out.

Results of the review
The H. pylori prevalence was 25% (range: 10 - 60).
The likelihood of active ulcer disease was 20% (range: 10 - 30).

The fraction of ulcers due to H. pylori was 75% (range: 60 - 90).

The ulcer healing rate after antisecretory therapy was 75% (range: 60 - 90).

The H. pylori eradication success rate (including compliance) was 80% (range: 70 - 90).

The recurrent symptom rate per year was 90% (range: 50 - 90) with active ulcer, 10% (range: 0 - 30) with healed ulcer, and 30% (range: 10 - 50) with no ulcer.

The ulcer recurrence rate per year was 72% (range: 60 - 90) with H. pylori infection and 20% (range: 10 - 30) with no infection.

The sensitivity of the H. pylori serological test was 85% (range: 75 - 90) and the specificity was 79% (range: 70 - 85).

**Measure of benefits used in the economic analysis**
The main clinical outcome derived from the decision model was the proportion of patients developing active peptic ulcer disease at one year. There was no significant difference between the alternatives (less than 1% of the patients developing active peptic ulcer disease at one year in both strategies). Hence, a cost-minimisation analysis was actually performed.

**Direct costs**
Discounting was not required since the costs were incurred during one year. The unit costs were reported separately from the quantities of resources used. The health service costs included in the analysis were for the H. pylori serological test, endoscopy, rapid urease test, proton-pump inhibitor therapy, H. pylori eradication therapy, primary care physician office visit, gastroenterologist office visits, and hospitalisation for ulcer complication with or without surgery. The cost/resource boundary adopted was that of the third-party payer. The costs were estimated on the basis of the national average charges allowed by the Health Care Financing Administration for Medicare reimbursement rates. The costs of proton-pump inhibitor therapy and H. pylori eradication therapy were derived from the University of Michigan Hospital pharmacy. The source of the resource use data was not reported. No price year was given.

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were carried out to assess the robustness of the estimated costs per patient treated to variations in the model inputs over the ranges reported under the 'Results of the Review' section. The key variables investigated were the prevalence of H. pylori, the likelihood of peptic ulcer disease in patients presenting with uncomplicated dyspepsia, and the fraction of ulcers attributable to H. pylori. The ranges were broader for the prevalence of H. pylori (5 - 95%) and the likelihood that a patient with uninvestigated dyspepsia has peptic ulcer disease (0 - 80%). These were considered particularly influential parameters.
Estimated benefits used in the economic analysis
See the 'Measure of Benefits used in the Economic Analysis' section.

Cost results
The cost per patient treated was $545 in the test-and-treat strategy and $529 in the empirical antisecretory therapy. The sensitivity analyses showed that the most efficient intervention depended on the prevalence of H. pylori, the likelihood of having peptic ulcer disease, and the proportion of ulcers that can be attributed to H. pylori. However, in general, the costs of the empirical proton-pump inhibitor therapy were lower than those of the test-and-treat option, although the cost difference was modest.

Below an H. pylori prevalence of approximately 20%, the combinations of H. pylori prevalence and likelihood of having peptic ulcer disease that are possible at a population level all represent circumstances under which empirical proton-pump inhibitor is less costly than the test-and-treat strategy. This is regardless of whether the fraction of ulcers attributable to H. pylori is 60 to 90%. The model was successfully validated using the authors' epidemiological data.

Synthesis of costs and benefits
Not relevant as a cost-minimisation analysis was carried out.

Authors' conclusions
The test-and-treat strategy and the empirical antisecretory treatment were similar, both in terms of the costs and clinical outcomes. The prevalence of Helicobacter pylori (H. pylori) played an important role at both the individual patient level and at the population level. At a disease prevalence of below 20%, the empirical proton-pump inhibitor therapy was slightly cheaper than the test-and-treat strategy.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. The two strategies were selected, as both represented currently used options for the treatment of patients with uninvestigated dyspepsia. You should decide whether they are widely used interventions in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used a review of published studies. The search methods and the design of some of the primary studies were reported. However, the primary study data were combined using narrative methods, and it was not stated whether the authors took into account differences such as sample population, comparators, and sample size when estimating the effectiveness. The inclusion and exclusion criteria of the review were not reported. Only some of the estimates used in the effectiveness study were investigated in the sensitivity analyses.

Validity of estimate of measure of benefit
No summary benefit measure was used since the clinical outcomes derived from the decision model were similar in the two study groups, as already reported in the literature. The analysis was therefore categorised as a cost-minimisation study.

Validity of estimate of costs
The analysis of the costs was conducted from the perspective of the third-party payer. It appears that all the relevant categories of costs have been included in the study. The unit costs were reported and a detailed breakdown of the costs was given. However, no price year was reported, thus making reflation exercise in other settings difficult. The costs and the quantities were treated deterministically and only a few sensitivity analyses were conducted. The source of the resource use data was not reported. The authors highlighted the fact that true costs, rather than charges, were used in the economic evaluation.
Other issues
The authors noted that a recent study of dyspeptic patients in primary care found H. pylori testing to be of little incremental value beyond the clinical history for predicting the presence of peptic ulcer disease, except for those at high risk of peptic ulcer disease (Weijnen et al., see Other Publications of Related Interest). This was consistent with the results of this study. The authors did not address the issue of the generalisability of the study results to other settings. Consequently, the level of the external validity of the analysis was fairly low. The study referred to patients with uninvestigated dyspepsia and this was reflected in the conclusions of the analysis. The authors commented on the limitations of the assumptions made in the study.

Implications of the study
The main implication of the study was that empirical proton-pump inhibitor therapy led to modest cost-savings in comparison with the test-and-treat strategy as the prevalence of H. pylori infection declines, as the risk of peptic ulcer disease falls and as the proportion of patients with H. pylori-negative peptic ulcer disease increases in the population. However, the authors stated that "the test-and-treat strategy may be favoured if any long-term benefit of H. pylori testing and treatment extends to patients without existing peptic ulcer disease". The authors noted that some caution is required when interpreting the study results, as recent studies show probability values differ from those used in the decision model.

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Bibliographic details

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Other publications of related interest


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Subject indexing assigned by NLM

MeSH
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Analysis /methods; Decision Support Techniques; Drug Therapy, Combination; Dyspepsia /drug therapy /economics /microbiology; Health Care Costs; Helicobacter Infections /complications /diagnosis /drug therapy; Helicobacter pylori; Humans; Models, Econometric; Peptic Ulcer /drug therapy /economics /microbiology; Primary Health Care /economics /methods; Proton Pump Inhibitors; United States

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