Primary prophylaxis of variceal bleeding in cirrhosis: a cost effectiveness analysis

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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 for primary prophylaxis of variceal bleeding in cirrhosis. The strategies investigated were propranolol, sclerotherapy, and shunt surgery.

Type of intervention
Secondary prevention.

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

Study population
A hypothetical cohort of cirrhotic patients stratified according to nine risk groups based on the combination of the Child's classes A, B, and C, and varices of types 1 (Plaquet's grades I and II), 2 (Plaquet's grades II and IV without red signs or Plaquet's grades I and II with red signs), and 3 (Plaquet's grades III or IV with red signs).

Setting
Hospital. The study was carried out in Ohio, USA.

Dates to which data relate
The effectiveness data were obtained from studies published in 1990 and 1992. The dates during which the resource and cost data were collected were not clearly stated, although the authors reported those data to be in 'agreement' with those from a study published in 1987. The price year was not clearly stated.

Source of effectiveness data
The estimates for odds ratio of variceal bleeding, risk of death and dropout rates were derived from a review of previously completed studies.

Modelling
A Markov model was used to estimate costs and benefits associated with each strategy. The model incorporated 21 states, among which were nine bleeding states, three states representing minor complications, major complications and death from any cause. The model covered a period of 5 years.

Outcomes assessed in the review
The odds ratio of variceal bleeding (relative to natural history or observation), the risk of death, and dropout rates were assessed.
Study designs and other criteria for inclusion in the review
Meta-analyses and large randomized controlled trials published during 1966-1995.

Sources searched to identify primary studies
MEDLINE was searched to identify studies.

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
Not clearly stated. Fourteen published studies were included in the review, of which at least five were meta-analyses.

Methods of combining primary studies
The results from published meta-analyses and single studies were not combined. Sensitivity analyses were used to explore the effects of the variations on the results.

Investigation of differences between primary studies
Not stated.

Results of the review
The odds ratio of variceal bleeding (VB) with propranolol ranged from 0.47 to 0.54. The risk of death with this therapy was considered to be zero. The authors also assumed that 15% of patients stop that therapy. For SCL, the odds ratio of VB ranged from 0.60 to 0.85, with a mortality of 0.00-0.02 (0.01 at baseline). The dropout rate was the same as for propranolol. The SUR strategy turned out to have an odds ratio of 0.31, with a mortality rate ranging from 0.01-0.16 for Child's classes A and B and 0.50 for Child's class C.

Methods used to derive estimates of effectiveness
Estimates of effectiveness were also determined from experts' opinion.

Estimates of effectiveness and key assumptions
A utility of 1.0 was given to living without VB or any complications from treatment; 0.98 was given to living without bleeding but with minor side effects of PRO; 0.95 was assigned to living without bleeding but with esophageal stricture caused by SCL; for living without bleeding but with hepatic encephalopathy secondary to SUR, a value of 0.90 was used for mild to moderate and 0.2 for severe mental impairment; a utility of 0.7 was assigned for living with recurrent episodes of bleeding; for death from any cause, a value of zero was assigned.

Measure of benefits used in the economic analysis
The measure of benefits used in the economic analyses were life years and quality-adjusted life years (QALYs).

Direct costs
Whilst some quantities of resource use were reported separately from the costs, these included operating and
complication (initial treatment failures) costs. The sources of costs were the study institution's billing and pharmacy departments, and actual data from case series of 25 admissions with VB diagnoses (cost of treating a VB episode). The price year was not clearly reported. The quantity/cost boundary adopted was that of the hospital. Discounting was not applied.

**Currency**
US dollars ($).

**Sensitivity analysis**
The effects of the variability in the published estimates of VB incidence and mortality, the probability of changing Child's class and variceal size were analysed. A threshold analysis was also performed in terms of the value of the risk of bleeding from esophageal varices (not receiving prophylactic therapy) needed in order to make a specific option more cost-effective than observation (no-therapy option).

**Estimated benefits used in the economic analysis**
The propranolol strategy, relative to no-therapy, was found to increase the life expectancy of most groups in a range of 0.1 to 0.2 years, and to yield 0.1-0.4 QALYs gained in all groups. All the other strategies were associated with negative or slight positive figures for life years and QALYs gained relative to the comparator of no-therapy.

**Cost results**
The cumulative 5-year costs (ranges) per patient were (lower and upper values corresponding to the A1 and C3 groups, respectively):

observation (comparator) $5,829-$33,338;
propranolol $5,371-$18,664;
SCL $11,997-$29,822;
SUR $23,649-31,901.

**Synthesis of costs and benefits**
The results were presented as the number of patients who need to be treated in order to prevent one first VB episode and the estimated cost over 5 years. Cost-utility ratios were not used to synthesize costs and benefits. The price year was not clearly reported. It was not stated whether discounting was applied to the estimates. The number of patients and costs over 5 years for the propranolol strategy ranged within 30-5 and $76,650-$12,775, respectively. The SCL option had figures of 50-10 and $441,000-$82,200, and the SUR option was 16-3 and $350,400-$65,700. The relative ranking between the options was robust to the changes explored in the sensitivity analysis. The threshold analysis (minimum bleeding risk over 5 years at which each therapy is more cost-effective than the no-therapy option) yielded values of 12%, for the propranolol, 61% for SCL, and 82% for SUR.

**Authors' conclusions**
This study supports the use of propranolol as the most cost-effective therapy for prophylaxis against initial VB in all risk groups of cirrhotic patients with esophageal varices. In patients with Child's A disease, propranolol is cost-effective, but the benefit of treating patients for longer than 5 years needs to be further evaluated. Prophylactic SCL and surgery cannot be recommended on the basis of these results.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of comparator is clear. The do-nothing option (i.e. clinical history of cirrhosis with esophageal varices) represented such a choice. You, as a user of this database, should consider whether these are widely used health technologies in your own setting.

**Validity of estimate of measure of benefit**

The internal validity of the study results needs to be discussed in terms of the validity of the studies included in the review and the analysis of differences which might be behind the variations found. Moreover, the utility values were derived from the authors’ own opinions, rather than directly derived from patients’ preferences.

Validity of the analysis of costs:

The cost analysis covered a period of 5 years, with a report of some quantities of resource use being made. However the price year was not stated and nor was it reported whether costs were discounted.

**Other issues**

The conclusions were justified in terms of the sensitivity analysis, which explored the variations found in the literature for crucial parameters in the model. The issue of generalisability was not adequately addressed.

**Implications of the study**

Although the study describes some of the most relevant factors in the economic analysis of therapies for the primary prophylaxis of variceal bleeding in cirrhotic patients, it has important weaknesses that need to be addressed in order to provide a valid picture of the most efficient therapy option in this area of health care.

**Source of funding**

None stated.

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