Cost effectiveness of screening for hepatitis C virus in asymptomatic, average-risk adults

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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
Screening strategies for hepatitis C in populations at average risk of infection were considered. Three screening strategies were analysed:

1. screening by third-generation enzyme-linked immunosorbent assay (ELISA), followed by confirmatory testing using polymerase chain reaction (PCR) alone;
2. screening by PCR alone; and
3. no screening.

Type of intervention
Screening.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of average-risk adults. The authors did not provide a definition of the "average-risk" population with respect to "high-risk" or "low-risk" populations. However, they reported that the study population should be without any specific complaints or symptoms. The age of the baseline cohort was 35 years. Two other age cohorts were considered, those aged 15 years and those over the age of 65 years.

Setting
The setting was primary care. The economic analysis was carried out in the USA.

Dates to which data relate
The effectiveness data were gathered from studies published between 1995 and 2001. The resource data were gathered from studies published between 1997 and 2001. Year 2001 prices were used.

Source of effectiveness data
The effectiveness data were derived from published studies.

Modelling
A Markov decision analytic model was created, using Monte Carlo simulations, to simulate the costs and the health outcomes assigned to each screening strategy. Eight health states were described. These corresponded to well, chronic hepatitis C, compensated cirrhosis with normal alanine aminotransferase levels, compensated cirrhosis with elevated alanine aminotransferase levels, decompensated cirrhosis, hepatocellular carcinoma, liver transplantation, and death.
The model was based on several assumptions. Two main assumptions were about the treatment of patients positive for the hepatitis C virus. Patients who tested positive would be referred for treatment, but only 20% of those with a positive test for hepatitis C would receive treatment. The treatment was a combination of interferon alpha and ribavirin.

The lifetime horizon was used.

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

- the prevalence of hepatitis C;
- the sensitivity and specificity of ELISA;
- the transition probabilities between disease states;
- the transmission rate;
- the treatment efficacy; and
- the quality of life assigned to the different health states.

**Study designs and other criteria for inclusion in the review**
The authors reported that treatment efficacy was obtained from randomised controlled trials. The study designs and other criteria for inclusion in the review were not specified for the other outcomes.

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

**Criteria used to ensure the validity of primary studies**
Not specified.

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

**Number of primary studies included**
The model data were derived from approximately 24 studies.

**Methods of combining primary studies**
The results of the individual primary studies were combined using a narrative method.

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

**Results of the review**
The prevalence of hepatitis C among 35 year-old adults in the USA was 0.038. The prevalence of chronic hepatitis C was estimated to be 0.029 in the same age cohort. The prevalence of chronic hepatitis C was estimated to be 0.003 for those aged 15 years and 0.007 for those over the age of 65 years.
The sensitivity of ELISA was 0.986 and the specificity was 0.99.

The Markov transition probabilities were reported in full (table 2).

The end-of-treatment response was 0.37 in patients with genotype 1 and 0.89 in patients with genotype 2 or 3.

The rate of relapse at the end of treatment was 0.24.

The annual rate of transmission in the USA population was 0.009. It was estimated to be 0.006 in the study population.

The health-state utility weights were reported in full (table 4).

**Methods used to derive estimates of effectiveness**

The authors made several assumptions to estimate the outcomes. The estimates were based on the literature, authors’ opinion, or calculations.

**Estimates of effectiveness and key assumptions**

The main assumptions were as follows:

- PCR is the ‘gold’ standard for hepatitis C testing and, therefore, the sensitivity and specificity were 1.00;
- all patients receiving the combination therapy would initially be assigned to a 6-month treatment course, and that approximately 20% would drop out after the first month; and
- patients receiving combination therapy would have a long-term relapse rate of 0.5% per year.

The utilities associated with chronic hepatitis C (0.96) and combination treatment (0.90), and also the disutility of learning a positive test result (0.02), were estimated from the literature and using authors’ opinions. The authors assumed that patients who became aware of their infection would reduce the probability of transmission by half.

**Measure of benefits used in the economic analysis**

The number of quality-adjusted life-years (QALYs) was used as the benefit measure. The quality of life was measured by health-state utility weights on a scale from 0 to 1, and was derived from the literature and authors’ opinions. The benefits were discounted at an annual rate of 3%.

**Direct costs**

A societal perspective was adopted. The direct costs included were for the screening tests, genotyping, complementary examination (including biopsy, complete blood count, liver ultrasound, liver profile, and visits), treatment and management care. The treatment costs covered the drugs, monitoring and follow-up. The unit costs were reported, but the quantities of resources used were not. Medicare fee schedules were used as a proxy for the cost of office visits, liver ultrasonography and liver profiles. The cost of ELISA, PCR and genotyping were based on charges from an independent laboratory, which were adjusted by an estimated 50% cost-to-charge ratio. The costs of drugs were derived from the Red Book 2000. The costs of management care were derived from published studies. All the costs were adjusted to 2001 US dollars. The total costs were derived using a decision analytic model. The source of the quantities was not reported. The costs were discounted at an rate of 3%, which was appropriate since the costs were incurred during more than 2 years.

**Statistical analysis of costs**

No statistical analysis of the costs was performed.
Indirect Costs
The loss of work owing to side effects from medication was included in the analysis. The authors valued time according to the average unskilled labour rate of $13.75 per hour. The quantities were based on authors' assumptions. The costs were discounted at a rate of 3%.

Currency
US dollars ($).

Sensitivity analysis
One- and two-way sensitivity analyses were performed on plausible ranges for clinical variables (95% confidence intervals were used when available) and on costs, using doubled or halved values. Extreme values were used for all utility weights, except for chronic hepatitis C. In addition, a Monte Carlo simulation was conducted on 10,000 trials.

Estimated benefits used in the economic analysis
The mean discounted QALYs for the no screening strategy was 23.596 QALYs. This was 0.002 more than the other screening strategies.

Cost results
The cost of no screening was much lower than the cost of the screening strategies. The mean cost of no screening was $390 per person, compared with $511 for ELISA-PCR and $572 for PCR alone.

Synthesis of costs and benefits
The no screening strategy was a dominant strategy as it provided marginally better outcomes at a lower cost. Therefore, a synthesis of the costs and benefits was not relevant.

The model was sensitive to the rate at which positively screened patients received antiviral therapy. When approximately 50% of patients who screened positive initiated treatment, the incremental cost-effectiveness ratio of screening with ELISA-PCR dropped below $50,000/QALY (a conventional threshold in health economics).

The model was also sensitive to the annual rate of progression to cirrhosis. A rate greater than 2.5% made the screening strategy ELISA-PCR cost-effective.

The model was not sensitive to the cost of screening, treatment or disease. Age also had little impact on the results.

When the disutility of knowledge of hepatitis C viral infection was less than 0.01, screening with ELISA-PCR was the most cost-effective strategy.

The Monte Carlo simulations showed that no screening strategy produced greater health benefits than ELISA-PCR in just over half of the trials, which also incurred lower costs in nearly all trials.

Screening with PCR alone was never cost-effective.

Authors' conclusions
The analysis does not support the widespread screening for hepatitis C among asymptomatic average-risk adults.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. The authors did not include recombinant immunoblot assay because it was less accurate and more expensive than the gold standard PCR. You should decide if any of the strategies...
compared in the study are widely used health technologies 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. The sources searched and the method used to select the data were not reported. It would appear that the effectiveness estimates were combined using narrative methods. The impact of differences between the primary studies was not investigated. Sensitivity analyses that varied the values of the effectiveness estimators were performed. However, the ranges of variation used in the sensitivity analyses were not justified, which limits the validity of the uncertainty results. The authors showed that the model was sensitive to changes in both the rate at which positively screened patients received antiviral therapy and the annual rate of progression to cirrhosis. The authors did not provide a clear definition of the average risks for hepatitis C infection.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled. It was unclear if the utility weights were derived from patient’s preferences or experts’ opinion. This fact limits the relevance of the quality of life measurements. The time horizon (until death) was appropriate for the study question. However, it seems that the natural mortality rate in the study population has not been considered in the Markov model. This omission might have biased the results in favour of the surgery strategy.

**Validity of estimate of costs**
All the categories of costs relevant to the perspective adopted appear to have been included in the analysis. The costs and the quantities were not reported separately. The price year was reported, considering some adjustments. Discounting appears to have been relevant, as the follow-up considered in the analysis was longer than several days. A sensitivity analysis was performed on the costs.

**Other issues**
The authors did not compare their results with those from other published studies. They also did not address the issue of the generalisability of the study results to other settings. The results were not reported selectively and the conclusions reflected the scope of the study. The authors did not report any limitations of their study. Sensitivity analyses were performed to account for variability in the cost or effectiveness data. Consequently, the external validity of the study may be high.

**Implications of the study**
The authors concluded that widespread screening of asymptomatic average-risk patients for hepatitis C cannot be recommended before the several questions are resolved. For example, the impact of hepatitis C diagnosis on quality of life and utilities; the proportion of newly diagnosed patients being treated; and the rate of progression of hepatitis C in asymptomatic average-risk patients.

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None stated.

**Bibliographic details**

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11755504

**Other publications of related interest**


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Subject indexing assigned by NLM

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