Cost-effectiveness comparison of current proton-pump inhibitors to treat gastro-oesophageal reflux disease in the UK

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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 proton-pump inhibitors (PPIs) to treat gastro-oesophageal reflux disease (GORD). Seven PPIs were compared. These were esomeprazole, lansoprazole capsules, lansoprazole oro-dispersible tablets, omeprazole (generic and branded), pantoprazole and rabeprazole.

Type of intervention
Treatment.

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

Study population
The study population comprised a hypothetical cohort of 1,000 patients who presented with symptoms of GORD, but whose diagnosis was unconfirmed by endoscopy. The target population was the same as the study population.

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

Dates to which data relate
The effectiveness evidence was derived from papers published from 1995 to 2004. The resource use and cost data were derived from papers published from 2002 to 2004. The price year was 2003.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and experts' opinions.

Modelling
A series of Markov models, consisting of 13 inter-connected models, was developed to evaluate both the cost-effectiveness and the cost-utility of PPIs in the treatment of GORD in the UK. The timeframe for the analysis was 1 year, running over thirteen 4-week cycles.

Outcomes assessed in the review
The outcomes assessed included:
the acute treatment healing rates,
the symptom relief rates,
the long-term treatment remission rates at 6 months,
the proportion of patients on different dosages of each drug for long-term treatment, and
quality of life.

**Study designs and other criteria for inclusion in the review**
The authors stated that randomised controlled trials (RCTs) were preferred for their review, but the results of observational studies were also included if no RCT was available. Studies were chosen for inclusion based on disease classification (erosive or non-erosive GORD). The reported outcomes had to fit with the model variable requirements.

**Sources searched to identify primary studies**
MEDLINE was searched for clinical trials and studies of PPIs in GORD. The key trials supporting each product were obtained from the prescribing information prepared for the European markets.

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

**Methods used to judge relevance and validity, and for extracting data**
The validity of the primary studies was judged by a panel of physicians reviewing the model and its parameters.

**Number of primary studies included**
The model rates and probabilities were derived from 19 papers.

**Methods of combining primary studies**
Not reported.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
For acute treatment, the following model parameters were reported in full in the paper:
the healing rates at 4 weeks and 8 weeks for erosive GORD,
the 4-week double-dose healing rate for erosive GORD, and
the symptom relief rates at 4 weeks for non-erosive GORD.
For long-term treatment, the remission rates at 6 months were reported in full for:
continuous maintenance treatment on high dose and step-down dose, and
on-demand treatment on high dose and step-down dose.
The remission rate at 12 months after the treatment stopped was also reported.
Methods used to derive estimates of effectiveness
Experts' opinions were used to derive estimates of effectiveness and to validate the authors' assumptions.

Estimates of effectiveness and key assumptions
Based on expert opinion, 50% of patients were assumed to stop treatment in the long term. The remainder received either continuous maintenance therapy or took their medication on demand.

The proportion of treated patients receiving on-demand therapy for PPIs was assumed to be 30%. Licensing approval for on-demand usage (in the case of esomeprazole and rabeprazole) was assumed to increase the percentage of patients being dosed in this manner to 50%.

Measure of benefits used in the economic analysis
The outcome measures used in the economic analysis were symptom-free days and quality-adjusted life-years (QALYs). The patients' quality of life was impaired in proportion to the frequency and severity of symptoms, irrespective of the presence or severity of oesophagitis.

Direct costs
The direct costs included costs for medications, prokinetic treatment, the Helicobacter pylori test, 1-week eradication therapy, medical visits and diagnostic procedures. Assumptions about medical resource use were based on a UK physician survey of patient management in clinical practice, which involved 10 gastroenterologists and 15 general physicians (Wahlquist et al. 2002, see Other Publications of Related Interest- below for bibliographic details). The unit costs of medication and medical visits were derived from published materials (BNF 2003, Personal and Social Services Research Unit 2003 and NHS Reference Costs 2003, see ,Other Publications of Related Interest- below for bibliographic details). Discounting was not relevant as the costs were estimated for 1 year. The quantities and the costs were reported separately. The price year was 2003.

Statistical analysis of costs
The costs were treated deterministically in the base-case analysis. In the sensitivity analysis, the costs were varied between +/- 10% of the base-case value.

Indirect Costs
The indirect costs were not included in the economic evaluation.

Currency
UK pounds sterling (€).

Sensitivity analysis
A probabilistic sensitivity analysis was carried out to evaluate the implications of the joint uncertainty in the model variables. Probabilities were assigned a beta distribution, based on the underlying proportion and sample size in the clinical trials and studies. The QALY weight for days with symptoms was also assumed to follow a beta distribution, with a standard deviation of 0.1. The costs were varied between +/- 10% of the base-case value. Cost-effectiveness acceptability curves for multiple interventions were drawn to summarise the probability of each PPI being the optimal treatment choice over a range of willingness-to-pay (WTP) values.

Estimated benefits used in the economic analysis
For 1,000 GORD patients treated according to current clinical practice, the numbers of symptom-free days obtained...
over 1 year were:

320,329 with rabeprazole,
317,940 with pantoprazole,
317,713 with generic omeprazole,
317,713 with branded omeprazole,
316,217 with esomeprazole,
315,675 with lansoprazole oro-dispersible tablets, and
315,675 with lansoprazole.

For 1,000 GORD patients treated according to current clinical practice, the QALYs gained over 1 year were:

982 with rabeprazole,
981 with pantoprazole,
980.9 with omeprazole generic,
980.9 with omeprazole branded,
980.3 with esomeprazole,
980.1 with lansoprazole oro-dispersible tablets, and
980.1 with lansoprazole.

Cost results
Treatment with generic omeprazole was the least costly over a year.

For 1,000 GORD patients, the annual total cost was:

285,227 with generic omeprazole,
294,184 with rabeprazole,
329,398 with pantoprazole,
399,128 with branded omeprazole,
357,254 with esomeprazole,
336,116 with lansoprazole oro-dispersible tablets, and
359,314 with lansoprazole.

Synthesis of costs and benefits
The authors calculated the incremental cost per symptom-free day and the incremental cost per QALY.

The results of the sensitivity analysis showed that only treatments with generic omeprazole and rabeprazole were
economically viable. Rabeprazole is a cost-effective treatment option compared with all other available PPIs. When compared with generic omeprazole, it had an incremental cost-effectiveness ratio of 3.42 per symptom-free day gained and 8,308/QALY.

The probabilistic sensitivity analysis found the above results to be robust. If society were willing to pay less than around 8,500 for a QALY gain then generic omeprazole would be the optimal treatment. At higher WTP values rabeprazole had the highest probability of being cost-effective in comparison with all other PPIs. Rabeprazole remained cost-effective independent of the choice of maintenance treatment (i.e. the proportion of patients remaining on continuous treatment versus on-demand treatment).

The authors tested the conservative assumption that PPIs are equally effective in treating non-erosive reflux disease (non-erosive GORD). The results showed that generic omeprazole and rabeprazole still dominated the other treatments, but the incremental cost-effectiveness ratio of rabeprazole versus generic omeprazole increased to between 25,260/QALY (if a common 50% rate was assumed) and 29,602/QALY (if a common 57% rate was assumed).

Authors’ conclusions
The current model, incorporating real-life treatment patterns, showed that only treatment scenarios with generic omeprazole and rabeprazole were economically viable and that rabeprazole was a cost-effective treatment option compared with all other available proton-pump inhibitors (PPIs).

CRD COMMENTARY - Selection of comparators
The authors justified their choice of the comparators examined in the study. All seven PPIs represented current practice, and the dosages were also reported. Thus, the comparators considered in the study were appropriately chosen. You should decide if they are widely used health technologies in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state whether a systematic review of the literature had been undertaken. The effectiveness estimates were combined using narrative methods. The authors did not consider the impact of differences between the primary studies when estimating effectiveness. Experts' opinions were also used to derive estimates of effectiveness and validate the model structure and assumptions, but the authors did not report the process by which the experts were selected. The assumptions based on expert opinion were investigated in sensitivity analyses, using ranges that appear to have been appropriate.

Validity of estimate of measure of benefit
The authors used symptom-free days and QALYs as the outcome measures. These enable the results to be compared with other treatments, as well as comparisons of cost-effectiveness and cost utility results across other disease areas. The estimation of health benefits was modelled. The instrument used to derive a measure of health benefit, a Markov model, was appropriate.

Validity of estimate of costs
The study reported the costs from the UK NHS perspective. Only the direct medical costs were included. Extensive information on the unit costs and sources of data was provided, which enhances the possibility of replicating the cost analysis in other settings. Resource use was mainly derived from expert opinion. The authors stated that the inclusion of costs other than the direct medical costs, for example the costs associated with lost productivity due to GORD symptoms, is likely to show even greater cost-advantages for the PPIs associated with a higher number of symptom-free days. The price year was reported, which will facilitate refiation exercises in other time periods.

Other issues
The authors stated that their results were not directly comparable with those from other studies because these studies
evaluated only sub-groups of patients and parts of the treatment options. The issue of generalisability to other settings was addressed. The authors did not present their results selectively. The authors reported, as a further limitation to their study, that they combined data from various sources.

**Implications of the study**
The results of this study indicated that rabeprazole is the treatment of choice for GORD, but do not preclude the possibility that other PPIs may be cost-effective for sub-groups of patients or for sub-sets of treatment approaches. The authors suggested the need for economic evaluations and the need to look further than drug acquisition costs.

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**Bibliographic details**

**Other publications of related interest**


British Medical Association, Royal Pharmaceutical Society of Great Britain. BNF 2003;46.


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Subject indexing assigned by NLM

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