A model of the health and economic impact of posttransfusion hepatitis C: application to cost-effectiveness analysis of further expansion of HCV screening protocols

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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
The impact of adding nucleic acid testing (NAT) for hepatitis C virus (HCV) to the existing, routine blood screening protocols that test for HCV antibodies in blood donors.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who received transfusion(s) in a hospital setting. The age of the patients ranged from new born to 104 years. The first, second and third quartiles were 52, 67 and 76 years, respectively. The authors reported that the patients' characteristics were comparable to those reported in the USA and other western countries.

Setting
The setting was secondary care. The economic study was carried out in Barcelona, Spain.

Dates to which data relate
The effectiveness data were collected from studies published between 1990 and 1999. The cost data were collected from studies published between 1995 and 1997. The price year was not reported.

Source of effectiveness data
The effectiveness data were taken from a review of completed studies.

Modelling
A Monte Carlo simulation of a Markov model was developed to represent the outcomes of patients transfused with HCV-infective blood. The model was then used to estimate the economic impact of post-transfusion hepatitis C, and to calculate the cost-effectiveness ratio of various HCV screening methods.

Kaplan-Meier plots were used to estimate the projected survival after transfusion-acquired infection, compared with the projected survival of controls without infection.

Outcomes assessed in the review
The following outcomes were used as input parameters for the model.

The short-term mortality risk due to underlying diseases in the 1st and 2nd post-transfusion years for three groups of patients: those aged up to 41 years, 41 to 65 years, and greater than 65 years.

The mortality risk after liver transplant in the first year, the second to third years, and the fourth to fifth years.

The quality of life assigned to four different health states: baseline health, symptomatic acute hepatitis, chronic hepatitis, and de-compensated hepatitis.

The quality of life assigned to patients after a liver transplant in the first quarter, the second to fourth quarters, and the second and subsequent years.

**Study designs and other criteria for inclusion in the review**

The authors’ reported that the studies included within the review were observational studies. No inclusion or exclusion criteria were reported.

**Sources searched to identify primary studies**

Not reported.

**Criteria used to ensure the validity of primary studies**

Not reported.

**Methods used to judge relevance and validity, and for extracting data**

Not reported.

**Number of primary studies included**

Approximately 9 primary studies were included in the review.

**Methods of combining primary studies**

Not reported.

**Investigation of differences between primary studies**

The differences between the primary data sources were not investigated or explained by the authors.

**Results of the review**

The inputs for the model were as follows.

The short-term mortality risk due to underlying diseases in the 1st and 2nd post-transfusion years: age up to 41 years, 0.08 and 0.02 quality-adjusted life-years (QALY); age 41 to 65 years, 0.22 and 0.06 QALY; and age greater than 65 years, 0.30 and 0.20 QALY.

The mortality risk after liver transplant: 0.0525 in the first year; 0.0063 in the second to third years; and 0.0050 in the fourth to fifth years.

The quality of life assigned to health states: 1.00 QALY for baseline health or asymptomatic chronic carrier; 0.70 QALY for symptomatic acute hepatitis (only for 3 months); 0.90 QALY for chronic hepatitis; and 0.50 QALY for de-compensated cirrhosis.
The quality of life preceding liver transplant: 0.50 QALY in the first quarter; 0.75 QALY in the second to fourth quarters; and 0.85 QALY in the second and subsequent years.

Measure of benefits used in the economic analysis
The measure of health benefit used was QALYs. The method for the valuation of health states was not reported. The QALYs were discounted at a rate of 3%. The authors reported the gain in quality-adjusted life expectancy for each HCV screening method, in terms of the number of hours per blood collection tested.

Direct costs
The costs and quantities were not reported separately. The study only included the direct health costs. The incremental cost of HCV antibody screening was estimated to be $5 per blood collection tested. The incremental cost of adding routine HCV NAT to the donor screening programme was estimated to be $10 (range: 5 - 25) per blood collection tested.

The cost of treating HCV-related complications was broken down as follows:
the cost of acute symptomatic hepatitis was $1,015;
the follow-up cost of treating asymptomatic chronic carriers was $164 per year;
the follow-up cost of treating chronic hepatitis was $328 per year;
the cost of interferon treatment in the first quarter was $1,588;
the cost of interferon treatment in the second to fourth quarters was $1,270 per quarter;
the cost of liver failure was $20,000 per year;
the cost of a liver transplant in the first quarter was $222,226;
the cost of a liver transplant in the second to fourth quarters was $21,276 per quarter;
the cost of a liver transplant in the second year was $23,488; and
the cost of a liver transplant in subsequent years was $12,688.

The cost of treating HCV-related complications and the cost estimates for HCV screening were obtained from published studies. The costs were discounted at an annual rate of 3%.

Statistical analysis of costs
No statistical analysis was conducted.

Indirect Costs
No indirect costs were included in the analyses.

Currency
US dollars ($). No currency conversions were reported.

Sensitivity analysis
One-way sensitivity analyses were performed. The parameters varied were the risk of HCV transmission, the cost of
HCV screening, the inflation of medical costs, the short-term mortality rate due to underlying disease, the patient's age, and the discount rate.

Estimated benefits used in the economic analysis
The gain in quality-adjusted life expectancy was:

17.65 hours per blood collection tested using surrogate markers, compared with no HCV screening;

12.83 hours per blood collection tested using HCV ELISA (antibody testing), compared with the use of surrogate markers; and

0.05 hours per blood collection tested using HCV RNA (NAT), compared with HCV ELISA.

Cost results
The present value of lifetime costs derived from treating PHTC was reported as $6,406 per patient in the main body of the text. However, this value was reported as $6,330 per patient in the abstract.

The comparative savings in the future cost of treating HCV-related complications were:

$27.58 per blood collection tested using surrogate markers, compared with no HCV testing;

$20.05 per blood collection tested using HCV ELISA (antibody testing), compared with surrogate markers;

$0.07 per blood collection tested using HCV RNA (NAT), compared with surrogate markers.

Synthesis of costs and benefits
The incremental cost-effectiveness ratio (ICER) for the introduction of HCV NAT, compared with current screening protocols, was $1,829,311 per QALY gained.

The sensitivity analysis varied the residual risk rate of post-transfusion hepatitis C after NAT implementation, but this only influenced the cost-effectiveness ratio to a limited extent. The ICER for a hypothetical "perfect test" that eliminated post-transfusion hepatitis C was $1.316 million per QALY gained. This was 28% below the baseline estimate.

The incremental cost-effectiveness of HCV NAT was only minimally sensitive to an inflated cost of treating medical liver diseases. At a hypothetical annual inflation rate of 12.5%, the cost-effectiveness of NAT declined to $1.529 million. This represented a decrease of 13% from the baseline estimate.

The incremental cost-effectiveness of HCV NAT was very sensitive to the patient's age. The ICER increased exponentially as the patient's age exceeded 60 years.

The short-term mortality due to underlying diseases had a far lower impact on the ICER. The ICER ranged from $1.448 million per QALY gained for patients who survived their underlying causes, to $2.317 million for those where the short-term mortality doubled the baseline estimate.

Authors' conclusions
The authors' concluded that post-transfusion hepatitis C had only a minimal impact on the patients' health, because of the advanced age of many of the recipients of the blood. The authors stated that the testing of blood donors for HCV antibodies resulted in net savings for the health care system, but the addition of HCV NAT would result in only minimal additional health benefits at a very high cost.
CRD COMMENTARY - Selection of comparators
No explicit justification was given for the choice of the comparator. However, it appears that the comparators represented current practice in the authors’ setting. You should decide if the comparator represents current practice 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 undertaken. No information was provided on the sources searched or how the studies were identified. In addition, the criteria on which the studies were selected and assessed were not described, and the methods used to extract the data were not provided. The authors used the data from the available studies selectively, and did not consider the impact of differences between the primary studies when estimating the effectiveness.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The Markov model used to derive the measure of health benefit, i.e. QALYs, was appropriate. However, it was not possible to assess how appropriate the QALY value used in the model were, because the authors did not report any details about the health state valuation methods.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted (national health service) were included in the analysis. Some of the costs were omitted from the analysis, but it seems unlikely that these omissions would have affected the authors’ conclusions. A sensitivity analysis of the unit costs was conducted using appropriate ranges for the parameters. The authors did not report the price year used or any currency conversions. Discounting was performed on future prices at a rate of 3% per annum. The discount rate was varied between 0 and 10% in the sensitivity analysis.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, and addressed the issue of generalisability to other settings. The authors reported that the main limitation of their study was the failure to take account of the possible impact of HCV RNA levels, viral genotypes or alcoholism on the course of the disease. However, they went on to state that this was because published data in this area were often scarce or contradictory, or reported in such a way that made mathematical modelling problematic.

Further limitations were evident. The authors stated that they omitted concurrent infection with other hepatotropic viruses because they were awaiting extended evidence on the role of these viruses in worsening the outcome of HCV infection. The authors did not provide the definitions of many of the abbreviations used in the paper. There also appears to have been a number of typographical errors in the paper, which in some instances, involved published results of the analysis. For example, the present value of the lifetime health costs incurred by patients with post-transfusion hepatitis C.

Implications of the study
The authors concluded that the routine screening of blood donors using HCV NAT would produce very little health benefit at a significantly high cost. They stated that this was because the health and economic gains that could be obtained from preventing post-transfusion hepatitis C had already been realised. Consequently, the authors reported that there was very little room left for further improvement. The authors argued that decisions about blood safety have been overly influenced by the political and emotional consequences of the Aids epidemic. They recommended that patients, physicians, policy makers and the public should make future decisions about the expansion of HCV screening programmes.

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