Case finding for hepatitis C in primary care: a cost utility analysis

Coon J T, Castelnuovo E, Pitt M, Cramp M, Siebert U, Stein K

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 study examined two alternative case-finding strategies for hepatitis C in primary care. Strategy one, the population approach, comprised an offer of testing to all those within a target age group. Strategy two, the targeted approach, offered testing to those known to be at highest risk of having contracted hepatitis C. Each programme was compared with a non case-finding arm in which individuals were permitted to spontaneously present for testing.

A series of testing and diagnostic procedures were available to both populations. These included the enzyme-linked immunosorbent assay (ELISA), reverse transcription polymerase chain reaction (PCR) and biopsy. Finally, patients confirmed with positive hepatitis C test results were offered treatment with pegylated interferon plus ribavirin at standard doses for a period of 48 weeks.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-utility analysis.

Study population
The study population differed according to the case-finding strategy. In the population approach, the study population comprised a hypothetical cohort of individuals aged 30 to 54 years who were attending a general practice for a non-urgent appointment. In the targeted approach, the study population included a hypothetical cohort of individuals already known to be at increased risk, such as those with a history of current or former injecting drug use.

Setting
The setting was primary care. The economic study was carried out in the UK.

Dates to which data relate
Much of the effectiveness data used to populate the model came from studies published between 1997 and 2006. The dates to which the resource use referred were not reported. The price year was 2004.

Source of effectiveness data
The clinical data used to populate the decision model were:

the prevalence of HCV and other epidemiological inputs,
the sensitivity and specificity of ELISA and PCR,
the rate of acceptance of PCR or ELISA in targeted and population strategies,
the mortality rates,
the rates of response to treatment, and
the transition probabilities across health states in the HCV simulation model.

Modelling
A standard decision tree was used to represent the patient pathway from the point of identifying individuals for testing to the offer of treatment with antiviral therapy. Then, a Markov model was developed to simulate the progression of hepatitis C in a hypothetical cohort of 10,000 eligible individuals. The time horizon of the model was lifetime (the average age of a typical patient was 37 years). The health states, cycle length and transition probabilities were reported in full.

Sources searched to identify primary studies
Data on the prevalence of HCV in the population strategy were derived from an unpublished source. This represented the only available UK estimate and was obtained through contact with experts. The prevalence of HCV in the targeted strategy was obtained from a published UK study. Other epidemiological data were obtained from UK databases. Test accuracy came from manufacturer's data (PCR) or a systematic review of the literature and meta-analysis (ELISA). Data on the treatment effect for antiviral therapies were obtained from randomised controlled trials (RCTs) or reviews of RCTs. Other published and unpublished sources were used to derive data on mortality, acceptance of tests and transition probabilities for disease progression. In general, UK estimates were used to populate the model.

Methods used to judge relevance and validity, and for extracting data
A review of the literature was undertaken. Commonly used databases (MEDLINE, EMBASE, the Cochrane Library and NHS EED) were searched to identify relevant studies from 1996 to 2004. Researchers and clinicians were also contacted. Only English language literature was searched. It would appear that the most recent and robust estimates were chosen from amongst those found in the literature. In particular, the authors stated that sources for clinical data were chosen on the basis of the methodological quality, publication date (favouring the most recent studies), relevance to the UK and appropriateness of the sample size. Given the lack of published evidence, some data were based on personal communications and expert opinion.

Measure of benefits used in the economic analysis
The summary benefit measure used was the quality-adjusted-life-years (QALYs). Quality of life weights were reported but their source was not stated. The benefits were discounted at a rate of 1.5%. Other model outputs, such as cases of decompensated cirrhosis, hepatocellular carcinoma and death, were also reported.

Direct costs
The analysis of the costs was conducted from the perspective of the NHS. It included the costs associated with patient identification and contact, time spent in discussion with the patient about HCV testing, diagnostic tests, genotyping, communication of test results, counselling, biopsy and specialist consultation. In addition, costs associated with model health states (different stages of hepatitis, liver transplant, etc.) were considered for the long-term analysis. The costs were broken down and most details on resource consumption and unit costs were provided. The authors stated that resource consumption and costs were based on recent UK estimates derived, for example, from the Office of National Statistics and Unit Costs of Health and Social Care. Discounting was relevant given the long timeframe of the analysis, and an annual rate of 6% was used. The price year was 2004.

Statistical analysis of costs
Normal distributions were assigned to the total costs for each model health state and means with standard errors were reported.
Indirect Costs
Inline with the perspective adopted, productivity costs were not included.

Currency
UK pounds sterling (€).

Sensitivity analysis
The issue of uncertainty was addressed by running a univariate sensitivity analysis on the clinical and economic inputs. The sources of the alternative values were not explicitly stated. An extensive probabilistic sensitivity analysis was also performed, and details of the distributions used for all model inputs were provided. In general, beta distributions were assigned to transition probabilities and utility weights, normal distributions to health state costs, and uniform distributions to patient characteristics.

Estimated benefits used in the economic analysis
The expected discounted (undiscounted) QALYs were 2.27 (3.10) with the population approach and 2.26 (3.09) with no case finding. The difference in discounted benefits (i.e. 0.011 QALYs) was in favour of the population approach.

The expected discounted (undiscounted) QALYs were 9.05 (12.36) with the targeted approach and 9.00 (12.29) with no case finding. The difference in discounted benefits (i.e. 0.046 QALYs) was in favour of the targeted approach.

Cost results
The expected discounted (undiscounted) costs were 570 (1,607) with the population approach and 400 (1,276) with no case finding. The incremental discounted costs for the population approach were 170.

The expected discounted (undiscounted) costs were 2,357 (6,241) with the targeted approach and 1,598 (5,094) with no case finding. The incremental discounted costs for the targeted approach were 170.

Synthesis of costs and benefits
Incremental cost-utility ratios were calculated to combine the costs and benefits.

The incremental cost per QALY gained with the population approach over no case finding was 15,493 (undiscounted 18,376).

The incremental cost per QALY gained with the targeted approach over no case finding was 16,493 (undiscounted 16,177).

The results of the probabilistic sensitivity analysis showed that, if the NHS willingness-to-pay for a QALY were assumed to be 30,000, then the probability that the population approach was cost-effective was 73%. The corresponding probability for the targeted approach was 77%.

The univariate sensitivity analysis showed that the model inputs with the greatest impact on the cost-utility ratio were the utility weights, the discount rate, and the rates of spontaneous and re-presentation of individuals for testing outside of case finding. For example, the use of a 3.5% discount rate (new NICE guidelines) for both the costs and benefits would make the cost-utility ratios less attractive, with an incremental cost per QALY of 35,000 for the population approach and 33,000 for the targeted approach. Similarly, if the rates of spontaneous and re-presentation of individuals for testing outside of case finding increased, then the incremental cost per QALY for the case-finding approaches also increased.
Authors' conclusions
Case finding for hepatitis C virus (HCV) in primary care was likely to be considered cost-effective from the perspective of the UK National Health Service (NHS). However, the analysis highlighted the fact that substantial uncertainties remain, especially for the impact of the interventions on quality of life aspects.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was appropriate. In effect, although no explicit justification was provided, the comparator appears to have represented current practice in the authors' setting. You should decide if the comparator represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came from a systematic review of the literature that aimed to include the most recent and valid sources of data. However, limited information on the review was provided. The authors reported the sources searched but not specific inclusion or exclusion criteria for the primary studies. The authors stated that data sources were selected on the basis of the methodological quality, publication date (favouring the most recent studies), relevance to the UK and appropriateness of the sample size. Details on each source of data were provided and it seems that the best evidence available was selected. Expert opinion was used when published data were not available. The issue of uncertainty around the clinical data was satisfactorily addressed through a probabilistic sensitivity analysis.

Validity of estimate of measure of benefit
The estimation of health benefit (QALY) was derived appropriately using a Markov model. The QALYs were appropriately discounted. The methods used to estimate the utility weights were not described and their source was not explicitly stated. Appropriate probability distributions were assigned to the utility weights. QALYs can be compared with the benefits of other health care interventions.

Validity of estimate of costs
The analysis of the costs was performed from the perspective of the NHS. It appears that all the relevant categories of costs have been included in the analysis. Details of the unit costs and the quantities of resources used were provided, which might help when replicating the analysis in other settings. The sources of the costs were reported, whereas details on the sources of resource consumption were less clear. The cost estimates were treated deterministically in the base-case, but stochastic distributions were assigned to economic inputs in the sensitivity analysis. Discounting was relevant and was appropriately performed. The price year was reported, which will facilitate reflation exercises in other time periods. Overall, the cost data were presented clearly.

Other issues
The authors noted the lack of published economic evaluations on case finding for HCV in the UK, which meant that comparisons with other studies were not possible. The issue of the generalisability of the study results to other settings was extensively addressed in the sensitivity analysis, in which alternative economic and clinical inputs were used. However, the results of the sensitivity analysis were reported selectively. The authors' conclusions reflected the scope of the analysis.

The authors pointed out some limitations of their study. For example, it was noted that some estimates used in the model were uncertain because of the lack of available published evidence. Further, the model did not consider treatment for people who are currently injecting drugs due to the controversial benefits of treatment in these individuals. Finally, the model results were highly sensitive to discounting and the use of current discount rates for costs and benefits (3.5%) resulted in a less attractive cost-effectiveness for the case-finding strategies.

Implications of the study
The results of the analysis support national and international guidelines on case finding for HCV. The authors stated that further research should provide the clinical estimates required in modelling studies, such as quality of life data and...
treatment effectiveness.

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