Helicobacter pylori "test and treat" or endoscopy for managing dyspepsia: an individual patient data meta-analysis


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
The study compared a Helicobacter (H.) pylori "test and treat" strategy (i.e. testing for H. pylori and treating the positive patients) versus prompt upper-gastrointestinal endoscopy for the management of dyspepsia.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adults suspected of having dyspepsia. The authors defined dyspepsia as a cluster of symptoms attributable to the upper gastrointestinal tract, including epigastric or upper abdominal pain, heartburn, regurgitation and nausea.

Setting
The setting was primary and secondary care. The economic study was carried out in the UK.

Dates to which data relate
The data for the meta analysis (including effectiveness and resource use data) were obtained from studies published between 1999 and 2003 and from the study results related to a personal communication from 2004. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies.

Outcomes assessed in the review
The outcomes assessed were the standardised mean difference (SMD), relative risk (RR) and associated 95% confidence interval (CI) for total dyspepsia symptom score, and the presence of dyspepsia at 12 months. In addition, sub-group analyses were performed by comparing both strategies for various sub-groups of patients. Specifically, females, males, patients with epigastric pain, patients with predominant heartburn, and patients aged 50 years or older.

Study designs and other criteria for inclusion in the review
Studies were included in the review if they were randomised controlled trials (RCTs) that compared a prompt endoscopy strategy with a "test and treat" approach for the initial management of dyspepsia in adults, either managed in
primary or in secondary care. The studies also had to have reported outcome data including symptom resolution, resource use, and cost-effectiveness. Dyspepsia was defined as a cluster of symptoms attributable to the upper gastrointestinal tract (see 'Study Population' section).

Sources searched to identify primary studies
To identify relevant trials, the prospective trials register of the Cochrane Library was supplemented with searches of the Cochrane database of RCTs and MEDLINE until December 2003.

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

Methods used to judge relevance and validity, and for extracting data
Original datasets were obtained directly from researchers and were standardised to allow direct comparisons among trials. Further details of the peer-reviewed analysis plan can be found elsewhere (Delaney et al. 2004, see 'Other Publications of Related Interest' below for bibliographic details).

Number of primary studies included
Five studies were identified.

Methods of combining primary studies
The primary studies were combined by a meta-analysis. The authors had access to individual patient trial data and the analysis was performed on an intention to treat basis.

Investigation of differences between primary studies
Where heterogeneity between the results of the trials was detected, a random-effects model was used.

Results of the review
Data for 1,924 patients (946 endoscopy and 978 "test and treat") were processed. The mean age was 40 years in the endoscopy group and 41 years in the "test and treat" group.

The SMD in symptom scores at 12 months for patients undergoing endoscopy compared with "test and treat" was -0.11 (95% CI: -0.28 - 0.07).

The RR of remaining symptomatic after 1 year was reduced with endoscopy compared with "test and treat" (RR 0.95, 95% CI: 0.92 - 0.99).

The results of the sub-group analysis showed there to be no statistically significant differences between the management strategies for female patients, male patients, patients with epigastric pain, patients with predominant heartburn, pylori-positive patients and pylori-negative patients. However, there was a small, statistically significant difference in favour of endoscopy for the sub-group of patients aged 50 years or older.

Measure of benefits used in the economic analysis
Being symptom-free at 12 months was considered to be the summary measure of benefit. This was directly estimated from the meta-analysis. Therefore, the reader is referred to the 'Results of the Review' section.

Direct costs
Although no perspective was reported, the direct costs considered in the economic analysis appear to have been those of the health service. They included primary and secondary care visits (i.e. general practitioner visits, outpatient visits and hospitalisations), the costs of prescribed drugs for dyspepsia (i.e. proton-pump inhibitors, histamine 2 receptor antagonists, prokinetics, antacids and eradication therapy) and investigational tests (i.e. urea breath test, endoscopy, barium meal and abdominal ultrasound). Cost estimations were based on actual data (i.e. total dyspepsia-related resource use for 1,771 patients) derived from the RCTs included in the review. The costs were obtained for a United States setting. Average retail prices were used for pharmaceuticals, while physician costs were obtained from the American Medical Association procedural codebook and the 2003 Medicare fee schedule.

Discounting was not carried out, but it was not relevant as the follow-up period was 12 months. The unit costs were presented separately for some items, but resource use quantities were not reported. The price year was not reported. The authors did not state any adjustments for protocol-driven costs. The estimated costs were reported as the weighted mean differences (WMD) in costs between prompt endoscopy and the "test and treat" strategy.

**Statistical analysis of costs**
The costs were treated stochastically (95% CIs were reported).

**Indirect Costs**
No indirect costs were reported.

**Currency**
US dollars ($).

**Sensitivity analysis**
There was a limited assessment of the uncertainty related to variability in the data. Only a one-way sensitivity analysis on the cost of endoscopy was performed. The cost of endoscopy was reduced to $80 (in line with charges in some European countries).

**Estimated benefits used in the economic analysis**
See the 'Results of the Review' section.

**Cost results**
The WMD in total cost per patient for prompt endoscopy versus "test and treat" was $389 (95% CI: 276 - 502). This indicated that prompt endoscopy cost more per patient than "test and treat".

Much of the increased burden related to prompt endoscopy patients was accounted for by the costs of investigations (WMD $318, 95% CI: 285 - 350).

**Synthesis of costs and benefits**
An incremental net benefit analysis, which considered a range of values for the willingness to pay per symptom-free patient, was performed. Mean net benefits for each of the trial arms were pooled.

Despite the small effect difference in favour of endoscopy, when the mean net benefit for each trial arm was pooled, increasing the value for willingness to pay per patient symptom-free (lambda) from $0 to $1,000 did not make prompt endoscopy a cost-effective approach (WMD -$330, 95% CI: -236 - -423).

Prompt endoscopy would become cost-effective if the willingness to pay per patient symptom-free of dyspepsia was $180,000 or higher.
The results of the sensitivity analysis showed that even with a cost of $80 per endoscopy, prompt endoscopy only became cost-effective when the willingness to pay per patient symptom-free of dyspepsia reached $40,000.

**Authors' conclusions**
Prompt endoscopy confers a small benefit in terms of cure of dyspepsia, but it costs more than "test and treat". It is not a cost-effective strategy for the initial management of dyspepsia when realistic levels of willingness to pay per patient symptom-free of dyspepsia are considered.

**CRD COMMENTARY - Selection of comparators**
The authors selected the "test and treat" strategy, based on current practice, as guidelines for different countries have recommended this approach. Prompt endoscopy was chosen because recent studies have selected it as a possible alternative to the "test and treat" strategy. The reader should decide if these are relevant technologies in their own setting.

**Validity of estimate of measure of effectiveness**
The authors did not state whether a systematic review of the literature had been performed. In spite of this, the study followed an analysis plan that had been peer-reviewed and published in the Cochrane Library (Delaney et al. 2004). Moreover, the prospective trials register was supplemented by searches of the Cochrane database of RCTs and MEDLINE. It is therefore likely that the methodology and conduct of the review were satisfactory. The estimates of effectiveness were arrived at by the use of meta-analysis techniques with patient level data. As the authors had access to patient level data, adjustments for differences in sample sizes were not necessary. The authors standardised the different study datasets before combining them. The estimates of effectiveness were estimated credibly from the studies identified.

The authors reported further limitations of their effectiveness data. For instance, the original trials were not blinded and, therefore, the possibility that this might have led to a small bias in favour of endoscopy cannot be excluded. Also, the follow-up period was only 12 months. However, they acknowledged that blinding in this case would have not been possible, and that long-term data were scarce.

**Validity of estimate of measure of benefit**
The authors derived the summary measure of benefits directly from the meta-analysis on individual patient data. The reader is therefore referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

**Validity of estimate of costs**
Although not explicitly stated, the analysis was performed from the perspective of a third-party payer. All the relevant cost categories from this perspective appear to have been considered in the analysis, and all relevant costs for each category seem to have been included. The unit costs for the main cost items were reported separately but the resource quantities used were not, hence limiting the reproducibility of the study in other settings. Appropriate statistical analyses of the costs were performed, which adds to the reliability of the results. A sensitivity analysis was performed on only one of the possible cost drivers to assess the robustness of the results. The price year was not reported. Currency conversions or discounting were not necessary and were not performed. The authors stated that the costs were reported in US dollars due to the lack of reference costs for Denmark and the Netherlands. However, the study was performed in the UK. It would therefore have been more useful had the costs been reported in UK pounds sterling.

**Other issues**
The authors compared their effectiveness results with those of the Cochrane Review, although appropriate cost-effectiveness comparisons with those results from other economic evaluations were not reported. The issue of generalisability was explicitly addressed when discussing the limitations of using USA fees. Specifically, the generalisability of the results to countries where the cost of endoscopy is much lower than in the USA might not be
implications of the study
the study showed that the cost of prompt endoscopy as a first-line approach for the management of dyspepsia without alarm symptoms is prohibitive in everyday clinical practice. a "test and treat" strategy seems to be preferable.

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