Recurrent duodenal ulcer haemorrhage: a pharmacoeconomic comparison of various management strategies
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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
Strategies to reduce recurrent duodenal ulcer (DU) bleeding were compared. The model evaluated three strategies, of which two pertained to the eradication of Helicobacter pylori (H. pylori) infection and one was a maintenance treatment.

Strategy A was empirical treatment for possible H. pylori infection followed by a proton-pump inhibitor (PPI) for 2 months.

Strategy B comprised a test for H. pylori infection, followed by eradication if positive or maintenance with a PPI if negative.

Strategy C was maintenance with a PPI alone.

The anti-H. pylori therapy included a combination treatment with three antibiotics (clarithromycin 1 g/day, ampicillin 1.5 g/day and tinidazole 1 g/day, all in divided doses) and a PPI (omeprazole 40 mg or lansoprazole 60 mg/day).

Type of intervention

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of middle-aged patients who had gastrointestinal bleeding from DU, which had already been controlled with endoscopic treatment (injection or thermal therapy) and pharmacotherapy (intravenous PPIs and somatostatin). They had no co-morbid illnesses and had not recently been using non-steroidal anti-inflammatory drugs (NSAIDs).

Setting
The setting was tertiary care. The economic study was conducted in a tertiary referral hospital in Northern India.

Dates to which data relate
The effectiveness data were obtained from studies published between 1993 and 2002. No information was provided on the dates to which the cost data referred.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of published studies.
Modelling
A decision tree analysis was undertaken, based on evidence from relevant articles and cost data, to calculate the expected costs and benefits of each of the three strategies over a 2-year period.

Outcomes assessed in the review
The main clinical effectiveness parameters included in the model were the probabilities of particular events occurring within each of the three strategies. These included:

- the probability that the ulcer healed;
- the probability that H. pylori was eradicated after initial therapy;
- the probability that H. pylori was eradicated after an unsuccessful initial regimen;
- the probability of a recurrent bleed after a healed ulcer;
- the probability of a recurrent bleed following endotherapy; and
- the probability of death after surgery.

Study designs and other criteria for inclusion in the review
Not stated.

Sources searched to identify primary studies
MEDLINE was searched for relevant articles to inform the effectiveness parameters. Cross-references from review articles were also searched.

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
Fourteen primary studies provided effectiveness evidence.

Methods of combining primary studies
It was unclear how data from the individual studies were combined to derive the probabilities of particular events. For some of the probabilities, only one primary study was used.

Investigation of differences between primary studies
Not stated.

Results of the review
The probability of haemostasis with endotherapy plus drugs was 80% (range: 60 - 100).

The probability of eradicating H. pylori with initial therapy was 70% (range: 50 - 90).
The probability of eradicating H. pylori after an unsuccessful regimen was 80% (range: 67 - 91).

The frequency of H. pylori infection in bleeding DU was 85% (range: 33 - 95).

The probability of ulcer healing with H. pylori eradication was 90% (range: 60 - 98).

The probability of ulcer healing despite failure to eradicate H. pylori was 60% (range: 57 - 61).

The probability of ulcer healing with PPIs was 90% (range: 70 - 95).

The probability of an active or recurrent ulcer with persistent H. pylori infection was 30% (range: 10 - 60).

The probability of a recurrent bleed with an active or recurrent ulcer was 30% (range: 10 - 60).

The probability of a recurrent bleed with a healed ulcer was 5% (range: 0 - 15).

The probability of a recurrent bleed with PPIs, without an anti-H. pylori drug, was 20% (range: 15 -30).

The probability of a recurrent bleed in patients with persistent ulcer who were on PPIs, without anti-H. pylori treatment, was 6% (range: 4 - 15).

The probability of death after surgery was 2% (range: 0 - 3).

**Measure of benefits used in the economic analysis**

The measure of benefit used was the quality-adjusted life-years (QALYs). Disutility values in patients with DU, its complications and treatment were derived from the literature (Groeneveld et al. 2001, see 'Other Publications of Related Interest' for bibliographic details).

**Direct costs**

The cost boundary adopted was that of the patient, since in India health care costs are borne by the patient. The quantities and the costs were not analysed separately. The direct costs measured included:

- the cost of endotherapy plus drugs to stop the bleed;
- the cost of hospitalisation in intensive care for one week;
- the cost of hospitalisation for 2 weeks;
- the cost of anti-H. pylori treatment for 2 weeks;
- the cost of treatment with PPIs for 2 months;
- the cost of maintenance treatment with PPIs for 2 years;
- the cost of retreatment for persistent H. pylori;
- the cost of diagnostic oesophagogastroduodenoscopy;
- the cost of a rapid urease test plus histology;
- the cost of emergency surgery for a bleeding DU; and
- the cost of a urea breath test.

The average costs were reported. The costs were obtained from a tertiary hospital in Northern India and a few other
private hospitals, based on records of hospital bills and discussions with physicians. It was unclear what year the cost data referred to. Although the time period of analysis was 2 years, it was unclear whether discounting was undertaken.

**Statistical analysis of costs**
The costs were treated deterministically as point estimates.

**Indirect Costs**
The indirect costs were not included in the study.

**Currency**
Indian rupees (INR). The study also reported the costs in US dollars ($). The conversion rate was INR 48 = $1.

**Sensitivity analysis**
A sensitivity analysis was conducted around the effectiveness and cost data to explore uncertainty in the model variables. The ranges over which the effectiveness variables were tested were derived from the literature, and were based on the lowest and highest probability values within the relevant articles. The range over which the cost estimates were tested was derived from hospital bills and discussions with physicians from a tertiary hospital, and other private hospitals in Northern India. A series of one- and two-way sensitivity analyses was undertaken. A one-way analysis was undertaken on:

- the probability of eradicating H. pylori after initial therapy;
- the frequency of H. pylori infection in bleeding DU;
- the probability of ulcer healing with H. pylori eradication; and
- the probability of ulcer healing with PPIs.

A two-way analysis was undertaken on:

- the probability of eradicating H. pylori after initial therapy;
- the probability of ulcer healing with H. pylori eradication; and
- the cost of maintenance treatment with PPIs for 2 years.

**Estimated benefits used in the economic analysis**
The QALYs gained with each of the three strategies was 1.9.

**Cost results**
The intervention cost per patient treated was INR 7,481 ($155.8) with strategy A, INR 8,198 ($170.8) with strategy B, and INR 14,500 ($302.1) with strategy C.

**Synthesis of costs and benefits**
The empirical H. pylori treatment followed by PPIs for 2 months was the most cost-effective strategy for the prevention of recurrent bleeding. The cost per QALY gained for each of the strategies was calculated.

The average cost-effectiveness ratios were INR 3,937.4 ($82.0) per QALY for strategy A, INR 4,314.7 ($89.9) per QALY for strategy B, and INR 7,631.6 ($158.9) per QALY for strategy C.
The one-way sensitivity analysis revealed that strategies A and B were competitive options. If the probability of H. pylori eradication was less than 58% and that of healing of a DU after H. pylori eradication was less than 73%, strategy B became the most cost-effective option. Strategy B also became the most cost-effective if the frequency of H. pylori infection was less than 58% in patients with a bleeding DU.

The two-way sensitivity analysis revealed that strategy B was the best option when the probability of ulcer healing following H. pylori eradication was less than 79% and the cost of maintenance PPI treatment for 2 years was more than INR 6,400 ($133.3).

Authors' conclusions
Anti-Helicobacter pylori (H. pylori) treatment followed by proton-pump inhibitors (PPIs) for 2 months was the most cost-effective strategy to prevent recurrent bleeding.

CRD COMMENTARY - Selection of comparators
The choice of the comparator was clear. Strategy C reflected current practice across a range of settings. The reader should consider whether this reflects current practice in their own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken and very little information on the nature and method of the review of the literature was provided. It was unclear how the estimates of effectiveness from the primary studies were combined, or whether the authors used data from the available studies selectively. It was also unclear whether the authors considered the impact of differences between the primary studies when estimating effectiveness.

Validity of estimate of measure of benefit
The measure of health benefit (QALYs) was derived from a decision tree model. Disutility values were derived from the literature and based on a single source. No other information was given. The authors acknowledged that potential events were not included in the model. Reinfection with H. pylori after eradication was not included, but the authors considered that this would not impact on the study conclusions.

Validity of estimate of costs
The costs were estimated from a patient perspective, since in India patients pay for their medical care. However, it was not clear whether all of the costs relevant to this perspective were included in the analysis, for example travel costs. The authors acknowledged that the estimated costs of maintenance PPI treatment were probably conservative, owing to the limited time horizon of 2 years. However, a sensitivity analysis of the costs was conducted to consider uncertainty in the cost of maintenance treatment with PPIs for 2 years. The costs and the quantities were not reported separately and no price year was given. Although discounting would have been appropriate given the 2-year time horizon of the study, it was unclear whether this was undertaken. Some cost data were also derived from hospital bills. These factors limit both the internal and external validity of the study.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, although the number of studies referred to was restricted because of the limited data on the cost-effectiveness of the different strategies. The issue of generalisability to other settings was addressed. The authors noted that the cost estimates in the study were derived from a developing country and the system of "out of patient's pocket". This, therefore, limits the generalisability of the results which would need to be considered with caution in a developed country. In addition, the authors considered that the typical patient in India was likely to exhibit different characteristics to those in developed countries. Patients in India with bleeding DU are less commonly elderly, do not have co-morbid illnesses, and are less often on NSAIDs than patients in most developed countries. The authors did not present their results selectively. The
study investigated different management strategies for recurrent DU haemorrhage and this was reflected in the conclusion. The authors also acknowledged that the time horizon of the study was low, but this was necessary because of the scarcity of data on longer term follow-up.

**Implications of the study**
The authors stated that all patients with bleeding DU should receive H. pylori eradication treatment, either empirical or test-based.

**Source of funding**
None stated.

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**Other publications of related interest**

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