The cost-effectiveness of competing strategies for the prevention of recurrent peptic ulcer hemorrhage

Ofman J, Wallace J, Badamgarav E, Chiu C F, Henning J, Laine L

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
Eleven strategies for the prevention of recurrent peptic ulcer haemorrhage were examined. There were three empirical strategies (1 to 3), four test-and-treat strategies (4 to 7) and four test/retest eradication strategies (8 to 11).

Strategy 1: empirical eradication strategy.
Strategy 2: empirical maintenance proton-pump inhibitor (PPI) therapy.
Strategy 3: empirical maintenance histamine-2 receptor antagonist (H2RA) therapy.
Strategy 4: eradication therapy for all Helicobacter pylori (H. pylori)-positive patients and maintenance PPI therapy for all H. pylori-negative patients.
Strategy 5: eradication therapy for all H. pylori-positive patients and maintenance H2RA therapy for all H. pylori-negative patients.
Strategy 6: "selective" eradication therapy for H. pylori-positive patients not receiving nonsteroidal anti-inflammatory drugs (NSAIDs) and maintenance PPI therapy for all H. pylori-negative and NSAID patients. The patients switched to selective cyclooxygenase-2 inhibitors if chronic NSAIDs were required.
Strategy 7: "selective" eradication therapy for H. pylori-positive patients not receiving NSAIDs and maintenance H2RA therapy for all H. pylori-negative and NSAID patients. The patients switched to selective cyclooxygenase-2 inhibitors if chronic NSAIDs were required.
Strategy 8: patients with an initial, negative biopsy urease test (Campylobacterlike organism, CLO) get retested with a carbon-labelled urea breath test (UBT). Eradication therapy was given to all H. pylori-positive patients and maintenance PPI therapy to all H. pylori-negative patients.
Strategy 9: patients with an initial negative CLO get retested with a carbon-labelled UBT. Eradication therapy was given to all H. pylori-positive patients and maintenance PPI therapy to all H. pylori-negative patients.
Strategy 10: patients with an initial, negative CLO get retested with a carbon-labelled UBT. "Selective" eradication therapy was given to H. pylori-positive patients not receiving NSAIDs, while maintenance PPI therapy was given to all H. pylori-negative and NSAID patients. The patients switched to selective cyclooxygenase-2 inhibitors if chronic NSAIDs were required.
Strategy 11: patients with initial negative CLO get retested with a carbon-labelled UBT. "Selective" eradication therapy was given to H. pylori-positive patients not receiving NSAIDs, while maintenance H2RA therapy was given to all H. pylori-negative and NSAID patients. The patients switched to selective cyclooxygenase-2 inhibitors if chronic NSAIDs were required.

Type of intervention
Diagnosis and treatment.
Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with an initial URH. Patients with oesophageal variceal bleeding or stress-related mucosal haemorrhage were excluded, as were those refractory or recurrent upper gastrointestinal haemorrhage.

Setting
The setting was not explicitly stated. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1988 and 2000. The resource use data came in part from studies published from 1993 to 1995. The costs were derived from 2000 estimates. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies, augmented by experts' assumptions.

Modelling
A decision tree model was constructed to estimate the costs and effectiveness of the alternative strategies for treating patients with URHs. The time horizon of the model was one year. The structure of the tree was not reported in the paper. As the physician was assumed to be unaware of false-positive or false-negative test results, a Bayesian analysis was considered in the model in order to assess the accuracy of diagnostic tests based on the underlying H. pylori status.

Outcomes assessed in the review
The outcomes assessed in the review were:

- the prevalence of H. pylori only;
- the prevalence of H. pylori and NSAID;
- the prevalence of NSAID only;
- the probability of H. pylori eradication with triple therapy or with quadruple therapy;
- the probability of recurrent haemorrhage in those testing H. pylori positive without treatment, after H. pylori eradication, with maintenance H2RA, or with maintenance PPI;
- the probability of recurrent haemorrhage in those testing H. pylori negative without treatment, with maintenance H2RA, or with maintenance PPI; and
- the sensitivity and specificity of the CLO, UBT and serology.

Study designs and other criteria for inclusion in the review
The authors stated that a systematic review of the literature was undertaken, but the design of the primary studies was not reported.
**Sources searched to identify primary studies**
MEDLINE and HealthSTAR were searched for relevant primary studies. English-language articles from 1985 were found by reviewing selected bibliographies.

**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**
Thirty-seven primary studies were included in the review.

**Methods of combining primary studies**
Weighted averages were calculated to place more emphasis on sample size when combining the primary studies. Estimates that biased the model against H. pylori eradication strategies were selected when possible.

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

**Results of the review**
The prevalence of H. pylori only was 37% (range: 13 - 51).

The prevalence of H. pylori and NSAID was 31% (range: 16 - 58).

The prevalence of NSAID only was 14% (range: 7 - 25).

The probability of H. pylori eradication was 85% (range: 45 - 98) with triple therapy and 80% (range: 45 - 98) with quadruple therapy.

The probability of recurrent haemorrhage in those testing H. pylori positive was 26% (range: 5 - 70) without treatment, 1% (range: 0 - 10) after H. pylori eradication, 7% (range: 4 - 15) with maintenance H2RA, and 6% (range: 4 - 15) with maintenance PPI.

The probability of recurrent haemorrhage in those testing H. pylori negative was 26% (range: 5 - 70) without treatment, 7% (range: 4 - 15) with maintenance H2RA, and 6% (range: 4 - 15) with maintenance PPI.

The sensitivity was 76% (range: 45 - 93) with the CLO, 95% (range: 90 - 99) with the UBT, and 90% (range: 80 - 95) with serology.

The specificity was 93% (range: 80 - 99) with the CLO, 95% (range: 80 - 99) with the UBT, and 80% (range: 70 - 90) with serology.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions, based on the opinions of a panel of expert gastroenterologists.

**Estimates of effectiveness and key assumptions**
The probability of NSAID discontinuation was 70% (range: 50 - 70). Patients who tested H. pylori negative with carbon-
labelled UBT, or completed quadruple drug therapy, were assumed by their physician to be cured and received no further anti-H. pylori therapy. It was assumed that the patients’ reports on NSAID usage were accurate. In addition, the physicians would attempt to discontinue NSAIDs in patients who did not need to remain on them, while those who actually needed NSAIDs were switched to selective cyclooxygenase-2 inhibitors.

**Measure of benefits used in the economic analysis**
The summary benefit measure was the rate of preventing recurrent URH. This was derived from the decision model.

**Direct costs**
Discounting was not carried out, which was appropriate as the time horizon of the model was one year. The unit costs were reported but details on resource use were not. The health services included in the economic evaluation were drugs, diagnostic tests, visits, haemorrhage treatment and hospital stay. A breakdown of the cost categories was provided. The cost/resource boundary of the study was that of the third-party payer. Resource use was estimated from the authors’ assumptions and published data. The unit costs were derived from the Drug Topics Red Book, American Medical Association Current Procedural Terminology codebook, and Medicare Reimbursement Fee Schedule. The price year was likely to have been 2000.

**Statistical analysis of costs**
The costs were treated deterministically in the base-case.

**Indirect Costs**
The indirect costs were not considered.

**Currency**
US dollars ($).

**Sensitivity analysis**
Sensitivity analyses were performed to investigate the robustness of the estimated cost-effectiveness ratios to variations in the model inputs (both costs and probability values) and assumptions. One-way and threshold analyses were carried out. The ranges tested were in part derived from the literature.

**Estimated benefits used in the economic analysis**
After one year, the rate of preventing recurrent URH was 0.9039 with strategy 1, 0.94 with strategy 2, 0.93 with strategy 3, 0.9567 with strategy 4, 0.9521 with strategy 5, 0.9497 with strategy 6, 0.9426 with strategy 7, 0.9601 with strategy 8, 0.9572 with strategy 9, 0.9508 with strategy 10, and 0.9447 with strategy 11.

**Cost results**
After one year, the estimated cost per patient was $1,217.70 with strategy 1, $1,922.80 with strategy 2, $1,246.80 with strategy 3, $1,387.30 with strategy 4, $1,088.90 with strategy 5, $1,659.10 with strategy 6, $1,199.50 with strategy 7, $1,258 with strategy 8, $1,069.70 with strategy 9, $1,590.40 with strategy 10, and $1,193.20 with strategy 11.

**Synthesis of costs and benefits**
Average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the eleven strategies.

The average cost per recurrent haemorrhage prevented was $1,347 with strategy 1, $2,045 with strategy 2, $1,341 with
strategy 3, $1,450 with strategy 4, $1,144 with strategy 5, $1,747 with strategy 6, $1,273 with strategy 7, $1,310 with strategy 8, $1,118 with strategy 9, $1,673 with strategy 10, and $1,263 with strategy 11.

The incremental analysis showed that after ranking all alternatives, strategy 8 was the only one that was not dominated. In general, all test/retest strategies were more cost-effective than test-and-treat strategies. "Selective" H. pylori eradication was not cost-effective within each sub-group of strategies. The model was sensitive to a few critical variables. More specifically, the cost of the carbon-labelled UBT, the H. pylori eradication rate, the haemorrhage rate, and the prevalence of H. pylori.

Authors' conclusions
The most cost-effective strategies for the prevention of recurrent ulcer-related haemorrhage (URH) were strategies that incorporated test/rest Helicobacter pylori (H. pylori) eradication with maintenance antisecretory therapy in H. pylori-negative patients.

CRD COMMENTARY - Selection of comparators
The authors provided a justification for the choice of the comparators. All the strategies were selected so as to cover the range of interventions for treating patients with URH. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a systematic review of the literature. The methods and conduct of the review were only reported in part. The authors described the sources searched and the method used to aggregate data coming from several sources. The designs of the primary studies were not described, which makes it difficult to assess the quality of the data that were used in the analysis. In addition, a group of experts made a number of assumptions. The method used to reach expert consensus was not provided. One strength of the analysis was the extensive use of sensitivity analyses.

Validity of estimate of measure of benefit
The summary benefit measure was specific to the disease considered in the study. This makes it difficult to compare with the benefits of other health care interventions. The measure was obtained from the decision model. This was likely to have been appropriate for representing the pattern of care for the population of patients under evaluation.

Validity of estimate of costs
The authors stated explicitly the perspective of the study. It appears that all the relevant categories of costs have been included in the analysis. A detailed breakdown of the costs was provided, but information on resource use was scarce and was mainly derived from the authors' assumptions. These assumptions reflected diagnostic and treatment patterns in the USA. The source of the cost data was reported. The costs were treated deterministically in the base-case, but several sensitivity analyses were carried out on the costs and resources used. The price year was reported, thus aiding reflation exercises in other settings. Discounting was not carried out. This was appropriate since the costs were incurred within a timeframe of one year.

Other issues
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Sensitivity analyses were carried out and these, in part, increased the external validity of the analysis. The authors noted some limitations to the validity of their study. More specifically, the use of assumptions, the uncertainty around the estimates derived from the literature, and the short timeframe of the analysis.
Implications of the study
The study results implied that, from the perspective of the third-party payer, the test/retest strategies with antisecretory therapy are the most cost-effective for the prevention of recurrent URH.

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