Including polymerase chain reaction in screening for hepatitis C virus RNA in blood donations is not cost-effective

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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 health intervention examined in the study was polymerase chain reaction (PCR) testing aimed at detecting the presence of hepatitis C virus (HCV) in blood donations.

Type of intervention
Screening.

Economic study type
Cost-effectiveness analysis.

Study population
The study population was represented by all recipients of blood donations to be screened for the presence of HCV in France.

Setting
The setting of the study was not explicitly stated. The economic study was carried out in France.

Dates to which data relate
Data on effectiveness evidence and resource use were derived from studies published between 1996 and 1999. No price year was reported.

Source of effectiveness data
The effectiveness evidence was derived from published studies and authors' assumptions.

Modelling
A decision model based on a Markov chain was constructed to simulate the natural progression of liver disease from chronic hepatitis C through six health states: chronic hepatitis C, compensated cirrhosis, decompensated cirrhosis, liver transplantation, hepatocellular carcinoma, and death. Annual transitional probabilities were estimated and used to move through the disease states. The medical treatment used was based on recombinant interferon-alpha (IFN) plus ribavirin for 12 months. The time horizon of the model was ten years.

Outcomes assessed in the review
The outcomes assessed in the review and used as model inputs were:

the number of HCV false negative tests (residual risk),
the potential decrease of this residual risk from adding PCR testing on each blood donation (strategy B') or on a pool size of 50 donations (strategy B''),

the sustained response rate of the combination therapy after 12 months, the sustained response rate for relapsers after an additional six months treatment, and the various transition probabilities between Markov states.

**Study designs and other criteria for inclusion in the review**
Not stated.

**Sources searched to identify primary studies**
Not stated.

**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**
Ten primary studies were used.

**Methods of combining primary studies**
A narrative method appears to have been used in which estimates from more than one source were combined. These were for the Markov transition probabilities and treatment effectiveness.

**Investigation of differences between primary studies**
Not stated.

**Results of the review**
The number of HCV false positive tests was 4.9 (range: 1.9 - 10.3) per million blood donations.

The potential decrease of this residual risk from adding PCR testing on each blood donation (strategy B') was 0.2 to 1.1 per million, which increased by 30% with pooling 50 donations (strategy B'').

The sustained response rate of the combination therapy after 12 months was 40% and the sustained response rate for relapsers after a further six months was 50%.

The Markov transition probabilities were fully reported in a diagram.

**Methods used to derive estimates of effectiveness**
Several assumptions were made by the authors, who were part of an expert committee set up by the French Ministry of Health to assess the advantages of PCR added to ELISA testing.

**Estimates of effectiveness and key assumptions**
The authors "estimated that among the total of blood donations in France (2,758,000 in 1996), 14 (5-30) HCV-infected
donations were negative for antibody with the current ELISA screening (strategy A) and that the addition of PCR
testing on each blood donation (strategy B') could potentially detect 12 (4-25) of these HCV-infected blood donations" and that "addition of PCR testing on pools (B'') could detect 11 (3-19) additional HCV-infected blood donations".

The average number of labile blood products for each donation was 1.2 and a 100% infection rate was maintained after transfusion of HCV-infected products.

The authors also assumed that:

20% of those infected would go into spontaneous remission;

the distribution of the survival rate in the general population of blood transfusion recipients was exponential,

25% of patients had contraindications for IFN treatment,

patients with no response had the same prognosis as patients not treated and received no long-term benefits from the treatment, and

patients with sustained response would not develop progressive diseases.

Measure of benefits used in the economic analysis
The benefit measures used in the economic analysis were the number of HCV infections averted, the number of cases of chronic hepatitis C averted, the number of severe hepatic disorders averted, and the number of years of life saved with strategy B' over strategy A and strategy B'' over strategy A.

Direct costs
A 3% discount rate was used since costs were incurred over a period of ten years. Unit costs were reported separately from quantities of resources for only a few items. The analysis of costs included the direct costs of the test minus savings due to HCV infections avoided. The direct costs included PCR testing (employees' wages, equipment, reagents, overheads and costs of identification) and the unit opportunity cost of replacing a blood donation. Cost savings reflected the avoided costs of treatments and included drug therapies, chronic hepatitis, cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, and transplantation for the first year and subsequent years. The cost/resource boundary adopted was that of the French health system. The estimation of costs and quantities was based on published data. No price year was reported.

Statistical analysis of costs
No statistical analysis of costs was carried out.

Indirect Costs
Indirect costs were not included.

Currency
Euros.

Sensitivity analysis
One-way sensitivity analyses were carried out to test the robustness of the estimated cost-effectiveness ratios. The number of additional cases detected with PCR testing in both strategy B' and B'' was varied within the reported ranges. Costs of treatment and follow-up and transitional probabilities were varied by 50%. Finally, 5% and 10% discount rates were used.
Estimated benefits used in the economic analysis
The average (range) number of additional HCV infections averted was 14 (5 - 30) with strategy B' and 13 (4 - 23) with strategy B" over strategy A.

The number of chronic hepatitis C averted was 1.7 (0.6 - 9.5) with strategy B' and 1.6 (0.5 - 2.8) with strategy B" over strategy A.

The number of severe hepatic disorders averted was 0.7 (0.3 - 3.8) with strategy B' and 0.6 (0.2 - 1.2) with strategy B" over strategy A.

The number of years of life saved was 0.2 (0.1 - 0.9) with strategy B' and 0.2 (0.1 - 0.4) with strategy B" over strategy A.

Cost results
The total costs of each strategy were not reported.

Synthesis of costs and benefits
An incremental analysis was carried out to combine costs and benefits of the strategies B' and B" over strategy A.

The average (range) net cost per additional HCV infection averted was 13.5 (37.8 - 6.3) million Euros with strategy B' and 1.4 (4.2 - 0.7) million Euros with strategy B" over strategy A.

The average (range) net cost per additional chronic hepatitis C averted was 111.1 (311.2 - 51) million Euros with strategy B' and 10.5 (34.5 - 5.9) million Euros with strategy B" over strategy A.

The average (range) net cost per additional severe hepatic disorder averted was 250.6 (702.1 - 117) million Euros with strategy B' and 23.7 (77.8 - 13.3) million Euros with strategy B" over strategy A.

The average (range) net cost per additional year of life saved was 891.1 (2,496.6 - 415) million Euros with strategy B' and 84.6 (276.7 - 47.5) million Euro with strategy B" over strategy A.

Sensitivity analyses showed that, even in a best-case scenario (30 avoided HCV infections and low PCR test cost), the incremental cost-effectiveness of both B strategies was too high and was not sensitive to variations in the remaining input parameters.

Authors' conclusions
The authors concluded that adding PCR to ELISA testing for the screening of HCV in blood donations was not a cost-effective intervention, mainly because of the high sensitivity of the ELISA test. The estimated incremental cost per life-year gained was far above the usually recommended thresholds for the adoption of new technologies.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The ELISA test was selected as it represented the standard screening test for the detection of HCV in blood donations. You, as a user of this database, should assess whether it represents a currently used screening test in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was derived from published studies, but a formal review of the literature was not undertaken and search methods were not reported. The validity of primary studies was not assessed and no analytic methodology was used to combine the effectiveness data, taking into account the differences between the studies. In addition the authors made numerous assumptions. An expert panel was used, but the approach was not described. To take into account uncertainty and variability in data, sensitivity analyses were carried out on most of the model inputs.
although few results were given.

**Validity of estimate of measure of benefit**
Several benefit measures were used in the economic analysis, although no account was taken of quality of life, for example via Quality-Adjusted Life Years (QALYs). All were modelled using a Markov process, which appears to have been appropriate to model the disease progression. Discounting of benefits was appropriately carried out.

**Validity of estimate of costs**
The cost analysis was carried out from the perspective of the French health system and it appears that all relevant categories of costs were included in the analysis. Both costs incurred with the screening test and costs avoided due to the efficacy of the interventions were included in the analysis. Costs and quantities were reported separately only for some cost items. No statistical analysis of costs was carried out, but several sensitivity analyses were performed. The price year was not reported, thus making reflation exercises to other settings difficult. Cost estimates were based on previously published data. Transparency would have been improved had the results of the costing and the sensitivity analysis been presented.

**Other issues**
The authors made few comparisons of their findings with those from other studies. The issue of the generalisability of the study results to other settings was addressed in terms of prevalence variability. For example, screening first time donors would be likely to be more cost-effective. Also, several sensitivity analyses were carried out. The authors acknowledged that several assumptions were made in the study and that the time horizon may not have been sufficient to capture long-term effects of PCR, but several sensitivity analyses were performed to test for different assumptions. However, the authors were selective in their presentation of the results.

**Implications of the study**
The main implication of the study is that testing for HCV is a controversial use of resources, and that "future discussions should integrate better the economic consequences of decisions about improvements of safety of the French blood transfusion system". However, as the authors pointed out, cost-effectiveness is not the only component in decision-making. In particular, one must account for individual preferences, including at a political level.

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None stated.

**Bibliographic details**
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