Economic evaluation of health care program for hepatitis C virus antibody screening

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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
A screen and treat strategy for hepatitis C (HCV) using HCV antibody tests and interferon (IFN). The strategy included three steps: (1) early detection of hepatitis C cases in the free-living population, (2) implementation of IFN for detected chronic active hepatitis cases, and (3) follow-up of cases who underwent IFN therapy.

Type of intervention
Screening and treatment.

Economic study type
Cost-benefit analysis.

Study population
Males and females aged over 30 years, in the general population of a Japanese prefecture.

Setting
Screening clinics in the districts of Saga prefecture, Japan.

Dates to which data relate
The effectiveness data were derived from a clinical study conducted between 1993 and 1995 and a review of studies reported in the literature, published between 1990 and 1996. The cost data were based on the same study between 1993 and 1995, and benefits were based on the findings of the single study and other studies published in the literature between 1990 and 1997. The price year was 1995.

Source of effectiveness data
The effectiveness data were derived from a single study, which was augmented by a review of epidemiological data in the literature.

Link between effectiveness and cost data
The cost data were derived retrospectively from the same sample that formed the clinical study.

Study sample
14,622 males and 42,124 females (aged 30-59) who were residents in Saga prefecture in Japan and who underwent the screening during the period 1993 and 1995. No power calculations were used to determine sample size.

Study design
This was a non-randomised trial with the estimated controls based on the natural history model of the clinical outcomes. The period of follow-up was until the end of the IFN treatment for the chronic active hepatitis patients, 1.5 years for asymptomatic HCV carriers who were suspected to be potential chronic active hepatitis cases and 10 years for the other asymptomatic HCV carriers. Loss to follow-up was not reported.

**Analysis of effectiveness**
The analysis of effectiveness was based on intention-to-treat. The outcomes assessed were reduction in the number of cases of hepatitis going on to develop liver cirrhosis or hepatoma.

**Effectiveness results**
Out of a total of 56,746 people who received screening, 1,486 (309 males and 1,177 females) received further thorough examination and 855 were found to require either treatments or regular follow-ups. Among these, 240 were found to have chronic active hepatitis and 186 underwent IFN treatment. 82 people were diagnosed as suffering from either cirrhosis of the liver or hepatoma and underwent different treatment programmes.

**Clinical conclusions**
(In conjunction with the review/model results) screening can effectively detect people suffering from chronic active hepatitis, liver cirrhosis or hepatoma and also those who, it is suspected, will develop the diseases in the future. In those suffering from chronic active hepatitis, IFN treatments can help prevent this from developing into more serious liver cirrhosis and hepatoma, and therefore lengthen people’s lives.

**Modelling**
The natural history of the clinical outcomes and associated costs were presented in a cost-consequences model.

**Outcomes assessed in the review**
The review assessed percentage of cases dying and their life expectancies (for males and females) who have chronic active hepatitis and one of the following sequelae: cirrhosis of the liver; cancer after the onset of cirrhosis; cancer.

**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**
10 studies were included in the review.

**Methods of combining primary studies**
Narrative method.

Investigation of differences between primary studies
Not stated.

Results of the review
According to the natural history of chronic active hepatitis sufferers:

- 53% of males (87% of females) die from the disease after 30 years;
- 40% of males (10% of females) develop cirrhosis of the liver - half of these cases die after 11 years and the remaining develop hepatoma after 8 years and then die 3.5 years later;
- 5% of males (1% of females) develop hepatoma after 20 years and then die 3.5 years later;
- 2% are cured naturally.

Measure of benefits used in the economic analysis
The benefits measured were the medical expenditures saved, based on the differing clinical outcomes, and gains in earned income by reductions of hepatoma, cirrhosis and hepatitis due to medical intervention, both of which would have resulted in losses of income had the health care programme not been implemented.

Direct costs
Direct costs included were:

1. Screening costs (set costs for HCV antibody, ZTT, ChE tests as it was not possible to calculate the costs for the HCV antibody test only);
2. Screening arrangement costs, such as various instruction costs for civil servants in the local areas, costs for health centre seminars, costs for screening manuals and other materials;
3. Thorough examination costs in hospitals, such as measurements of HCV-RNA and ultrasonic examination;
4. Costs for high level HCV carriers, including costs for IFN treatment, such as IFN medication costs, examination costs, hospitalisation costs and treatment costs for side effects. Direct costs also included the cost of follow-up examinations for asymptomatic HCV carriers (for the following 1.5 years for those who are suspected to develop into chronic active hepatitis and for the following 10 years for other asymptomatic high level HCV carriers);
5. Costs for low level HCV carriers including follow-up examination for the following 10 years.

Direct costs were calculated based on the costs recorded in the prefectural hospitals during the period 1993 to 1995. A discount rate of 3% was used as the standard discount rate for the cost calculation. Overall quantities and costs were reported separately. The price year was not given.

Statistical analysis of costs
Not undertaken.

Indirect Costs
Indirect costs included were lost earned income due to thorough examination, IFN treatments, and follow-up examinations. Indirect costs were calculated based on the 1998 Japanese government reports on the national living
standard. A discount rate of 3% was used as the standard discount rate. Costs and quantities were reported separately.

Currency
Japanese yen (Y).

Sensitivity analysis
Four sensitivity analyses were conducted.

Firstly, cost-benefit ratios were examined with three levels of discount rate (1%, 3%, and 5%).

Secondly the HCV carrier rate was changed to see the changes in the cost-benefit ratio with three levels of discount rates.

Thirdly, cost-benefit ratios were observed (with 3% discount rate) with different levels of HCV carrier rates with four different levels of Complete Responder (CR) in IFN treatments (29.8%, 34.8%, 24.8%, and 19.8%).

Fourthly, cost-benefit ratios were observed (with 3% discount rate) with different levels of HCV carrier rates with four different levels (35%, 45%, 25%, and 15%) of early detection rate for chronic active hepatitis who are targeted for IFN treatments.

Estimated benefits used in the economic analysis
The total estimated medical expenditure saved was ¥1,830,941,000 and the total gained earned income was ¥1,269,553,000 by being spared later treatments and due to prolonged life (standard discount rate of 3%).

For the 5% discount rate, total medical expenditure saved was ¥1,389,870,000 and total gained earned income was ¥932,230,000.

For the 1% discount rate, total medical expenditure saved was ¥2,457,969,000 and total gained earned income was ¥1,787,271,000.

Cost results
The total direct costs were ¥1,071,412,000 and total indirect costs were ¥266,153,000 for the standard discount rate of 3%.

For the 5% discount rate, total direct costs were ¥1,057,480,000 and total indirect costs were ¥258,223,000.

For the 1% discount rate, total direct costs were ¥1,087,707,000 and total indirect costs were ¥273,466,000.

Synthesis of costs and benefits
Cost-benefit ratios were calculated with the standard discount rate of 3% and also with discount rates of 5% and 1%. As the ratios were above unity with different discount rates as long as HCV carrier rate was above 1%, this screen and treat programme is useful. In the sensitivity analyses: the cost-benefit ratios were all found to be above unity. It was also found that if the HCV carrier rate was 1% or above, the cost-benefits were above unity except for one case in which the cost-benefit was below unity when the HCV carrier rate was 1% and the discount rate was 5%. Additionally, as long the HCV carrier rate was above 1%, cost benefits were above unity even if CR was lower than the rate set by the 95% reliability limit. The results showed that even with the detection rate of 15%, cost-benefits were above unity if the HCV carrier rate were over 1%.

Authors’ conclusions
This screen and treat programme was found to be useful as long as the HCV carrier rate was above 1%. As such, the
programme can be used even in areas where the cases of chronic active hepatitis are not particularly high.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of comparator, no screening, was clear and justified.

**Validity of estimate of measure of benefit**
The internal validity of the study is likely to be high, but it should be noted that the screening programme's demonstrated benefit is predicated on the prevalence of hepatitis C, which in the chosen prefecture, was higher than average. Mortality rates from hepatoma and cirrhosis are among the highest in Japan. The reader should be aware that lower prevalence would reduce the net benefit in monetary terms of the programme, although the authors demonstrated that screening and treating would be beneficial in other areas with lower prevalence rates. The authors also conducted thorough and inclusive sensitivity analyses to test the robustness of their results in relation to key parameters affecting the potential benefits of IFN.

**Validity of estimate of costs**
The authors conducted a detailed and valid cost analysis, which included both direct and indirect costs, discounting, reporting of a price year and clear explanations of how cost totals were calculated for each element of the programme. Extensive sensitivity analyses were also conducted on key cost parameters over plausible ranges. As such the derived cost-benefit ratios are likely to have high validity.

**Other issues**
It would have been useful for the study to analyse various high prevalence sub-groups in the population (such as intravenous drug users) with much higher prevalence levels to determine the relative costs and benefits of targeted screening. This would have yielded much higher benefits and would inform other settings regarding the appropriateness of universal versus targeted screening. The effect of false positive and false negative results was not investigated, although the consequences of using an HCV genotyping test (PCR) were discussed (which would improve the sensitivity and specificity of the screening test). Generalisability to other Japanese prefectures was discussed, and other studies from both Japan and abroad were used to compare the results of the present study.

**Implications of the study**
In terms of costs and benefits, as long as the prevalence of HCV in the target population is greater than 1%, the programme is argued by the authors to offer a cost saving.

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None stated.

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