Helicobacter pylori eradication is superior to ulcer healing with or without maintenance therapy to prevent further ulcer haemorrhage

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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
Three strategies for the prevention of recurrent ulcer haemorrhage were examined. Strategy 1 was the treatment of Helicobacter pylori (H. pylori) infection. Strategy 2 was initial ulcer healing treatment followed by subsequent maintenance therapy with an H2-receptor antagonist. Strategy 3 was ulcer treatment alone (i.e. without treatment of H. pylori infection or subsequent management therapy).

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
No explicit details of the study population were reported. However, it was likely to comprise individuals with PUD.

Setting
The setting was not explicitly reported, but it was likely to have been that of the hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1993 and 2000. The dates to which the cost data related were not reported. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies. Although not explicitly stated, it appears that the review was a systematic review of the literature.

Modelling
A decision model was constructed using Data 3.5 decision analysis software (Treeage Inc., Williamstown) to compare the three treatment strategies for ulcer disease over a 12-month period. The probabilities for ulcer recurrence with bleeding, ulcer recurrence with pain but without bleeding, and death were derived from the results of the meta-analysis. The ranges for the sensitivity analysis were also derived from the results of the meta-analysis.

Outcomes assessed in the review
The main outcomes searched for in the review were the rates of eradication of H. pylori infection, and the rates of ulcer...
recurrence with bleeding. However, during the review, a further outcome was assessed and used to derive input parameters for the model. This outcome was the rates of ulcer recurrence with pain but without bleeding.

**Study designs and other criteria for inclusion in the review**
The authors searched for randomised controlled trials. The included publications had to provide information on the diagnosis of H. pylori, the therapy used to treat it, and the therapy used in the control group. They also had to describe compliance with medications, the frequency of non-steroidal anti-inflammatory drug usage, and the duration of follow-up. Three studies published as abstracts were excluded from the meta-analysis.

**Sources searched to identify primary studies**
MEDLINE was searched for articles published from January 1966 to December 2000. The authors also searched for publications in abstract form using article references and official proceedings of all major North America and European meetings. Duplicate publications were excluded. If more than one version of the same trial was retrieved, the one with the most recent data was used.

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

**Methods used to judge relevance and validity, and for extracting data**
All authors independently reviewed each study. Agreement was reached for all included studies.

**Number of primary studies included**
Seven studies were included in the review.

**Methods of combining primary studies**
The results of the individual primary studies were combined in a meta-analysis.

**Investigation of differences between primary studies**
The homogeneity of the trials was assessed using the Breslow-Day method, before pooling the data for the subsequent meta-analysis. Among trials comparing treatment of H. pylori infection with ulcer healing treatment alone (4 trials), there was no significant heterogeneity among the trials, \( p=0.36 \). There was also no significant heterogeneity among trials comparing treatment of H. pylori infection with initial ulcer healing treatment followed by maintenance therapy (3 trials), \( p=0.81 \). The trials were therefore combined in a meta-analysis.

**Results of the review**
When comparing treatment of H. pylori infection with ulcer treatment alone, the pooled relative risk reduction (RR) for recurrent bleeding was 79% (range: 50 - 100). The pooled absolute RR was 17% (95% confidence interval, CI: 9 - 25) and the number-needed-to-treat (NNT) to prevent one recurrent ulcer haemorrhage was 6 (95% CI: 4 - 11).

The pooled relative RR for recurrent ulcer with pain but without bleeding was 85% (range: 69 - 94). The pooled absolute RR was 25% (95% CI: 16 - 34) and the NNT to prevent one painful recurrence was 4 (95% CI: 3 - 6).

The pooled relative RR for recurrent ulcer with bleeding or pain was 81% (range: 75 - 88). The pooled absolute RR was 41% (95% CI: 30 - 52) and the NNT was 2 (95% CI: 2 - 3).

When comparing treatment of H. pylori infection with initial ulcer-healing treatment followed by maintenance therapy, the pooled relative RR for recurrent ulcer bleeding was 72% (range: 49 - 100). The pooled absolute RR was 4.1% (95%
CI: 0.6 - 7.5) and the NNT to prevent one recurrent ulcer haemorrhage was 25 (95% CI: 13 - 167).

The pooled relative RR for ulcer recurrence with pain but no bleeding was 79% (range: 76 - 100). The absolute RR was 7.4% (95% CI: 3 - 12) and the NNT to prevent one painful ulcer recurrence was 13 (95% CI: 8 - 33).

The pooled relative RR for ulcer recurrence with bleeding or pain was 77% (range: 77 - 89). The pooled absolute RR was 12% (95% CI: 6 - 17) and the NNT to prevent one ulcer recurrence with bleeding or pain was 9 (95% CI: 6 - 17).

For the treatment of H. pylori infection, the probability of ulcer recurrence with bleeding was 2.5% (sensitivity analysis range: 0 - 10). The probability of ulcer recurrence with pain without bleeding was 2.5% (sensitivity analysis range: 0 - 10).

For ulcer healing with maintenance H2-receptor antagonist, the probability of ulcer recurrence with bleeding was 6% (sensitivity analysis range: 2 - 13). The probability of ulcer recurrence with pain without bleeding was 10% (sensitivity analysis range: 5 - 20).

For ulcer healing with no maintenance therapy, the probability of ulcer recurrence with bleeding was 22% (sensitivity analysis range: 18 - 33). The probability of ulcer recurrence with pain without bleeding was 30% (sensitivity analysis range: 20 - 40).

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

No summary benefit measure was used in the economic analysis.

**Direct costs**

The perspective of the study was not explicitly reported, but it appears to have been that of the hospital. The direct costs used in the analysis were the costs of the drugs, upper endoscopy, hospitalisation for complicated ulcer recurrence (with bleeding), uncomplicated ulcer recurrence (pain but no bleeding; no hospitalisation required), and the treatment of a complication that proved fatal. The cost data were derived from the authors’ institution, and no further details were reported. The resource quantities and the costs were not reported separately. Discounting was not relevant since the costs were incurred during 12 months. The price year and the dates when the resource quantities were measured were not reported.

**Statistical analysis of costs**

The costs were treated deterministically.

**Indirect Costs**

The indirect costs were not reported.

**Currency**

US dollars ($).

**Sensitivity analysis**

Sensitivity analyses were carried out to investigate variability in the data. A one-way sensitivity analysis was carried out for the three strategies on the probabilities of ulcer recurrence with bleeding, and without bleeding but with pain after H. pylori eradication. The ranges used were derived from the meta-analysis. A one-way sensitivity analysis on the cost parameters was also carried out. The costs were varied between 50 and 1,000% of the initial estimates, but a justification for the choice of range was not reported. The authors also conducted a threshold analysis.
Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The estimated 1-year costs were $620 for treatment of H. pylori infection, $1,260 for initial ulcer healing treatment followed by subsequent maintenance therapy, and $4,280 for initial ulcer healing treatment alone.

Synthesis of costs and benefits
The costs and benefits were not combined. The threshold analysis revealed that possible changes in the optimal management strategy (from treatment of H. pylori infection to initial ulcer healing treatment, followed by maintenance therapy) could occur in two cases. More specifically, if the risk of a complicated ulcer recurrence after H. pylori eradication became higher than 6%, or if the cost of treating H. pylori (including the cost of confirming eradication) was over $741. The sensitivity analysis showed that the results were mainly dependent on the estimated costs associated with the treatment of complications, both fatal and nonfatal.

Authors’ conclusions
Effective treatment of Helicobacter pylori (H. pylori) infection was the least costly strategy for the prevention of recurrent ulcer haemorrhage. However, it should be noted that, if treatment of H. pylori infection does not decrease the incidence of complicated recurrences to below 6%, maintenance therapy may be a more reasonable option.

CRD COMMENTARY - Selection of comparators
The choice of the comparators was explicitly stated. Long-term maintenance antisecretory treatment after the initial ulcer bleed reflected standard practice in the authors' setting. The authors justified their choice of H. pylori infection treatment on the grounds of the absence of data concerning its superiority to standard practice. You should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been carried out. However, they did report the methodology of the review in full detail. The effectiveness estimates from the primary studies were combined in a meta-analysis and the homogeneity of the primary studies was statistically tested. The authors included only randomised controlled trials in the analysis, thereby ensuring the quality of the efficacy estimates. A number of sensitivity analyses relating to the efficacy estimates were also conducted. This analysis demonstrated the robustness of the results to changes in the base-case parameter estimates. Overall, the validity of the estimates obtained is likely to be high.

Validity of estimate of measure of benefit
There was no summary measure of benefit. The authors stated that they conducted a cost-minimisation analysis. However, they did not provide evidence of equivalent effectiveness, as one would normally expect in such an analysis.

Validity of estimate of costs
The perspective adopted in the analysis. The authors limited their analysis to the direct hospital costs, which suggests that the perspective was that of the hospital. Whilst relevant categories of costs were included, the use of summary costs meant that it was impossible to assess what aspects of costs were included within each category. For example, it was not evident whether overhead costs were included in the analysis. The authors used their own setting as the source of the prices and unit costs. It was not stated whether charges were used to proxy prices. The date to which the prices related was not reported. Although the authors conducted a one-way sensitivity analysis in which the costs were varied between 50 and 1,000%, the justification for these ranges was not reported.
Other issues
The authors compared their results with published studies comparing treatment of H. pylori infection with initial ulcer healing and subsequent maintenance therapy. They stated that, although these studies showed no statistically significant benefit of either treatment approach over the other, the pooled results (through meta-analysis) demonstrated a small but statistically significant advantage in treating H. pylori infection over maintenance therapy. The generalisability of the results to other settings or countries was not specifically discussed. Although a sensitivity analysis was conducted on the cost items, only the results of the threshold analysis were reported.

Implications of the study
The authors did not make any recommendations for policy change or practice. No further research was explicitly identified.

Source of funding
None stated.

Bibliographic details
Sharma V K, Sahai A V, Corder F A, Howden C W. Helicobacter pylori eradication is superior to ulcer healing with or without maintenance therapy to prevent further ulcer haemorrhage. Alimentary Pharmacology and Therapeutics 2001; 15(12): 1939-1947

PubMedID
11736725

Indexing Status
Subject indexing assigned by NLM

MeSH
Anti-Bacterial Agents /therapeutic use; Anti-Ulcer Agents /therapeutic use; Bismuth /therapeutic use; Drug Therapy, Combination; Helicobacter Infections /drug therapy /economics /microbiology; Helicobacter pylori /drug effects; Humans; MEDLINE; Metronidazole /therapeutic use; Omeprazole /therapeutic use; Organometallic Compounds /therapeutic use; Peptic Ulcer Hemorrhage /economics /prevention & control; Randomized Controlled Trials as Topic; Ranitidine /therapeutic use; Recurrence; Risk Factors; Salicylates /therapeutic use; Sensitivity and Specificity

AccessionNumber
22002000105

Date bibliographic record published
31/12/2004

Date abstract record published
31/12/2004