Effectiveness and costs of omeprazole vs ranitidine for treatment of symptomatic gastroesophageal reflux disease in primary care clinics in West Virginia

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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
This study considered omeprazole sodium (20 mg once daily) and ranitidine hydrochloride (150 mg twice daily) for the treatment of symptomatic gastroesophageal reflux disease (GERD).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who had been diagnosed with GERD and, in the opinion of a physician, needed to start medication. GERD was defined as frequency of heartburn and/or acid regurgitation despite non-prescription treatment for at least 2 weeks. The patients were aged 18 years or older, had not been treated with any proton-pump inhibitor or histamine2 receptor antagonist in the preceding 30 days, were not pregnant or breastfeeding, and did not have any clinical evidence of renal or hepatic impairment.

Setting
The setting was primary care. The study was conducted in Charleston (WV), USA.

Dates to which data relate
The study dates were not reported. The resource use data were also collected as part of the effectiveness study. The price year was 1998.

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

Link between effectiveness and cost data
The resource use information was collected prospectively from the same patient sample as that used in the effectiveness analysis.

Study sample
No power calculations to estimate the required sample size were reported. Overall, 268 patients were recruited to the study. Of these, 138 (51.5%) were randomised to receive omeprazole and 130 (48.5%) to receive ranitidine. The paper did not report the characteristics of those patients who were invited to take part in the study but refused, nor did it give
details of any patients excluded after the initial selection. The authors did not compare the characteristics of their sample population with the population of patients with symptomatic GERD requiring medical treatment.

**Study design**
The study was a multi-centre, open-label, randomised controlled trial. The patients were randomised to treatment with either omeprazole or ranitidine by computer. Following randomisation the patients were issued with a 30-day supply of the appropriate drug. Neither the patients nor physicians were blinded to the treatment group. The control of further prescriptions and other medical care was handed over to the patients’ usual physician. Five clinics affiliated to a university-based department of family medicine participated in the study. The patients were enrolled over 24 months and followed up for 24 weeks. The outcome data were collected at 2, 4, 12 and 24 weeks through telephone interviews by a trained research co-ordinator, who was blind to the patients' treatment group. Seventeen patients (6.3%) were lost to follow-up, 8 (5.8%) from the omeprazole treatment arm and 9 (6.9%) from the ranitidine group. The characteristics of these patients were not statistically significantly different from those who stayed in the study.

**Analysis of effectiveness**
The effectiveness data were analysed on an intention to treat basis. The effectiveness of the two treatments was assessed by the resolution of heartburn symptoms, scores on the Gastrointestinal Symptom Rating Scale (GSRS) and quality of life. Quality of life was measured using the Psychological General Well-Being (PGWB) Index and the Short-Form 36 (SF-36) Health Survey.

The two treatment groups were similar in their age, gender, ethnic group, whether they were treated at an urban centre, co-morbidity and health-related quality of life. The only statistically significant difference noted between the two groups was that the ranitidine treatment group reported a slightly higher score on the GSRS (4.3 versus 3.9), (p=0.06).

**Effectiveness results**
After 2 weeks of treatment, 49.0% of the patients in the omeprazole group and 33.3% of those in the ranitidine group did not have any heartburn symptoms, (p=0.007). At 4 weeks, the proportions of patients not reporting any heartburn symptoms had increased to 58.7% in the omeprazole group and 35.0% in the ranitidine treatment group, (p<0.001).

Four weeks after the start of treatment, the omeprazole group reported a lower adjusted mean GSRS reflux score (2.53) than the ranitidine group (2.89), (p=0.005). There was no statistically significant difference between the mean adjusted GSRS reflux scores in the two treatment groups at 3 and 6 months after the start of the treatment.

There were no statistically significant differences in the health-related quality of life between the two treatment groups.

No details of adverse effects experienced by the patients were reported.

**Clinical conclusions**
The authors concluded that patients treated with omeprazole were more likely to report the resolution of heartburn symptoms and other GERD-related symptoms in the 4 weeks following the start of treatment. Differences between the two groups did not remain significant 3 and 6 months after starting treatment. Further, there were no differences in the health-related quality of life of the two treatment groups.

**Measure of benefits used in the economic analysis**
A cost-minimisation analysis was undertaken, as the analysis of the effectiveness data did not provide conclusive evidence that one of the treatment options resulted in greater long-term resolution of symptoms or differences in the health-related quality of life.

**Direct costs**
The costs to the health service were included in this study. Details of the number of physician, specialist and emergency department visits, diagnostic procedures and use of prescription medications were collected from interviews with the patients. These were conducted at 2, 4, 12 and 24 weeks following the start of the treatment. The results were verified by consulting the patient's medical notes.

The cost of outpatient appointments, diagnostic services and inpatient stays were based on the actual charges from the university accounting and billing system. The costs of medications were taken from the Red Book average wholesale prices. No data were collected for over-the-counter medication for heartburn since it was deemed unfeasible to collect accurate data. Since data were collected for all of the medical costs, no imputation was required.

The resource quantities and the unit costs were not reported separately. The price year used was 1998. The costs were not discounted, which was appropriate given that they related to a 6-month period.

**Statistical analysis of costs**
Medical costs were log transformed before they were analysed. An ordinary least-squares regression analysis was performed to compare the mean treatment costs by intervention group. The analyses used age, gender, clinic location, co-morbidity and baseline scores on the physical element of the SF-36. The price data appear to have been treated in a deterministic manner.

**Indirect Costs**
No indirect costs were included in the study.

**Currency**
US dollars ($).

**Sensitivity analysis**
No sensitivity analysis was performed.

**Estimated benefits used in the economic analysis**
See the 'Effectiveness Results' section.

**Cost results**
The mean total cost of treatment over 6 months was $8,371 (standard deviation, SD=$2,408) in the omeprazole group and $9,286 (SD=$2,268) in the ranitidine group, (p=0.64).

The mean inpatient costs were $7,174 (SD=$2,313) in the omeprazole group and $8,128 (SD=$2,189) in the ranitidine group, (p=0.28).

The mean outpatient costs were $1,198 (SD=$158) in the omeprazole group and $1,158 (SD=$129) in the ranitidine group, (p=0.76).

The authors analysed the medical costs on the basis of whether treatment was continued for less than or more than 8 weeks. Treatment for less than 8 weeks resulted in medical costs of $8,862 (SD=$3,165) with omeprazole and $7,568 (SD=$2,756) with ranitidine. If the treatment was continued for 8 or more weeks, the medical costs in the omeprazole group fell to $7,749 (SD=$3,734), whereas those in the ranitidine group increased to $11,656 (SD=$3,840), (p=0.03).

**Synthesis of costs and benefits**
A cost-minimisation analysis was undertaken, therefore the costs and benefits were not synthesised.
Authors' conclusions
The use of omeprazole and ranitidine resulted in improved clinical symptoms in patients with symptomatic gastroesophageal reflux disease (GERD). However, there was no statistically significant difference between the two regimens after 24 weeks of treatment. The total costs for the omeprazole group were $915 lower than those for the ranitidine group. Further, the results indicated that the costs are lower if omeprazole treatment is continued beyond 8 weeks.

CRD COMMENTARY - Selection of comparators
There was no explicit justification for the use of the comparator. You should consider if either of the treatment regimens included in the study represent current practice in your own setting.

Validity of estimate of measure of effectiveness
The study design was appropriate to address the study hypothesis. The quality of the effectiveness data would have been improved had the patient and their attending physicians been blind to the intervention group. It was noted, however, that this would have made it difficult for the treatment of the patients to be completely handed over to their usual physician in the manner used in this study. By analysing the effectiveness data on an intention to treat basis, the authors appropriately took account of the potential changes to treatment after randomisation. As the authors did not compare the study sample to the study population, it is not possible to comment on how representative the sample was. The authors stated that many of the patients whose care was funded by Medicaid were, in line with the scheme's policy, transferred off treatment with omeprazole after 8 to 12 weeks. They acknowledged that this might have had an impact on the effectiveness results. The authors argued that the patient groups were similar at baseline, but they did not compare the proportion of each group whose medical care was funded by Medicaid. Consequently, this potentially confounding factor was not included in the analysis.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of benefit as a cost-minimisation analysis was undertaken.

Validity of estimate of costs
The paper did not explicitly state the perspective from which the study was undertaken. However, it appears to have been that of the health care service. All the relevant costs to this perspective appear to have been included, except for the over-the-counter medication for heartburn. In some cases hospital charges were used instead of the true opportunity costs. This may be suitable for a health service perspective, but not for a societal perspective. The paper did not report the medical costs in sufficient detail to allow adequate recalculation of the results for other settings. The fact that the resource quantities and the unit costs were not reported separately also limits the generalisability of the results. However, the price date was reported, which does help the generalisability.

Uncertainty in the cost data was investigated through appropriate statistical analysis. However, the prices used in the study appear to have been treated in a deterministic manner and they were not subjected to a sensitivity analysis.

Other issues
The authors compared the results of their study with a number of other appropriate studies. However, they did not directly address the generalisability of the results to other settings. The authors presented their results in a comprehensive manner and acknowledged limitations to their study, a number of which have been highlighted already. In addition, they reported that the introduction of non-prescription ranitidine might have influenced the results even though the non-prescription drug was at a lower dosage.

Implications of the study
The authors suggest that the recommendation to limit treatment with omeprazole to 8 weeks does not result in reduced medical costs and may result in worse clinical outcomes.
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