Cost effectiveness of alternative Helicobacter pylori eradication strategies in the management of duodenal ulcer


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
Using one of nine strategies in the treatment of uncomplicated duodenal ulcer (DU). The nine strategies were the results of some therapeutic permutations in the context of three broadly defined sets of health technologies, including intermittent acid suppression, maintenance acid suppression, and H. pylori eradication.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients with uncomplicated duodenal ulcer.

Setting
Hospital. The economic study was carried out in Ontario, Canada.

Dates to which data relate
The data relating to H pylori eradication rates were extracted from papers published between 1992 and 1995. The dates relating to other clinical outcomes and resources used were not specified. 1995 prices were used.

Source of effectiveness data
The clinical probabilities were estimated based on a review of previously published literature. A decision analytic model (decision tree) was constructed to estimate the primary measure of effectiveness.

Modelling
A decision analytic model (a decision tree) was constructed to calculate the primary outcome and the expected costs of the alternative health technologies using the clinical probabilities estimated from the published papers.

Outcomes assessed in the review
The clinical probabilities estimated in the review consisted of ulcer healing probabilities, ulcer recurrence probabilities, and H pylori eradication probabilities.

Study designs and other criteria for inclusion in the review
The study included randomised controlled trials dealing with adults whose duodenal ulcer (DU) fulfilled two criteria: (1) it was larger than 5mm diameter and (2) its healing was identified by endoscopy at set intervals (e.g. four weeks, eight weeks).

**Sources searched to identify primary studies**
MEDLINE and other sources were used to identify the primary studies although specific details of the "other sources" were not given.

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

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

**Number of primary studies included**
The study included 26 ranitidine trials and 24 omeprazole trials. A recent meta-analysis was the main source of the H pylori eradication probabilities. The total number of primary studies included in the review was not explicitly specified and could not be derived from the references given in the paper.

**Methods of combining primary studies**
The only method mentioned for the combination of primary studies was pooling of data from the trials for each regimen to estimate the required clinical probabilities.

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

**Results of the review**
The ulcer healing probabilities for ranitidine at four weeks and eight weeks were 72% and 86%, respectively. The corresponding values for omeprazole were 64% at two weeks and 87% at four weeks. The ulcer recurrence probability at six months in the placebo group was 56%. The corresponding value for patients given continuous maintenance ranitidine was 12%, and 53% for patients with H pylori. An adjustment rate of 0.75 was used to estimate the endoscopically detected recurrence rates. The eradication rates and 95% confidence intervals for C1 to C6 were reported (with the exception of C2 which was not reported).

The eradication rate (and confidence intervals) were:

- C1: 61% (57-66)
- C3: 84% (79-90)
- C4: 85% (75-96)
- C5: 91% (88-94)
- C6: 86% (80-92).

**Methods used to derive estimates of effectiveness**
A decision analytic model (decision tree) was constructed to estimate the total expected ulcer time per patient over the...
12-month period of the model and ulcer-free time per healing episode.

**Estimates of effectiveness and key assumptions**
Ulcer-free time per healing episode was 2.15 weeks for a 4-weeks episode of omeprazole therapy, and four to six ulcer-free weeks for an 8-week episode of treatment with ranitidine. The total expected ulcer weeks per patient over the 12-month period for all strategies were: A1 (5.7), A2 (3.1), B1 (4.0), C1 (2.4), C2 (2.3), C3 (2.1), C4 (2.1), C5 (2.0) and C6 (3.8).

**Measure of benefits used in the economic analysis**
The measure of benefits was the total expected ulcer time per patient over the 12-month period.

**Direct costs**
Drug regimens were reported separately for each strategy. The resources used for the treatment of patients with symptoms of ulcer recurrence were not reported separately. The expected costs per patient were estimated for each health technology. Unit price was calculated and reported for all the drug regimens used in the study. Physician and hospital service costs were calculated but not reported in the paper. The costs were calculated from a governmental third-party payer's perspective. The sources of cost data consisted of a district database, a small survey of local pharmacies, an expert physician panel in association with a modified Delphi technique, and two district health organisations. The costs were adjusted to 1995 prices. The cost of endoscopy was omitted from the study since it was common across all health technologies. The costs of side effects were not considered in the study.

**Indirect Costs**
Not reported.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
A set of one-way sensitivity analyses was performed, although the parameters on which the analyses were carried out were not explicitly stated. The estimated 95% confidence intervals of eradication rates were used to perform a set of one-way sensitivity analysis.

**Estimated benefits used in the economic analysis**
The total expected ulcer weeks per patient over the 12-month period for all strategies were: A1 (5.7), A2 (3.1), B1 (4.0), C1 (2.4), C2 (2.3), C3 (2.1), C4 (2.1), C5 (2.0) and C6 (3.8). The side-effects of the treatment approaches were not considered in the economic analysis.

**Cost results**
The expected costs per patient (CAN$) over the 12-month period for all strategies were: A1 (Can$306), A2 (Can$343), B1 (Can$353), C1 (Can$387), C2 (Can$482), C3 (Can$292), C4 (Can$337), C5 (Can$306), and C6 (Can$226). The costs of side effects were not considered in the study.

**Synthesis of costs and benefits**
A comprehensive synthesis of cost and benefits for all strategies was not carried out since the intermittent strategies (A1 and A2) and the continuous maintenance strategy (B1) were dominated by H pylori eradication strategies C3 and C5. Incremental cost-effectiveness ratios (relative to strategy C6) were calculated to select the cost-effective strategies...
among the six H pylori eradication strategies. The incremental cost-effectiveness calculations revealed that strategies C3 and C5 with an incremental cost-effectiveness ratio of around Can$40 per ulcer-free week were the most cost-effective strategies of all. The values of the incremental cost-effectiveness ratios were not reported for all the H pylori strategies. The sensitivity analysis established the general robustness of the results to alternative assumptions. However, the results were sensitive to alterations in some of the eradication probabilities, for example if the eradication rate for strategy C6 were to be reduced from the baseline value of 86% to 50%, the strategy's status would change from being the least costly to the second most costly eradication therapy.

Authors' conclusions
The authors concluded that their analysis revealed that a move towards treatments targeted at H pylori eradication would both save money and improve health. Although bismuth triple therapy is the least costly of the eradication strategies, better outcomes for a modest increase in the cost can be achieved with omeprazole and two antibiotics given in a seven-day regimen, particularly strategies C3 and C5.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator is clear. The comparator was assumed to be a widely employed approach in the management of duodenal ulcer (DU). You should consider whether this is a widely used health technology in your own setting.

Validity of estimate of measure of benefit
As mentioned by the authors, the main shortcomings of the study affecting its internal validity are:

(1) the study did not take into account the side effects of the treatment strategies (complications and antibiotic resistance),

(2) the study did not consider the issue of noncompliance, and

(3) H pylori regimens selected for the study may seem outdated, which was due to the rapid change in the management of DU.

Validity of estimate of costs
Insufficient details were provided of the resources required and the costs included. Costs were only from the third-party payer's perspective and did not consider cost incurred by others in society such as patients.

Other issues
The cost data, from district organisations in Ontario, may not be generalisable to other settings or countries.

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