Dyspepsia management in primary care: a decision analysis of competing strategies

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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
Four alternative strategies available for the treatment of uninvestigated dyspepsia were considered.

One was an initial test and treat strategy (T&T), beginning with a serum enzyme-linked immunosorbent assay for Helicobacter pylori (H. pylori). Patients who test positive receive a 14-day course of antibiotic therapy for H. pylori eradication, whereas those who test negative receive a 6-week trial of once-daily proton-pump inhibitor (PPI). Patients nonresponding or those who relapse would follow a 6-week course of once-daily PPI, while persistently symptomatic patients would subsequently progress to endoscopy (EGD; i.e. T&T-PPI-EGD strategy).

The other strategies were:

- an initial PPI trial, followed by EGD for nonresponders (PPI-EGD strategy);
- an initial PPI trial, followed by T&T for nonresponders, followed by EGD for persistently symptomatic patients (PPI-T&T-EGD strategy); and
- an initial T&T, followed by EDG for nonresponders (T&T-EDG strategy).

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study considered a hypothetical cohort of patients younger than 45 years of age, presenting to their primary care provider for the first time with a complaint of recurrent upper abdominal pain or discomfort. Patients were excluded if they presented "alarm" symptoms (e.g. bleeding, weight loss, dysphagia, anorexia, vomiting), or if they had predominant symptom of acid reflux or regurgitation. They were also excluded if they were taking long-term nonsteroidal anti-inflammatory drugs.

Setting
The setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1987 and 2001. The study did not report the dates when the resource data were gathered. The price year appears to have been 2000.

Source of effectiveness data
NHS Economic Evaluation Database (NHS EED)
Produced by the Centre for Reviews and Dissemination
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The evidence was derived from a systematic review of published studies, and from authors’ assumptions.

**Modelling**
A decision tree was designed to compute the cost-effectiveness of the four strategies for the treatment of uninvestigated dyspepsia. The time horizon considered was 1 year.

**Outcomes assessed in the review**
The following clinical and effectiveness data were obtained from the literature review and included as inputs in the model:

- the probability that the cause of dyspepsia is nonulcer dyspepsia (NUD);
- the probability that NUD is H. pylori positive;
- the probability that the cause of dyspepsia is peptic ulcer disease (PUD);
- the probability that PUD is H. pylori positive;
- the probability that the cause of dyspepsia is oesophagitis;
- the probability that oesophagitis is H. pylori positive;
- the probability that the cause of dyspepsia is gastric cancer;
- the probability that gastric cancer is H. pylori positive;
- the probability that H. pylori is successfully eradicated by the first round of antibiotic therapy;
- the probability that H. pylori is successfully eradicated by the second round of antibiotic therapy;
- the probability that a patient with NUD has initial symptom improvement 1 year after anti-H. pylori therapy;
- the probability that a patient with NUD has sustained symptom improvement 1 year after anti-H. pylori therapy;
- the probability that a patient with PUD has initial symptom improvement with anti-H. pylori therapy;
- the probability that a patient with PUD has symptom improvement after 1 year of continuous PPI therapy;
- the probability that a patient with oesophagitis has initial symptom improvement with the PPI trial;
- the probability that a patient with oesophagitis has sustained symptom improvement after 1 year of continuous PPI therapy; and

- the probability that a patient with gastric cancer has initial symptom improvement with the PPI trial.

**Study designs and other criteria for inclusion in the review**
The authors reported that studies published between 1985 and 2001, and those identified by reviewing bibliographies of key references, were considered for inclusion in the review. No other inclusion criteria were reported.
Sources searched to identify primary studies
MEDLINE, HealthSTAR and the Cochrane Database of Systematic Reviews were searched.

Criteria used to ensure the validity of primary studies
Although the authors commented that they relied most heavily on those studies with highest quality, they did not report any criteria used to assess the validity of the primary studies.

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

Number of primary studies included
Seventy studies were included in the review.

Methods of combining primary studies
The authors used data from the included studies selectively. The range of results coming from the included studies was used in the sensitivity analysis as a range for some of the parameters.

Investigation of differences between primary studies
The authors did not investigate differences between the primary studies.

Results of the review
The following values were included as parameters of the model:

the probability that the cause of dyspepsia is NUD, 66%;
the probability that NUD is H. pylori positive, 48%;
the probability that the cause of dyspepsia is PUD, 23%;
the probability that PUD is H. pylori positive, 90%;
the probability that the cause of dyspepsia is oesophagitis, 10%;
the probability that oesophagitis is H. pylori positive, 40%;
the probability that cause of dyspepsia is gastric cancer, 0.5%;
the probability that gastric cancer is H. pylori positive, 85%;
the probability that the first round of antibiotic therapy successfully eradicates H. pylori, 85%;
the probability that the second round of antibiotic therapy successfully eradicates H. pylori, 80%;
the probability that a patient with NUD has initial symptom improvement 1 year after anti-H. pylori therapy, 48%;
the probability that a patient with NUD has sustained symptom improvement 1 year after anti-H. pylori therapy, 33%;
the probability that a patient with PUD has initial symptom improvement with anti-H. pylori therapy, 85%;
the probability that a patient with PUD has sustained symptom improvement 1 year after anti-H. pylori therapy, 70%;
the probability that a patient with oesophagitis has initial symptom improvement with anti-H. pylori therapy, 25%;
the probability that a patient with NUD has initial improvement with the PPI trial, 38%;
the probability that a patient with PUD has initial symptom improvement with the PPI trial, 80%;
the probability that a patient with PUD has sustained symptom improvement after 1 year of continuous PPI therapy, 75%;
the probability that a patient with oesophagitis has initial symptom improvement with the PPI trial, 80%;
the probability that a patient with oesophagitis has sustained symptom improvement after 1 year of continuous PPI therapy, 70%;
the probability that a patient with gastric cancer has initial symptom improvement with the PPI trial, 33%.

Methods used to derive estimates of effectiveness
The authors formulated several assumptions to derive some of the effectiveness estimators.

Estimates of effectiveness and key assumptions
The authors assumed the following:

the probability that a patient with oesophagitis has sustained symptom improvement after 1 year of anti-H. pylori therapy was 15%;
the probability that a patient with gastric cancer has initial symptom improvement with anti-H. pylori therapy was 10%;
the probability that a patient with gastric cancer has sustained symptom improvement after 1 year of continuous PPI therapy was 2%;
the probability that a patient with NUD has sustained symptom improvement with the PPI trial was 28%; and
the probability that a patient with gastric cancer has sustained symptom improvement 1 year after anti-H. pylori therapy was 2%.

Measure of benefits used in the economic analysis
The measures of benefits used were the quality-adjusted life-years (QALYs) and the number of symptom-free patients after 1 year. The utilities from mild, moderate and severe dyspepsia symptoms were obtained from a study that used the time trade-off method in a sample of 73 patients. These utilities were combined to calculate base-case QALYs, assuming that 50% of the cohort had severe dyspepsia, 25% had moderate dyspepsia and 25% had mild dyspepsia.

Direct costs
The cost/resource boundary adopted was that of a third-party payer. The broad expenditure areas were drug costs, diagnostic procedure costs, endoscopic costs and physicians’ fees. Most of the resources used were reported separately from the costs, or could be easily derived from the data reported in the paper. The source of the resource use data was not reported. The drug costs were collected from the 2000 Red Book of average wholesale prices for pharmaceuticals. The costs for EGD, diagnostic procedures and physician services were obtained from the 2000 American Medical Association Current Procedural Terminology Code Book and the 2000 Medicare Fee Schedule. The costs were estimated using both actual data and authors’ assumptions. The price year appears to have been 2000.
Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
No indirect costs were included.

Currency
US dollars ($).

Sensitivity analysis
The area of uncertainty investigated was variability in both the effectiveness parameters and cost data. The authors developed a second model in which patients with persistent symptoms were not tested for H. pylori. One-way sensitivity analyses were carried out to evaluate the effects on the results of varying individual cost and probability estimates over the ranges observed in the literature. Two-way sensitivity analyses and threshold analyses were also performed on the most clinically significant and potentially influential variables. Monte Carlo simulations were performed to assess second-order uncertainty around base-case estimates of the model. Simulations of 100, 500, 1,000 and 2,000 trials were carried out.

Estimated benefits used in the economic analysis
The T&T-PPI-EGD, and PPI-T&T-EGD strategies showed 84% symptom-free patients and 0.98 QALYs, compared with 75% symptom-free patients and 0.92 QALYs for the T&T-EGD strategy, and 78% symptom-free patients and 0.97 QALYs for the PPI-EGD strategy.

Cost results
The authors reported a cost per patient of $1,628 for the PPI-EGD strategy, $1,902 for the T&T-EGD strategy, $1,680 for the T&T-PPI-EGD strategy and $1,788 for the PPI-T&T-EGD strategy. The cost estimation included those costs incurred due to complications associated with EGD and the use of antibiotics.

Synthesis of costs and benefits
In both the cost-effectiveness and cost-utility analyses, an average and a marginal analysis were performed.

The average cost-effectiveness in terms of cost per symptom-free at 1 year was $2,535 for the T&T-EGD strategy, $1,996 for the T&T-PPI-EGD strategy, $2,078 for the PPI-EGD strategy and $2,124 for the PPI-T&T-EGD strategy. The average cost-utility in terms of cost per QALY gained was $2,067 for the T&T-EGD strategy, $1,714 for the T&T-PPI-EGD strategy, $1,678 for the PPI-EGD strategy and $1,824 for the PPI-T&T-EGD strategy. The T&T-EGD strategy was a dominated alternative in the marginal analysis of both the cost-effectiveness and the cost-utility analyses.

The results of the threshold sensitivity analysis showed that PPI-EGD was the most cost-effective alternative under the following assumptions:

the cost of upper endoscopy without a rapid urease test was lower than $152 (baseline value $544);

the cost of 14 days of anti-H. pylori therapy was more than $450 (baseline value $304);

the cost of 1 month of PPI therapy was less than $45 (baseline value $90);

the probability that H. pylori is eradicated by the first round of antibiotic therapy was less than 60%;

the probability that symptoms of NUD initially improve with anti-H. pylori therapy was less than 15%;
the probability that oesophagitis is the cause of dyspepsia was more than 70%;
the probability that PUD is the cause of dyspepsia was less than 8%;
the probability of NUD as the cause of dyspepsia was less than 25%;
the probability that PUD is H. pylori positive was less than 50%; and
the probability that NUD is H. pylori positive was less than 12%.

The two-way sensitivity analysis showed that the T&T-PPI-EGD strategy remained the most cost-effective as long as:
the cost of EGD remained above $250 and the probability of NUD symptom improvement with H. pylori eradication remained above 36%;
when the cost of antibiotic therapy remained below $360 and the probability of oesophagitis remained below 55%.

The current guidelines (i.e. T&T-EGD) did not become cost-effective under any combination of costs or probability estimates.

The results of the Monte Carlo simulations were comparable to those of the base-case analysis.

Authors' conclusions
The current guidelines for the treatment of uninvestigated dyspepsia are not cost-effective in comparison with proton-pump inhibitor (PPI)-based approaches. Each of the three PPI-based strategies in the study appears to have reduced unnecessary invasive procedures, while achieving improved symptom control and quality of life at a lower overall cost, compared with the current American Gastroenterological Association guidelines.

CRD COMMENTARY - Selection of comparators
The T&T-EGD strategy was explicitly chosen as the comparator since it represents standard practice in the USA for uncomplicated dyspepsia in a primary care setting. You must decide whether this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
Although the authors stated that a systematic review of the literature was undertaken and they searched for literature using MEDLINE, HealthSTAR, and the Cochrane Library, a full systematic review may not have been undertaken for all the effectiveness parameters. This is a common practice in modelling studies. However, it does not always ensure that the best data available are used in the model. The authors appear to have used data from the studies selectively and did not consider the impact of differences between the studies when estimating the effectiveness. Although the authors stated that they relied mostly on those sources with the highest methodological quality, they did not report how the quality of the studies was assessed or how the data extraction was performed. To compensate for this limitation, the authors conducted a thorough sensitivity analysis in all areas of uncertainty. A positive point of the study was that all the sources used to derive estimates of effectiveness were clearly identified.

Validity of estimate of measure of benefit
QALYs and the number of symptom-free patients after 1 year were the benefit measures used for the economic analysis. These would appear to be valid measures of benefit. Moreover, the use of QALYs allows comparisons of study results across different interventions.

Validity of estimate of costs
The perspective of a third-party payer was adopted in the study. Relevant cost categories were included for this
perspective. The sources of the resource use data were not reported and the price year was not clearly identified (although it appears to have been 2000). The resource quantities were reported separately, or could be derived from the information provided in the paper, thus enhancing the reproducibility of the study to other settings. To assess uncertainty, extensive sensitivity analyses on the cost parameters used were performed.

**Other issues**
The authors compared their findings with those from other studies, which, in general, showed the findings to be in agreement. The cost estimates are likely to be specific to the USA and, as the authors reported, may not be generalisable to other settings. The authors acknowledged several limitations of their study. First, where data were equivocal or absent, the assigned values tended to bias the model in favour of current guidelines. Second, a 1-year time horizon might be inadequate to realistically portray the natural history of dyspeptic patients. Third, patients rendered asymptomatic with PPI therapy were assumed to continue once-daily PPI therapy indefinitely, when in reality this does not happen. However, extensive sensitivity analyses were performed and the results of the model were shown to be robust. Although several Monte Carlo simulations were performed to evaluate second-order uncertainty, the results of these simulations were reported as deterministic and, consequently, the level of second-order uncertainty surrounding the study results could not be appropriately assessed from the paper.

**Implications of the study**
The results of the study supported the conclusion that the endorsement of current guidelines should be reappraised. In addition, a prospective trial comparing alternative PPI-based treatment strategies should be conducted.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**
11984514

**Other publications of related interest**


**Indexing Status**
Subject indexing assigned by NLM
MeSH
Cost-Benefit Analysis; Decision Support Techniques; Dyspepsia /drug therapy; Enzyme Inhibitors /therapeutic use; Health Care Costs; Helicobacter Infections /drug therapy; Humans; Primary Health Care; Proton Pump Inhibitors

AccessionNumber
22002006351

Date bibliographic record published
31/01/2006

Date abstract record published
31/01/2006