Cost-effectiveness of proton pump inhibitor therapy for acute peptic ulcer-related bleeding

Erstad B 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
The study evaluated the use of adjunctive oral and intravenous proton-pump inhibitor (PPI) therapies for patients with acute peptic ulcer-related bleeding of sufficient severity to warrant hospitalisation. Four clinical scenarios were considered.

Scenario 1 was diagnostic endoscopy and oral PPI therapy (40 mg twice daily of omeprazole or the equivalent dose of another PPI for 5 days).

Scenario 2 was diagnostic and therapeutic endoscopy with high-dose intravenous (i.v.) PPI therapy (80 mg bolus followed by 8 mg/hour for 72 hours).

Scenario 3 was diagnostic and therapeutic endoscopy with oral PPI therapy (40 mg twice daily of omeprazole or the equivalent dose of another PPI for 5 days).

Scenario 4 was diagnostic and therapeutic endoscopy without PPI therapy.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis and cost-utility analysis.

Study population
The study population comprised hospitalised patients with acute peptic ulcer-related bleeding who, based on endoscopic findings, were at high risk for re-bleeding. Patients considered to have a high risk of re-bleeding were those with active bleeding, visible vessels (bleeding or not bleeding) and adherent clots.

Setting
The setting was tertiary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data and some of the resource use data were derived from studies published between 1997 and 2003. The price year was not stated.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies and expert opinion.

Modelling
A decision tree model was used to estimate the costs and effectiveness of the therapies evaluated in the study. The structure of the model was reported. The time horizon considered was 30 days. The model assumed that confirmatory endoscopy was performed within 24 hours of the preliminary clinical diagnosis of acute peptic ulcer-related bleeding. Further, it was assumed that all patients would require at least 24 hours of hospitalisation.

Outcomes assessed in the review
The outcomes assessed were the probabilities of immediate surgery, recurrent bleeding and surgery for recurrent bleeding.

Study designs and other criteria for inclusion in the review
The author stated that the effectiveness evidence was collected from prospective, randomised placebo-controlled trials involving PPI therapy.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
The validity of the primary studies seems to have been ensured since only prospective, randomised placebo-controlled trials were selected.

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

Number of primary studies included
At least six trials were included in the review.

Methods of combining primary studies
A narrative method was used to combine the studies.

Investigation of differences between primary studies
No differences between the primary studies were investigated.

Results of the review
The probability of immediate surgery was 0.010.

The probability of patients requiring no surgery but diagnostic endoscopy was 0.66.

The probabilities of recurrent bleeding were 0.109 for scenario 1, 0.67 for scenario 2, 0.70 for scenario 3 and 0.225 for scenario 4.

The probabilities of surgery for recurrent bleeding were as follows:

after therapeutic endoscopy (no PPI), 0.150;

following repeat therapeutic endoscopy after previous therapeutic endoscopy (no PPI), 0.170;

after therapeutic endoscopy and i.v. PPI, 0.250;
following repeat therapeutic endoscopy after previous therapeutic endoscopy and i.v. PPI, 0.170;

after therapeutic endoscopy and oral PPI, 0.330; and

after oral PPI (no therapeutic endoscopy), 0.670.

**Methods used to derive estimates of effectiveness**
The probability of death related to surgery was derived using data available in a trial and expert opinion.

**Estimates of effectiveness and key assumptions**
The probability of death was estimated to be 0.1.

**Measure of benefits used in the economic analysis**
The summary measures of benefit used were the episodes of bleeding averted and the quality-adjusted life-years (QALYs) gained. The episodes of bleeding averted were obtained from the effectiveness analysis. The quality of life values associated with each health state were obtained from a published article (Teng et al. 2000, see 'Other Publications of Related Interest' below for bibliographic details).

**Direct costs**
Discounting was not relevant because of the short time horizon of the study. The direct costs included in the economic analysis were those related to endoscopy, length of stay, PPI therapy, blood transfusions, surgery and death. No adverse effect-related costs were included in the analysis, based on the minimal impact of their inclusion in a preliminary analysis. Moreover, no significant adverse effects due to PPI therapies had been reported. In addition, all other costs related to acute peptic ulcer-related bleeding, such as those related to the patient being seen in an emergency department, were presumed to be similar for all scenarios and were not included in the analysis. The costs were presented separately from the quantities of resource used. The unit costs were obtained from the literature and were updated using the Consumer Price Index. The price year was not stated. Although the trials used in the effectiveness analysis involved omeprazole, the costs of PPI therapy was based on pantoprazole with presumed dose equivalency.

**Statistical analysis of costs**
The costs were treated deterministically.

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

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses (with threshold analyses) were performed by decreasing and increasing all baseline costs by 50%. The author stated that a two-way sensitivity analysis was used to compare the PPI scenarios, but no further details were reported.

**Estimated benefits used in the economic analysis**
Compared with placebo, the proportion of episodes of bleeding averted was 29.40% in scenario 1, 30.79% in scenario 2, 30.70% in scenario 3 and 25.58% in scenario 4.
Compared with placebo, the QALYs gained were 0.5421 in scenario 1, 0.5435 in scenario 2, 0.5434 in scenario 3 and 0.5424 in scenario 4.

Cost results
The costs per patient were $2,999 in scenario 1, $2,614 in scenario 2, $2,688 in scenario 3 and $3,187 in scenario 4.

Synthesis of costs and benefits
The use of an i.v. PPI in conjunction with therapeutic endoscopy (i.e. scenario 2) was the dominant strategy since it presented superior effectiveness and lower costs. The findings were similar using either episodes of bleeding averted or QALYs gained for the effectiveness measure.

The costs per bleeding episode averted were $10,201 in scenario 1, $8,490 in scenario 2, $8,756 in scenario 3 and $12,459 in scenario 4.

The costs per QALY gained were $5,533 in scenario 1, $4,810 in scenario 2, $4,946 in scenario 3 and $5,876 in scenario 4.

The sensitivity analyses showed that the only variables that would alter the optimal choice of therapy were the cost of length of stay and the costs of PPI.

Authors' conclusions
High-dose intravenous (i.v.) proton-pump inhibitor (PPI) therapy in conjunction with therapeutic endoscopy was the most cost-effective approach in patients with acute peptic ulcer bleeding who, based on endoscopic findings, are at high risk for re-bleeding.

CRD COMMENTARY - Selection of comparators
The selection of the comparators was clear. The author compared all the strategies of interest in randomised trials that involved PPI and endoscopy therapies. Moreover, the author justified why other therapeutic options (e.g. angiographic therapy or operative interventions) were not included in the analysis. You should decide if the clinical scenarios analysed in this study are relevant to your own setting.

Validity of estimate of measure of effectiveness
The inclusion of only clinical trials in the review ensured the validity of the primary studies used. However, the search methods were not reported and a systematic review of the literature was not undertaken. It has to be considered that the effectiveness evidence for the PPI therapies was obtained from trials that involved omeprazole, whereas the economic analysis considered pantoprazole. The author argued that, according to the comparative information available, it was reasonable to assume that these PPIs were equally efficacious in equipotent doses.

Validity of estimate of measure of benefit
The summary measures of benefit used in the economic evaluation were appropriate. The episodes of bleeding averted is a common measure in analyses performed on populations similar to the one used in this study. Moreover, the use of QALYs as a measure of benefit enables comparisons with other studies performed in other populations. However, the author did not report the methodological approach used to derive the utility weights. In addition, a range of utility values was not explored in the sensitivity analysis.

Validity of estimate of costs
The resource quantities and the costs were reported separately, which enhances the possibility of conducting reflation exercises in other settings. However, the price year was not stated, hence impeding any future reflation exercises.
Sensitivity analyses of the cost estimations were performed. Discounting was not applied, which was appropriate given the time horizon of the study. The perspective adopted was explicitly reported, and all the costs relevant to the hospital perspective seem to have been considered. The use of a broader perspective and the inclusion of indirect costs would have been interesting.

Other issues
The author compared his findings with those of other studies and drew similar conclusions. The issue of generalisability was not explicitly addressed, but sensitivity analyses were performed. However, it was difficult to assess the external validity of the analysis since few details on the two-way sensitivity analyses were reported. Moreover, although the author stated that the costs were updated using the Consumer Price Index, the price year was not reported.

The author reported a number of limitations to the study. First, the outcomes were based on published literature and assumptions which may be prone to uncertainty. Second, it was assumed that the efficacy derived from studies conducted in countries outside the USA would be applicable in this country. Third, additional assumptions would be required with respect to the cost-effectiveness determinations based on QALYs, as the QALYs were not derived from the same studies used to determine the probabilities of clinical scenarios. Finally, the cost estimations were conservative since they did not consider the additional costs that may be required to purchase such products during the periodic shortages that occur due to donation and shelf-life issues.

Implications of the study
The study results supported the use of high-dose intravenous PPI in conjunction with therapeutic endoscopy in patients with acute peptic ulcer bleeding who, based on endoscopic findings, are at high risk for re-bleeding. The author stated that the results of the study should be corroborated using data from studies carried out with PPIs other than omeprazole. As mentioned earlier, it should be borne in mind that the effectiveness evidence was based on omeprazole, while the economic analysis was based on pantoprazole.

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Other publications of related interest

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