Cost-effectiveness analysis of proton pump inhibitors compared to omeprazole in the healing of reflux oesophagitis

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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 use of esomeprazole (40 mg), a proton-pump inhibitor (PPI), in the treatment of gastro-oesophageal reflux disease (GORD).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients requiring treatment for GORD.

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

Dates to which data relate
The effectiveness data were derived from a study published in 2001. The resource use information was derived from studies published in 2001 and 2002. The costs were evaluated in 1999/2000 values.

Source of effectiveness data
The effectiveness evidence was derived from a completed study, which consisted of a meta-analysis (Edwards et al., see Other Publications of Related Interest).

Modelling
A modelling approach, based on a simple decision tree, was used to assess the cost-effectiveness of the alternative treatment strategies for GORD. The structure of the tree, which was depicted in the article, was based on data derived from a survey of UK general physicians and gastroenterologists. The model considered both the follow-up of unhealed patients and the switch to different dosages during maintenance therapy.

Outcomes assessed in the review
The outcomes assessed in the published review were the relative risk (RR) for healing with esomeprazole, lansoprazole, pantoprazole and rabeprazole relative to omeprazole at 4 and 8 weeks. These RR values were then converted into probability values ("calculated" healing rates) used in the decision model. The additional healing rates at 8 weeks, if not healed at 4 weeks, were also derived from the systematic review.
Study designs and other criteria for inclusion in the review
Not reported.

Sources searched to identify primary studies
Not stated.

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
Not stated.

Methods of combining primary studies
A meta-analysis was used to combine the primary studies.

Investigation of differences between primary studies
Not stated.

Results of the review
The RR for healing relative to omeprazole at 4 weeks was 1.14 (98% confidence interval, CI: 1.10 - 1.18) for esomeprazole, 1.02 (98% CI: 0.97 - 1.08) for lansoprazole, 0.99 (98% CI: 0.91 - 1.07) for pantoprazole, and 1.00 (98% CI: 0.87 - 1.14) for rabeprazole.

The RR for healing relative to omeprazole at 8 weeks was 1.08 (98% CI: 1.05 - 1.10) for esomeprazole, 1.01 (98% CI: 0.97 - 1.06) for lansoprazole, 0.98 (98% CI: 0.93 - 1.04) for pantoprazole, and 0.98 (98% CI: 0.91 - 1.05) for rabeprazole.

The "calculated" healing rates at 4 weeks used in the decision model were 65.1% for omeprazole, 74.2% (95% CI: 71.6 - 76.8) for esomeprazole, 66.4% (95% CI: 63.1 - 70.3) for lansoprazole, 64.4% (95% CI: 59.2 - 69.7) for pantoprazole, and 65.1% (95% CI: 56.6 - 74.2) for rabeprazole.

The "calculated" healing rates at 8 weeks used in the decision model were 82.2% for omeprazole, 88.8% (95% CI: 86.3 - 90.4) for esomeprazole, 83.0% (95% CI: 79.7 - 87.1) for lansoprazole, 80.6% (95% CI: 76.4 - 85.5) for pantoprazole, and 80.6% (95% CI: 74.8 - 86.3) for rabeprazole.

The additional healing rates at 8 weeks, if not healed at 4 weeks, were 49% for omeprazole, 56.5% (95% CI: 51.8 - 58.7) for esomeprazole, 49.5% (95% CI: 45 - 56.7) for lansoprazole, 45.3% (95% CI: 42.2 - 52.2) for pantoprazole, and 44.3% (95% CI: 41.9 - 46.9) for rabeprazole.

Measure of benefits used in the economic analysis
The summary benefit measure was the proportion of patients healed at 8 weeks. This was derived from the modelling approach described earlier.
Direct costs
Discounting was irrelevant because of the short time horizon of the study. The unit costs were reported, but details of the quantities of resources used were not. The health services included in the economic evaluation were study drugs, endoscopy, general practitioner visit and outpatient visit. The cost/resource boundary of the NHS was adopted. Resource use was estimated mainly using data from a survey of UK general physicians and gastroenterologists. Other resource use data were derived from published studies. The costs were based on the British National Formulary, personnel social service research units, the Chartered Institute of Public Finance & Accountancy, and a published study. All the costs reflected national expenses. The prices were estimated in 1999/2000 values.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were not considered.

Currency
UK pounds sterling (GBP).

Sensitivity analysis
Sensitivity analyses were carried out to assess the robustness of the estimated cost-effectiveness ratios to variations in all the model inputs. This was done using a Monte Carlo simulation of 1,000 patients, in which all inputs were varied simultaneously and distribution probabilities were attached to each input. The choice of the probabilistic distribution for the most critical inputs was discussed. Upper and lower CIs were set at ±10%.

Estimated benefits used in the economic analysis
The proportion of patients healed at 8 weeks was 0.822 with omeprazole, 0.888 with esomeprazole, 0.830 with lansoprazole, and 0.806 with both pantoprazole and rabeprazole.

Cost results
The mean cost per patient was 117.02 with omeprazole, 106.73 with esomeprazole, 107.43 with lansoprazole, 108.70 with pantoprazole, and 108.59 with rabeprazole.

Synthesis of costs and benefits
The average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the alternative treatment strategies.

The mean cost per patient healed was 142.36 with omeprazole, 120.19 with esomeprazole, 129.43 with lansoprazole, 134.86 with pantoprazole, and 134.73 with rabeprazole.

The incremental analysis revealed that, in the base-case, esomeprazole was the most effective and least costly treatment. Thus, it dominated the remaining alternatives.

Lansoprazole dominated omeprazole although the effectiveness advantage was negligible.

Lansoprazole was only slightly more costly than esomeprazole. Thus, cost neutrality was the most likely scenario although esomeprazole was more effective.

The sensitivity analysis revealed that the estimated costs were robust to input changes but, with the exception of
esomeprazole, the expected number of patients healed at 8 weeks was sensitive to input variations. In particular, the Monte Carlo simulation showed that among all PPIs, only esomeprazole was both more effective and less costly than omeprazole.

After excluding omeprazole, the other PPIs were cost neutral compared with esomeprazole, which had a significant advantage in efficacy over them.

**Authors' conclusions**

Esomeprazole was more cost-effective than omeprazole for the treatment of gastro-oesophageal reflux disease (GORD) since it was as costly as omeprazole but more effective. Other proton-pump inhibitors (PPIs) also proved to be more cost-effective than omeprazole, but their efficacy profile was worse than that with esomeprazole.

**CRD COMMENTARY - Selection of comparators**

The rationale for the choice of the comparators was clear. All drugs were selected because they represented currently licensed treatments for GORD in the UK. The reasons for the choice of omeprazole as the basic comparator were reported. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness evidence came from a systematic review, the details of which had been published. No information on the number of studies involved in the analysis, the study design, validity and methods used to combine the studies, were reported. Therefore, it was difficult to assess the robustness of the source of evidence. The primary effectiveness data were converted into probability values using an approach that was described in detail. Therefore, all the steps of the calculations were quite transparent. However, for an overall commentary on the validity of the effectiveness measure, it would be helpful to refer to the review (see Other Publications of Related Interest). The authors stated that the systematic review was chosen to provide the evidence, owing to the lack of a head-to-head comparison based on a large clinical trial.

**Validity of estimate of measure of benefit**

The summary benefit measure represented a typical measure used in studies considering GORD. Accordingly, it was quite specific to the interventions under evaluation and it would be difficult to compare it with the benefits of other health care interventions. The benefit measure was obtained from a modelling approach that mirrored the standard treatment of patients with GORD. However, the authors stated that the outcomes for patients who remained unhealed at 8 weeks were not considered. Quality of life issues were not directly considered when the impact of the treatment on patient health was assessed.

**Validity of estimate of costs**

The authors explicitly stated the perspective adopted in the study. As such, it appears that all the relevant categories of costs have been included in the analysis. The unit costs were provided, as were the years during which the costs were estimated. The bulk of the evidence on resource use was also given. This enhances the possibility of replicating the study in other settings and carrying out reflation exercises. The costs were treated deterministically, but extensive sensitivity analyses were conducted to address the issue of variability in data. The data source for each item was reported.

**Other issues**

The authors did not compare their findings with those from other published studies. They also did not address the issue of the generalisability of the study results to other settings. This adversely affected the external validity of the analysis. However, sensitivity analyses were conducted on all model inputs. The authors stressed the fact that the model did not consider the outcomes of patients who were not healed after 8 weeks of treatment, and this biased the results against the most effective strategies. Therefore, this should be considered a conservative assumption.
Implications of the study
The authors suggested that the decision model should be updated as soon as more robust data becomes available.

Source of funding
None stated.

Bibliographic details

Other publications of related interest

Indexing Status
Subject indexing assigned by CRD

MeSH
Cost-Benefit Analysis; Dose-Response Relationship, Drug; Drug Administration Schedule; Enzyme Inhibitors /administration & dosage; Gastroesophageal Reflux /drug therapy; Models, Economic; Omeprazole /administration & dosage /economics; Proton Pumps /antagonists & inhibitors; Treatment Outcome

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