Cost effectiveness of rabeprazole versus generic ranitidine for symptom resolution in patients with erosive esophagitis


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 rabeprazole (RAB), 20 mg/day for 8 weeks, and ranitidine (RAN), 150 mg 4 times daily for 8 weeks, as initial and maintenance therapy in patients with erosive oesophagitis.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of ambulatory care patients with gastroesophageal reflux disease (GERD) symptoms for at least 3 months and endoscopically established erosive oesophagitis (grades 2 - 4 modified Hetzel-Dent grading scale). Patients with concomitant motility disorders, complications of GERD (e.g. strictures or Barrett’s oesophagus), or recent treatment with antisecretory therapy were not considered.

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

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1990 and 1998. The price year was 1998.

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

Modelling
A decision tree model was constructed to determine the costs and benefits of RAB versus RAN in the treatment of patients with erosive oesophagitis. The model incorporated an acute phase and a 1-year maintenance phase. The structure of the tree was based on actual patterns of patient treatment. Thus, empirical approaches, such as drug switching, were allowed. The time horizon of the model was one year.

Patients in the RAB arm received treatment for 8 weeks. Those who remained symptomatic received an additional 8-week course of RAB at higher dosage (40 mg/day). If symptoms persisted, a second high-dose 8-week RAB course was provided. If symptoms still persisted, patients underwent surgical consultation, while those non-surgical candidates received maintenance therapy with RAB 20 mg/day. Those who became asymptomatic received maintenance therapy
with RAB 20 mg/day, but if symptoms recurred, a high-dose 8-week RAB course was provided.

Patients in the RAN arm received RAN (150 mg 4 times daily), while those with persistent symptoms were switched to an 8-week RAB course (20 mg/day) and treated as in the RAB arm. Patients who became asymptomatic received RAN 150 mg twice daily as maintenance therapy. If recurrences were experienced, then the patients received RAN 300 mg twice a day. If symptoms still persisted, the patients were switched to RAB 40 mg/day, followed by maintenance RAB therapy.

**Outcomes assessed in the review**
The outcomes estimated from the literature were:

- the probabilities of complete symptom relief after initial and maintenance therapy,
- the recurrence rates, and
- the probability of non-responsive patients ultimately achieving symptom relief.

Symptom relief was defined as the complete resolution of heartburn.

**Study designs and other criteria for inclusion in the review**
Data on drug efficacy were obtained directly from randomised clinical trials. A systematic review was carried out to identify relevant studies that could provide the remaining probability values required in the model. The inclusion criteria for the review were not reported.

**Sources searched to identify primary studies**
MEDLINE and HealthSTAR were searched from 1985 onwards (to the present) for relevant studies.

**Criteria used to ensure the validity of primary studies**
The validity of efficacy data was ensured by the use of clinical trials. However, the validity of other sources could not be examined.

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

**Number of primary studies included**
Seventeen primary studies provided the data.

**Methods of combining primary studies**
The primary studies appear to have been combined using a narrative method.

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

**Results of the review**
The probability of complete symptom relief was 0.50 (range: 0.35 - 0.80) with RAB and 0.28 (range: 0.22 - 0.64) with RAN.
The probability of complete symptom relief after receiving RAB 40 mg/day for 8 weeks was 0.73 (range: 0.65 - 0.97).

The probability of complete symptom relief with RAB after failing RAN was 0.73 (range: 0.65 - 0.97).

The annual recurrence rates for maintenance therapy were 0.15 (range: 0.12 - 0.18) with RAB 20 mg/day, 0.55 (range: 0.45 - 0.90) with RAN 150 mg twice daily, and 0.55 (range: 0.46 - 0.68) with RAN 300 mg twice daily.

The probability of non-responsive patients ultimately achieving symptom relief was 0.20 (range: 0.11 - 0.60).

Methods used to derive estimates of effectiveness
An informal survey of four gastroenterologists and two general surgeons was carried out to identify some probabilities associated with treatment.

Estimates of effectiveness and key assumptions
The probability of being a candidate for surgery after receiving a surgical evaluation was 0.90 (range: 0.80 - 0.99). The probability of a candidate for surgery choosing to have surgery was 0.50 (range: 0.40 - 0.80).

Measure of benefits used in the economic analysis
The summary benefit measure was the percentage of symptom recurrences prevented. This was defined as either the complete absence of heartburn, or heartburn occurring on less than 25% of the days since the preceding clinical visit. The benefit measure was derived using the decision model.

Direct costs
Discounting was not relevant since the costs were estimated for one year. The unit costs were presented separately from the quantities of resources used. The health services included in the economic evaluation were drugs, endoscopy, inpatient and outpatient physician visits, surgical evaluation, and surgery (laparoscopic Nissen fundoplication). Endoscopy included the procedure, visit to the gastroenterologist, and facility fee. Surgical evaluation comprised oesophageal manometry, barium upper gastrointestinal X-ray, and surgical consultation. The perspective of the third-party payer was adopted. Resource use was derived from published medical literature and experts’ opinions. The costs were derived from Medicare reimbursement charges for hospitalisations, procedures and physician visits, while the average procedural charges came from two hospital-based endoscopic centres in California. A cost-to-charge ratio of 0.50 was applied to convert charges into costs. The drug costs were derived from average wholesale prices and the authors made some assumptions when the cost data were not available. The price year was 1998.

Statistical analysis of costs
No statistical analyses of the costs were performed.

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

Currency
US dollars ($).

Sensitivity analysis
Univariate sensitivity analyses were performed to examine the impact of variations in model inputs on the estimated cost-effectiveness ratios. The ranges observed in the literature were used. Two-way sensitivity analyses were carried out on the most relevant parameters. The authors investigated also the effect of using generic cimetidine as a comparator in
the analysis. Threshold analyses were also conducted to identify how each model input should change in order for RAN and RAB to be equally cost-effective.

Estimated benefits used in the economic analysis
The percentage of symptom recurrences prevented was 74% with RAB and 41% with RAN.

Cost results
The average cost per patient was $2,020 with RAB and $1,917 with RAN.

Synthesis of costs and benefits
Average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the treatment strategies. The average cost per symptomatic recurrence prevented was $2,748 with RAB and $4,719 with RAN. The incremental cost per additional symptomatic recurrence prevented with RAB over RAN was $313.

The sensitivity analysis showed that the results of the base-case were generally robust to variations in the model inputs. The threshold analysis suggested that large changes in model parameters were required for the two treatments to be of comparable cost-effectiveness. For example, the rate of symptom relief with RAN 150 mg 4 times daily had to increase by 171%, or the recurrence rate with RAN 150 twice daily had to decrease by 40%. Even greater variations were required for other model inputs. The inclusion of cimetidine did not change the results of the analysis, as the average cost-effectiveness ratio of RAB remained the lowest.

Authors’ conclusions
In a clinically realistic decision-analytic model, rabeprazole (RAB) was more cost-effective than ranitidine (RAN) for the treatment of patients with erosive oesophagitis.

CRD COMMENTARY - Selection of comparators
The authors did not provide an explicit justification for the choice of the comparators, but stated that RAN and RAB had recently been compared in several clinical trials. The use of an alternative drug (cimetidine) was also investigated. The authors acknowledged that there were other available treatment strategies that are frequently recommended in clinical practice. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from data derived from the literature. The data on drug efficacy were identified selectively, while a systematic review of the literature was conducted to identify other model inputs. The most commonly used electronic databases were searched, but the methods and conduct of the review were not reported. In addition, no information on the primary studies was provided. Finally, some data were derived using experts’ opinions. The issue of uncertainty was investigated in the sensitivity analysis, where all model inputs were varied. Moreover, when uncertainty existed in the medical literature, conservative assumptions, which were biased against RAB, were made.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. As such, it is hardly comparable with the benefits of other health care interventions. It was obtained using the modelling approach. The authors stated that the analysis focused on symptomatic rather than on endoscopic outcomes, which could have been more relevant.

Validity of estimate of costs
The authors reported explicitly the perspective of the study. All the relevant categories of costs were included in the
analysis. The unit costs were clearly reported, as was information on resource use. This enables the study to be replicated in other contexts. Some data were derived using experts' opinions. As reimbursement charges were used, a cost-to-charge ratio was applied to estimate the true costs of the services. The price year was reported, which aids reflation exercises in other settings. The costs were treated deterministically in the base-case, but were varied in the sensitivity analysis. The authors stated that resource use reflected typical clinical treatment patterns in the USA.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. They also did not explicitly address the issue of the generalisability of their results to other settings. However, the external validity of the analysis was in part enhanced by the sensitivity analysis. The authors noted some limitations to the validity of their analysis. First, some medical data were not robust because of the low quality of the sources used. Second, quality of life issues were not considered. Third, medication compliance was not considered, although it could be higher for once-daily rather than multiple-dose medications. Finally, the indirect costs were not considered, although it could be speculated that more effective treatments were likely to have a more favourable impact on such costs.

Implications of the study
The study results supported the use of RAB in the treatment of patients with erosive oesophagitis. The authors noted that further research should investigate the quality of life associated with the treatment of patients suffering from erosive oesophagitis.

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Bibliographic details

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Other publications of related interest
Humphries TJ, Spera A, Breiter J, et al. Rabeprazole sodium once daily is superior to ranitidine 150 mg four times a day in the healing of erosive or ulcerative gastroesophageal reflux disease. (abstract). Gastroenterology 1996;110:A139.


Indexing Status
Subject indexing assigned by NLM

MeSH
2-Pyridinylmethylsulfinylbenzimidazoles; Benzimidazoles /administration & dosage /economics; Cost-Benefit Analysis; Decision Trees; Drug Costs /statistics & numerical data; Drugs, Generic; Enzyme Inhibitors /administration & dosage /economics; Esophagitis, Peptic /drug therapy /etiology; Gastroesophageal Reflux /complications /drug therapy /physiopathology; Health Care Costs /statistics & numerical data; Histamine H2 Antagonists /administration & dosage