The clinical and economic value of a short course of omeprazole in patients with noncardiac chest pain


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 the omeprazole test, compared with placebo, as a diagnostic test for detecting gastroesophageal reflux disease (GERD) in patients with noncardiac chest pain (NCCP). The omeprazole test consisted of a short course of high-dose omeprazole.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with at least three episodes per week of unexplained chest pain for a minimum of 3 months. A cardiologist referred the patients after a diagnostic evaluation had failed to reveal a cardiac cause for the chest pain. The average age of the population was 60 years. The study population consisted of mainly men. Patients were excluded for the following reasons:
if they had a medical contraindication for omeprazole therapy;
if they had already been empirically tested with an anti-reflux regimen;
if they had a history of peptic ulcer disease;
if they were unable to provide informed consent; or
if they were unable to complete all stages of the study.

Setting
The setting was secondary care. The economic study was conducted in Tucson, Arizona, USA.

Dates to which data relate
The effectiveness evidence and resource use data were collected between January and December 1996. The price year was 1997.

Source of effectiveness data
The effectiveness data were derived from a single study.
Link between effectiveness and cost data
The costing was carried out retrospectively using the same sample as that used in the effectiveness study.

Study sample
The study did not report any power calculations to determine the sample size. A total of 39 patients (38 males) were enrolled into the study. All the patients underwent an initial diagnostic evaluation with upper endoscopy and ambulatory 24-hour oesophageal pH monitoring. The patients were classified as either GERD positive (n=23) or GERD negative (n=14). Within each of these strata, the patients were randomly assigned to receive either omeprazole for 7 days, followed by a comparable dose of placebo for 7 days, or placebo initially, followed by omeprazole. The two treatments were separated by a 7-day washout period. The patients were randomised following an initial referral by a cardiologist who failed to confirm a cardiac cause for the chest pain.

The initial study sample comprised mainly men. The authors reported that there was no published evidence on the ratio of males to females who present with NCCP. It was therefore not possible to determine if the initial study sample was appropriate for the clinical study question.

Study design
This was a randomised double-blind, placebo-controlled crossover trial conducted in a single centre. The patients were randomised using a stratified block randomisation scheme with a block size of 4. The duration of follow-up was 5 weeks. Two patients were lost to follow-up because they did not complete all the symptom assessment diaries. The patients and clinicians were blinded to the treatment for the assessment of the outcomes. This was achieved using a placebo capsule identical in appearance to omeprazole.

Analysis of effectiveness
The analysis of the clinical study used treatment completers only.

The primary health outcomes used in the analysis were a change of less than 50% in the symptom intensity score, an improvement of at least 50% in the symptom intensity score, or the complete disappearance of the symptoms. The results for GERD positive and GERD negative patients were reported separately.

The sensitivity and specificity for the omeprazole test were also reported.

The two groups, GERD positive and GERD negative, were comparable at baseline in terms of their age and symptom intensity assessment of chest pain. No adjustments were made for confounding factors.

Effectiveness results
The results for the GERD positive group were as follows.

The symptom intensity for chest pain improved significantly during the administration of omeprazole compared with placebo, (p<0.0005).

Eighteen patients had a positive omeprazole test: 12 (52%) had complete resolution of their chest pain during the treatment period and 6 (26%) had at least 50% improvement in their chest pain.

During the administration of placebo, 11 (50%) had no improvement in the reported symptom score of their chest pain, whereas 5 (23%) had at least 50% improvement in their chest pain. A placebo effect was seen, where 11 (50%) patients reported some improvement in their chest pain during placebo administration.

The results for the GERD negative group were as follows.

The symptom intensity for chest pain was similar during administration of omeprazole and placebo.
Two patients had a positive omeprazole test: 1 patient had complete resolution of chest pain during the treatment period, which was significantly less than in the GERD-positive group (no p-value reported) and 1 patient had at least 50% improvement in chest pain.

During the administration of placebo, only 1 patient had complete resolution of their chest pain.

The sensitivity of the omeprazole test was 78.3% (95% confidence interval: 61.4 - 95.1) and the specificity was 85.7% (95% confidence interval: 67.4 - 100).

Clinical conclusions
The omeprazole test was sensitive and specific for diagnosing GERD in patients experiencing NCCP.

Modelling
A decision-analytic model was used to evaluate the potential economic impact of the omeprazole test, compared with a conventional diagnostic strategy, for patients with NCCP. A cost-minimisation analysis was performed.

Measure of benefits used in the economic analysis
No summary measure of benefits was used in the economic analysis. To justify the use of a cost-minimisation analysis, the authors assumed that the initial diagnostic procedure (omeprazole or endoscopy plus 24-hour oesophageal pH monitoring) would not affect the long-term outcome of patients with NCCP.

Direct costs
The costs and the quantities were reported separately. The study included the direct costs associated with the diagnosis of GERD. These included the costs of upper gastrointestinal endoscopy ($497.40), the ambulatory 24-hour oesophageal test ($315.74), oesophageal manometry ($342.25), the omeprazole test ($76.23), the omeprazole healing and maintenance course ($1,524.75), and diltiazem ($184.95).

The costs were estimated using a decision-analytic model. The cost estimates were taken from the Medicare Fee Schedule and the Red Book of wholesale prices for pharmaceuticals. The price year was 1997. The probability estimates for the model were derived from published literature and the results of the randomised controlled trial. The input parameters used in the model to derive cost estimates were:

the prevalence of GERD, 62%;
the sensitivity of the omeprazole test, 78%;
the specificity of the omeprazole test, 86%;
the sensitivity of ambulatory 24-hour oesophageal pH monitoring, 85%; and
the specificity of ambulatory 24-hour oesophageal pH monitoring, 85%.

The time horizon used for the cost estimates was one year. Discounting was not carried out because of the short timeframe of the study (one year).

Statistical analysis of costs
No statistical analysis of costs was reported.

Indirect Costs
No indirect costs were reported.
Currency
US dollars ($). No currency conversion rates were reported.

Sensitivity analysis
One-way sensitivity analyses were used to estimate the impact of the following input parameters in the decision-analytic model:

- the cost of the omeprazole test;
- the cost of upper gastrointestinal endoscopy;
- the cost of ambulatory 24-hour oesophageal pH monitoring;
- the cost of oesophageal manometry; and
- the test characteristics of ambulatory 24-hour oesophageal monitoring.

Estimated benefits used in the economic analysis
No summary measure of health benefit was used in the economic analysis. See the 'Effectiveness Results' section.

Cost results
Compared with a conventional diagnostic strategy, the omeprazole test saved $573 (28% reduction in the total cost) per average patient with NCCP referred for gastroenterology evaluation.

Synthesis of costs and benefits
Not relevant since the authors reported a cost-minimisation analysis.

The one-way sensitivity analyses found that the model was not sensitive to the costs of upper gastrointestinal endoscopy, ambulatory 24-hour oesophageal pH monitoring and oesophageal manometry. The analysis was also insensitive to the test characteristics of ambulatory 24-hour oesophageal monitoring. The omeprazole test was not, however, the preferred strategy if its negative predictive value was less than 2%.

The sensitivity analysis also found that the cost of the omeprazole test must be greater than $649 for the conventional diagnostic strategy to become less costly.

Authors’ conclusions
The omeprazole test was sensitive and specific for diagnosing GERD in patients with NCCP. The test resulted in significant cost-savings and a decreased use of diagnostic tests.

CRD COMMENTARY - Selection of comparators
The choice of the comparator for the effectiveness component of this study (no test) differed to that used in the cost-minimisation analysis (conventional diagnostic strategy). The choice of the comparator for the cost-minimisation analysis was explicitly justified. You should decide if this is a widely used diagnostic strategy in your own setting. The authors used a placebo test as a comparator for the intervention diagnostic strategy. This allowed the efficacy of the diagnostic test to be evaluated. It was not possible to relate the results of the effectiveness component of the study to the those of the cost-minimisation analysis, because two different comparators were used.

Validity of estimate of measure of effectiveness
The study design was appropriate for the study hypothesis. The study sample may not have been representative of the study population because it comprised mainly men. However, the authors reported that the ratio of males to females with new NCCP in the general population was unknown. The study did not report the use of a power calculation to determine the sample size. It was therefore not possible to assess if the study sample was sufficient to detect a statistical difference. A randomised controlled trial was conducted but the outcomes were assessed for treatment completers only.

**Validity of estimate of measure of benefit**

A summary measure of benefit was not used because the authors assumed that the long-term outcomes in NCCP were unlikely to be affected by the initial diagnostic strategy. A cost-minimisation analysis was reported. The authors assumed that all the outcome measures for the omeprazole test were equivalent to those for a conventional diagnostic strategy. This assumption was not supported by published evidence. Further, the authors compared the omeprazole test with the diagnostic strategy used to determine the sensitivity and specificity of the omeprazole test. This implies a higher rate of accuracy with the conventional diagnostic strategy than with the omeprazole test. If more patients have false negative or false positive omeprazole tests that result in inappropriate or no therapy being administered, on account of a misdiagnosis or delay in diagnosis, the assumption of equivalence in long-term outcomes is not supported. In this event, the analysis would be reduced to a cost analysis, and hence a partial economic evaluation.

**Validity of estimate of costs**

The authors conducted the study from the perspective of a third-party payer. The majority of the costs relevant to this perspective were included in the analysis. Some relevant costs were omitted from the analysis, such as the cost associated with side-effects. Two patients experienced side-effects taking omeprazole, although neither required discontinuation of treatment. The omission of the costs associated with side-effects is unlikely to have affected the authors' conclusions. The costs and quantities were not reported separately. It was unclear if the study used the costs or charges associated with the diagnostic tests. Discounting was unnecessary since all the costs were incurred over a one-year timeframe.

The resource use was estimated from a single study (for the omeprazole test) and the published literature (for the comparator). A sensitivity analysis was conducted and the ranges used for the input parameters appear to have been appropriate.

**Other issues**

The authors made appropriate comparisons of their results with the findings from other studies. The authors appear to have presented their results selectively. The issue of generalisability to other settings was not addressed. The effectiveness study enrolled mainly men and this may limit the generalisability to the general population. The authors acknowledged that this was a limitation of their study. It was unclear if a similar study population was used for the cost-minimisation analysis. The authors did not provide evidence to support their assumption that the long-term outcomes of the alternative diagnostic approaches were equivalent.

**Implications of the study**

The authors suggested that the omeprazole test is an accurate, simple, and clinically practical method of diagnosing GERD-related NCCP. The use of the omeprazole test as the initial diagnostic strategy may result in significant cost-savings to health plans and third-party payers.

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