Economic evaluation of empirical antisecretory therapy versus Helicobacter pylori test for management of dyspepsia: a randomized trial in primary care

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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
The analysis compared three regimens for the management of dyspepsia in primary care.

Strategy A was empirical antisecretory therapy, consisting of esomeprazole 20 mg twice daily for 1 week.

Strategy B was Helicobacter pylori (H. pylori) test-and-eradicate. H. pylori testing was carried out using the urea breath test (UBT), whilst eradication treatment included esomeprazole 20 mg, amoxicillin 1,000 mg and clarithromycin 500 mg twice daily for 1 week.

Strategy C was a combination strategy, specifically esomeprazole 20 mg twice daily for 1 week followed by H. pylori testing if symptoms improved, and eradication therapy if H. pylori positive.

Due to the risk of a false-negative result, patients treated according to strategies B and C were denied a proton-pump inhibitor for at least 1 week before the UBT.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients from 106 general practices. Patients were eligible if they presented with dyspeptic symptoms for more than 2 weeks, and if the general practitioner (GP) found indication for investigation or treatment. Criteria for exclusion included alarm symptoms, ongoing treatment with antisecretory drugs, ongoing use of non-steroidal anti-inflammatory drugs, serious or terminal disease, alcohol or drug abuse, and previous surgery of the upper gastrointestinal tract. Further exclusion criteria were non-Danish speaking, age below 18 years, and pregnancy or lactation.

Setting
The setting was primary care. The economic study was carried out in the County of Funen, Denmark.

Dates to which data relate
The effectiveness evidence and resource use data were gathered between June 2001 and October 2003. The unit costs were for 2004.

Source of effectiveness data
The effectiveness data were derived from a single study.

**Link between effectiveness and cost data**
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

**Study sample**
The analysis was based on 722 patients registered with 106 general practitioners. Of these patients, 222 were allocated to strategy A, 250 to strategy B and 250 to strategy C.

**Study design**
The analysis was based on a randomised controlled trial. Randomisation occurred at the practice level. The method of randomisation was not stated. There was no mention of blinding, but this might have been difficult to achieve. The duration of follow-up was 1 year.

**Analysis of effectiveness**
The basis for the analysis of effectiveness (intention to treat or treatment completers) was not stated. However, it would appear that there was no loss to follow-up. The primary health outcomes were the mean proportion of days without dyspeptic symptoms during the 1-year follow-up, and the proportion in each group who were symptom free after 1 year. The three groups were shown to be relatively comparable at baseline. However, there were fewer smokers and females in strategy A than the other two strategies. No adjustment for these differences was made in the analysis.

**Effectiveness results**
The mean proportion of days without dyspeptic symptoms during the 1-year follow-up period was:

- 0.59 (95% confidence interval, CI: 0.54 to 0.63) in the strategy A group,
- 0.57 (95% CI: 0.53 to 0.60) in the strategy B group, and
- 0.53 (95% CI: 0.49 to 0.58) in the combination group, (p=0.16).

At 12 months, 23% in the strategy A group, 26% in the strategy B group and 22% in the combination group had no dyspeptic symptoms.

**Clinical conclusions**
Strategy A conferred a small but insignificant benefit over the other two alternatives.

**Measure of benefits used in the economic analysis**
The measures of benefits used were the proportion of days without dyspeptic symptoms during the 1-year follow-up and the proportion of patients who were symptom free after 1 year.

**Direct costs**
The costs and the quantities were not reported separately. The direct costs included in the analysis were the costs of endoscopies and endoscope depreciation, the H. pylori test costs, drug costs, primary care consultation costs, and patient transport costs associated with GP visits or visits to outpatient clinics. The estimation of the costs was derived from a variety of sources; the cost of endoscopies was based on current charges from the National Board of Health, Denmark. Provision for depreciation of equipment was determined from information about investment costs and durability of endoscopies. The cost of a GP consultation was agreed by the Danish General Practitioners Organisation and the
National Health Insurance.

The estimation of the quantities was derived from actual data. Visits to GPs were registered by the patients. The number of endoscopies was obtained from the patient administrative system. Information on the use of medication was collected from the Odense University Pharmacoepidemiologic database. Study protocol visits to GPs were not included as they occurred equally in the three randomisation groups.

The unit costs were for 2004. Discounting was not performed but it was not necessary given the relatively short follow-up (1 year).

**Statistical analysis of costs**
Point estimates were used for the costs and no statistical analysis of the costs was reported.

**Indirect Costs**
The indirect costs included in the analysis were the value of time related to the number of sick-leave days, and time for visits to the GP and outpatient clinics. The cost of time was estimated by applying hourly wages based on gender-and occupation-specific salaries. Time costs were assumed to be zero for patients who were unemployed.

**Currency**
Danish kroner (DKK).

**Sensitivity analysis**
A one-way sensitivity analysis was performed on the unit costs for endoscopies (DKK 5,000 and DKK 1,000), the cheapest and most expensive drugs per class, the prevalence of H. pylori infection (twice and half of the present infection rate) and the opportunity cost of time (half and one quarter of the wage rate).

**Estimated benefits used in the economic analysis**
The benefits were taken directly from the clinical study. See the 'Effectiveness Results' section.

**Cost results**
The mean yearly average cost per patient was DKK 7,157 for empirical treatment, DKK 5,458 for H. pylori test-and-eradicate, and DKK 3,870 for the combination strategy.

**Synthesis of costs and benefits**
A synthesis of the costs and benefits was carried out by calculating an incremental cost-effectiveness ratio using the proportion of days without dyspeptic symptoms.

The incremental cost-effectiveness going from the combination strategy to empirical antisecretory treatment and to H. pylori test alone was DKK 54,783 and DKK 39,700, respectively, per additional proportion of days without dyspeptic symptoms.

The authors also produced average cost-effectiveness ratios.

The cost-effectiveness ratio was DKK 12,131 for empirical treatment, DKK 9,576 for the H. pylori test and DKK 7,301 for the combination strategy.

According to the one-way sensitivity analyses, the opportunity costs of patients' time had the greatest influence on the cost-effectiveness analyses, but none of the sensitivity analyses changed the direction of cost-effectiveness among strategies.
Authors' conclusions
Empirical antisecretory therapy conferred a small and insignificant benefit, but cost more than strategies based on a test for Helicobacter pylori (H. pylori) and was probably not a cost-effective strategy for the management of dyspepsia in primary care.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator was clear. It was chosen because it reflected standard practice in the authors' setting. You should consider whether this is a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a randomised controlled trial, which was appropriate for the study question. However, the three groups were not comparable at baseline, as strategy A had fewer females and fewer smokers than strategies B and C. No adjustment was made for these differences. It was not clear if, or how, these differences would affect the estimate of effectiveness.

Validity of estimate of measure of benefit
The estimate of benefit was obtained directly from the effectiveness analysis. The reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
The authors reported that the study had been conducted from a societal perspective. As such, it appears that all the relevant categories of cost have been included in the analysis. The costs and the quantities were not reported separately, which will limit the generalisability of the authors' conclusions. A sensitivity analysis of the quantities was not conducted and this may limit the interpretation of the study findings. A sensitivity analysis of the prices was conducted. Discounting was appropriately not conducted.

Other issues
The authors made appropriate comparisons of their findings with those from other studies and, where differences were found, they were generally attributed to the use of different study populations. The issue of generalisability to other settings was partially addressed by performing sensitivity analysis on the cost items. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported some further limitations of their study, for instance the lack of a validated outcome measure for dyspepsia patients which could have been used in the analysis.

Implications of the study
The authors suggested that empirical antisecretory therapy is not a cost-effective strategy for the management of dyspepsia in primary care. They made no explicit recommendations for changes in policy or practice.

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Bibliographic details