Costs and clinical outcomes of primary prophylaxis of variceal bleeding in patients with hepatic cirrhosis: a decision analytic model
Saab S, DeRosa V, Nieto J, Durazo F, Han S, Roth B

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 use of primary prophylaxis with a non-selective beta-blocker for patients with hepatic cirrhosis. Three strategies were compared:

strategy one, all patients were given beta-blockers;

strategy two, patients underwent upper endoscopic screening, and those found to have large oesophageal varices (grade III to IV) were given beta-blockers. Under the screening strategy, patients with small varices (grade I to II) were re-screened after 1 year, and patients without varices were re-screened after 2 years; and

strategy three, patients were given no prophylaxis.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The hypothetical study population consisted of patients with hepatic cirrhosis and no history of oesophageal variceal bleed.

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

Dates to which data relate

Source of effectiveness data
The effectiveness data were based on a review of the literature.

Modelling
A model was used to estimate the lifetime costs and effects of each of the prevention strategies. A Markov, cohort-based model was employed consisting of four health states: cirrhosis without variceal bleed, cirrhosis with variceal bleed, recurrent variceal bleed, and death. The model simulation ran over a patient lifetime. Markov cycle lengths were not reported and it was not clear if transition probabilities were time dependant.
Outcomes assessed in the review
The outcomes assessed in the review were variceal size distribution and rates of growth, risk of variceal bleed, the mortality rate associated with oesophageal variceal haemorrhage, the rate of complications with endoscopic screening, the efficacy of beta-blockers as primary prophylaxis, and the probability of intolerance to beta-blockers.

Study designs and other criteria for inclusion in the review
The authors did not specify the types of study design included in the review.

Sources searched to identify primary studies
The authors did not specify the sources searched to identify primary studies.

Criteria used to ensure the validity of primary studies
The authors did not specify the criteria used to determine the validity of the primary studies.

Methods used to judge relevance and validity, and for extracting data
The methods used to judge relevance and validity, and to extract data, were not detailed in the study.

Number of primary studies included
Ten studies were used to inform the efficacy of beta-blockers in the model.

Methods of combining primary studies
The method used to combine results from the primary studies was not specified.

Investigation of differences between primary studies
The authors did not investigate differences between the primary studies.

Results of the review
The results of the review indicated that the risk of bleeding with small or moderate varices could be reduced from 0.1 (range: 0.05 - 0.15) to 0.013 (range: 0.007 - 0.020) with the use of beta-blockers, and the risk of bleeding with large varices could be reduced from 0.2 (range: 0.02 - 0.3) to 0.12 (range: 0.06 - 0.18). Other model input parameters derived from the literature were fully reported in the paper.

Measure of benefits used in the economic analysis
The measure of benefits used in the economic analysis was quality-adjusted life-years (QALYs) gained. The estimated utility values were obtained from 9 clinicians using the Delphi panel method. Each clinician was asked to complete a questionnaire to value the quality of life of patients with compensated and decompensated cirrhosis, and with and without beta-blockers, between 0 (death) and 1 (perfect health). They were also asked to rate their confidence on a scale of 1 to 5. The clinicians were asked to complete the questionnaire twice, with the summary information from the first questionnaire being provided before completion of the second questionnaire.

Direct costs
Resource use quantities were not reported alongside costs. The direct costs to the hospital were included in the analysis. The costs included treatment with beta-blockers, the cost of screening upper endoscopy and treatment of any complications, the cost of managing oesophageal varices, the cost of routine care for cirrhosis and the cost of dying.
The costs were based on a review of published studies. The model considered a lifetime perspective, and so discounting was relevant, but it was unclear whether it was used in the base case analysis. The study reported average costs. The price year was 2000, but the method used to adjust for inflation was not specified.

**Statistical analysis of costs**
The cost data were treated as point estimates. This was appropriate given the lack of patient level data.

**Indirect Costs**
Indirect costs were not included in the analysis.

**Currency**
US dollars ($).

**Sensitivity analysis**
Several model parameters were tested in one-way simple sensitivity analyses. The parameters explored included the rate of compliance, the discount rate, the risk of bleeding with and without beta-blockers, the costs of drugs, esophagogastroduodenoscopy, complications, dying and variceal bleeds and the probability of death from variceal bleed. The areas investigated were variability in the data and generalisability of results. The method used to derive the ranges used in the sensitivity analyses was unclear.

**Estimated benefits used in the economic analysis**
No prophylaxis (strategy 3) resulted in 4.84 QALYs per patient over a lifetime perspective. The screening strategy (strategy 2) was associated with 5.72 QALYs per patient, and universal prophylaxis with beta-blockers (strategy 1) was associated with 6.65 QALYs per patient. Side effects from treatment may be incorporated in the utility values associated with use of beta-blockers. It was unclear whether discounting was used in the base case analysis.

**Cost results**
The cost per patient of no prophylaxis (strategy 3) was estimated to be $36,700 over a lifetime perspective.

The cost per patient of screening with endoscopy (strategy 2) was estimated to be $37,300, and the cost of universal prophylaxis with beta-blockers (strategy 1) was estimated to be $34,100.

It was unclear whether discounting was used in the base case analysis.

The cost of complications with endoscopy was included in the analysis.

**Synthesis of costs and benefits**
Costs and benefits were combined as cost per QALY saved for some comparisons. Universal prophylaxis with beta-blockers (strategy 1) was found to be a dominant strategy as it was the least costly and most effective. This result was robust to the one-way sensitivity analyses conducted.

**Authors’ conclusions**
The authors concluded that universal prophylaxis is cost-effective.

**CRD COMMENTARY - Selection of comparators**
The choice of endoscopic screening as comparator was justified as representing current practice in the authors' setting.
'No prophylaxis' is a relevant comparator, so was also included. The authors admitted that there might have been other relevant treatment strategies in this area that were not represented in this model. You should decide whether this analysis considers all the comparators relevant to your own setting.

Validity of estimate of measure of effectiveness
The authors did not state whether a systematic review of the literature had been undertaken. Sources searched, inclusion criteria and data extraction methods were not reported. This introduces the possibility that the data used to inform the model were not fully representative of the available evidence. It was unclear how data from the separate studies were combined in the review. The authors did not consider the impact of differences between the primary studies when estimating effectiveness. These facts make it difficult to assess if the best available evidence has been used to populate the decision model.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. A Markov state transition model was used to extrapolate data beyond the trial endpoints by assuming that the baseline risk of events and the relative risk of treatment remained constant over time. The authors admitted that their model does not consider the effects of ageing. You must consider whether the assumptions used in the model are reasonable.

Validity of estimate of costs
All categories of cost relevant to the perspective adopted were included in the analysis. Costs were not reported separately from quantities, and this may limit the generalisability of the results. Sensitivity analysis was undertaken around the cost estimates. It is unclear whether discounting was used in the base case analysis. The authors stated that all costs were reported in terms of dollars for the year 2000, but any adjustments were not reported.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability to other settings was addressed through the use of one-way sensitivity analyses. However, one-way sensitivity analysis cannot account for the combined uncertainty in all model parameters. The authors did not present their results selectively. The authors reported a number of further limitations to the study, including the use of expert opinion to derive utility estimates, and the failure to consider indirect costs, which may be particularly large with endoscopic screening.

Implications of the study
The authors recommended that universal prophylaxis with beta-blockers be considered a cost-effective strategy for patients with hepatic cirrhosis.

Source of funding
None stated.

Bibliographic details

PubMedID
12738453

DOI
10.1111/j.1572-0241.2003.07392.x

Indexing Status
Subject indexing assigned by NLM

MeSH
Adrenergic beta-Antagonists /economics /therapeutic use; Adult; Decision Support Techniques; Endoscopy, Gastrointestinal /economics /statistics & numerical data; Esophageal and Gastric Varices /economics /etiology /prevention & control; Follow-Up Studies; Gastrointestinal Hemorrhage /economics /etiology /prevention & control; Health Care Costs /statistics & numerical data; Humans; Liver Cirrhosis /complications /economics /therapy; Markov Chains; Outcome Assessment (Health Care) /economics /statistics & numerical data; Quality of Life; Sensitivity and Specificity; Severity of Illness Index

AccessionNumber
22003000855

Date bibliographic record published
31/03/2005

Date abstract record published
31/03/2005