Six-month management of patients following treatment for gastroesophageal reflux disease symptoms: a Norwegian randomized, prospective study comparing the costs and effectiveness of esomeprazole and ranitidine treatment strategies in a general medical practitioners setting


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 treatment of symptom-free gastroesophageal reflux disease (GERD) with esomeprazole 20 mg/day, esomeprazole 20 mg on-demand, or ranitidine 150 mg twice daily.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised adults with symptom-free GERD (no more than 1 day with mild heartburn in the previous 7 days) following treatment with esomeprazole 40 mg once daily for 4 weeks.

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

Dates to which data relate
The effectiveness and resource use data referred to the period between September 2000 and May 2002. The price year was 2001.

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

Link between effectiveness and cost data
The resource use data were collected retrospectively from the same patient sample that provided the effectiveness data.

Study sample
A total of 2,156 individuals were recruited to the study but 254 were excluded prior to randomisation. Of the remaining 1,902 patients, 658 received continuous esomeprazole, 634 received esomeprazole on-demand, and 610 received continuous ranitidine. The study sample was based on sample size calculations that would allow the detection of a difference of NOK 200 in direct medical costs. Details of how the patients were recruited were not given in the paper.
Study design
The study was a multi-centre, randomised controlled trial that appears to have included 281 general practice clinics. The paper did not indicate how the patients were randomised to the three treatment groups. There does not appear to have been any blinding to treatment group. The patients were followed up for 6 months but loss to follow-up was not reported in this paper.

Analysis of effectiveness
The primary health outcomes assessed were patient satisfaction (measured on a 7-point Likert scale), relapse rate, and heartburn symptoms at the 6-month follow-up. The analysis of the effectiveness data was carried out on an intention to treat basis. The three treatment groups were shown to be comparable in terms of their age, gender and symptom severity at baseline.

Effectiveness results
In the continuous esomeprazole group, 82.2% of patients were completely or very satisfied with their treatment, compared with 75.4% in the esomeprazole on-demand group and 33.5% in the ranitidine group.

More patients had no heartburn symptoms in the continuous esomeprazole group (72.2%) than in the esomeprazole on-demand group (45.1%) and ranitidine group (32.5%).

The proportion of patients who had at least one relapse was lowest in the continuous esomeprazole group (7.0%) than in the other two groups (10.9% in the esomeprazole on-demand group and 34.4% in the ranitidine group).

Clinical conclusions
The authors concluded that treatment with continuous esomeprazole is more clinically effective than either on-demand esomeprazole or ranitidine.

Measure of benefits used in the economic analysis
In the methods section of the paper, the authors stated that they would conduct a cost-consequences analysis. However, they went on to calculate cost-utility ratios in the discussion. The measure of health benefit used was the number of quality-adjusted life-years (QALYs) gained. The authors took health state valuations from a previous study and applied them to their study data.

Direct costs
The direct medical costs incurred by the healthcare payer and the patient, and transportation costs were included in the analysis. The resource use data were collected from the same patient sample that provided the clinical effectiveness data. The unit costs of prescription medication were taken as retail prices using nationally accepted formulae, while over-the-counter prescription unit costs were calculated using listed wholesale prices. The unit costs of physician visits and tests were taken from nationally agreed unit costs. The paper provided breakdowns of the unit costs and the total costs in each category. The price year was 2001.

Statistical analysis of costs
The differences between costs in the three treatment arms were tested using F-tests.

Indirect Costs
The indirect costs of lost productivity and lost leisure time were included in the analysis. The resource use data were collected from the same patient sample that provided the clinical effectiveness data, while the unit costs were taken from national Norwegian figures. The paper specified unit costs and provided a breakdown of the total cost of each indirect cost. The price year was 2001.
Currency
Norwegian kroner (NOK) converted to Euros (EUR) at a rate of EUR 1.00 = NOK 8.049.

Sensitivity analysis
Uncertainty in the cost data was investigated using one-way sensitivity analyses with an arbitrary variation in costs of 25% or one based on variation in medication retail prices.

Estimated benefits used in the economic analysis
Over the 6 months of the study, the authors calculated that treatment with continuous esomeprazole resulted in 0.413 QALYs, treatment with on-demand esomeprazole resulted in 0.406 QALYs, and treatment with ranitidine resulted in 0.396 QALYs.

Cost results
For the 6 months of the study, the total costs (direct and indirect) were EUR 295.8 in the continuous esomeprazole group, EUR 221.5 in the on-demand esomeprazole group, and EUR 286.6 in the ranitidine group.

Synthesis of costs and benefits
The incremental cost-effectiveness ratios only included direct medical costs.

The incremental cost per QALY of continuous esomeprazole compared with ranitidine was about EUR 1,600.

The incremental cost per QALY of continuous esomeprazole compared with on-demand esomeprazole was about EUR 11,000.

The sensitivity analyses showed that the study results were not sensitive to changes in cost data, with on-demand esomeprazole remaining the lowest cost option in all cases.

Authors' conclusions
Both continuous esomeprazole and on-demand esomeprazole are cost-effective treatment options in comparison with ranitidine.

CRD COMMENTARY - Selection of comparators
This study compared three treatment regimens for the treatment of symptom-free GERD but did not provide a rationale for their choices. You should consider how these options compare with usual practice in your own setting prior to applying the results of this study.

Validity of estimate of measure of effectiveness
The measure of clinical effectiveness was taken from a randomised controlled trial, which was appropriate for the study question. The authors did not compare their patient sample with the wider patient population, so it is not clear whether it was representative. All three patient groups were shown to be comparable at baseline in terms of their age, gender and symptom severity. The analysis of the clinical effectiveness data was conducted on an intention to treat basis. However, there were no details of any statistical tests on the clinical effectiveness data, which means that the level of uncertainty around this data cannot be assessed.

Validity of estimate of measure of benefit
Although the authors stated that they undertook a cost-consequences analysis, they calculated incremental cost-utility
ratios. Health state valuations were taken from a published study and were applied to the results of the randomised controlled trial.

Validity of estimate of costs
A societal perspective was adopted in the economic analysis. All appropriate costs appear to have been included, although the indirect costs were not included in the cost-utility ratios. Breakdowns of the unit costs and costs by category were provided, which adds to the generalisability of the study. However, no clear breakdown of resource use was provided. The differences in costs between the three patient groups were tested using appropriate statistical tests. Sensitivity analyses were undertaken to assess variation in the cost data. This means that the extent of uncertainty around the cost data was investigated, but the impact of variation in the clinical effectiveness data on cost-utility was not considered. The authors acknowledged that they used some price data as a proxy for cost information but suggested that this is unlikely to have altered their results. A clear price year was reported, which will facilitate future reflation exercises.

Other issues
The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. This study aimed to estimate the costs of the three treatments in Norway, thus the authors did not consider how their findings might be applied to other countries. The authors acknowledged that their resource use data were obtained through patient recall, which may be subject to recall bias. They also noted that their patient population comprised patients who had been treated with 40 mg/day esomeprazole prior to receiving one of the study treatments, and that this may have affected the subsequent efficacy of the treatments included in the trial.

Implications of the study
The authors did not make any direct recommendations for changes in practice or for further research.

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