Is it cost-effective to treat recurrent hepatitis C infection in orthotopic liver transplantation patients?

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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 use of antiviral therapy for hepatitis C virus (HCV) infection in the post-orthotopic liver transplantation (OLT) setting. Antiviral therapy was administered for one year. The authors used a combination of interferon and ribavirin (IFN-RIB) as the basis for the current treatment.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised three age cohorts of 1,000 men and 1,000 women (45, 55 and 65 years old) who underwent OLT for HCV. All were assumed to have recurrent HCV after OLT.

Setting
The setting was secondary care. The economic analysis was conducted in the USA.

Dates to which data relate
The effectiveness data were gathered from studies published between 1990 and 2001. The cost data were derived from studies published between 1997 and 2000. The price year was 2000.

Source of effectiveness data
The effectiveness data were derived from a review of the literature.

Modelling
A Markov-based decision analytic model was created using DATA 3.5 software to simulate the costs and health outcomes for each cohort assigned to each of the two treatment strategies. The reference case was a cohort of 1,000 men aged 55 years. The authors used the combination of IFN-RIB as the basis for the current treatment. The four health states described were alive with recurrent HCV infection, compensated cirrhosis, decompensated cirrhosis and death. The lifetime horizon was used. To validate the model, the authors compared the survival distribution generated for the reference cohort with that available from the United Network for Organ Sharing (UNOS) database, using log-rank test, (p<0.05).

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

- the sustained viral response rate with antiviral therapy,
- the annual rate of progression of recurrent HCV to cirrhosis,
- the annual rate of hepatic decompensation,
- the annual rate of death from decompensation,
- the yearly mortality rate, and
- the compliance rate.

**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**
Fifteen primary studies were included in the analysis.

**Methods of combining primary studies**
Not stated.

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

**Results of the review**
The sustained viral response rate with IFN-RIB was 20% (range: 10 - 40).

The risk of developing cirrhosis was 0.04% (range: 0.00 - 0.08).

The annual rate of hepatic decompensation was 0.42 (range: 0.20 - 0.60).

The annual rate of death from decompensation was 0.429.

The yearly mortality rate for women was 0.0732 in those aged 45 years, 0.0944 in those aged 55 years, and 0.2077 in those aged 65 years.

The yearly mortality rate for men was 0.0704 in those aged 45 years, 0.1206 in those aged 55 years, and 0.1418 in
those aged 65 years.

Methods used to derive estimates of effectiveness
The authors made several assumptions to estimate the outcomes.

Estimates of effectiveness and key assumptions
The authors assumed the following:

that there would no longer be any benefit to patients who relapsed;

that a sustained viral response indicated no further progression of liver disease caused by HCV;

that antiviral therapy did not increase the risk of rejection;

that HCV did not spontaneously clear;

that death from natural causes was a constant percentage extrapolated from the UNOS database for non-HCV-related deaths post-OLT;

that patients did not undergo re-OLT for cirrhosis caused by recurrent HCV;

that routine post-OLT care did not differ between the two strategies;

that the compliance rate was 80% (range: 60 - 100) (there was a discrepancy between the figures in the text and the table);

that the mean duration of treatment for patients who could not complete antiviral therapy was 6 months; and

that there would be no benefit for patients who did not complete the 12 months of therapy.

Measure of benefits used in the economic analysis
The benefit measures were the number of cases of cirrhosis prevented, the number of deaths prevented, and the number of life-years saved (LYS). The authors used the declining exponential approximation of life expectancy (DEALE) to calculate the annual mortality rate. Various mortality rates per year were calculated according to age and gender (equation provided). The benefits were not discounted.

Direct costs
The perspective of the health service provider was adopted. Only the direct costs were included. These were for antiviral therapy, for treating compensated cirrhosis and decompensated cirrhosis, and for dying. The cost of dying was not explained. The cost of antiviral therapy covered antiviral drugs, haematologic growth factors, laboratory tests and clinic visits. The costs of antiviral therapy and treatment of decompensated cirrhosis were derived from published studies. The cost of dying was estimated in charges and converted using an assumed cost-to-charge ratio of 0.65. The resource quantities and the costs were not reported separately. All of the costs were likely to have been adjusted to the year 2000. The lifetime horizon was used. The costs were discounted at the recommended annual rate of 3% (Gold et al., see Other Publications of Related Interest).

Statistical analysis of costs
No statistical analysis of the costs was performed.

Indirect Costs
The indirect costs were not included in the analysis.

**Currency**

US dollars ($).

**Sensitivity analysis**

One-way sensitivity analyses were performed for sustained response rate, compliance, cirrhosis rate, and decompensation rate, over the ranges estimated (see prior sections). Also, for the discount rate (0 - 5%), annual drug cost ($1,300 - $25,300) and the cost of dying ($30,000 - $90,000). Two-way sensitivity analyses were performed to compare the effects of changing sustained viral response and antiviral therapy costs, and changing the sustained viral response rate and cirrhosis rate.

**Estimated benefits used in the economic analysis**

With the treatment, 29 cases of cirrhosis and 7 deaths were prevented.

The life expectancy was 6.63 years with treatment and 6.22 years in the absence of treatment. Thus, antiviral therapy increased the life expectancy by 0.4 years relative to no treatment.

The survival curves of data from both the treatment and no treatment strategies were not significantly different from the UNOS database (using log-rank test, p>0.05).

**Cost results**

The total direct cost was $45,600 with treatment and $33,600 in the absence of treatment. Thus, the incremental cost associated with antiviral therapy was $12,011.

**Synthesis of costs and benefits**

Compared with no treatment, the incremental cost-effectiveness ratio (ICER) associated with antiviral therapy was $29,100 per LYS.

The model was sensitive to sustained viral response, annual costs of antiviral drugs, cirrhosis rate, and age and gender of the cohort. For example, at a sustained viral response rate of 10%, the ICER was $57,900 per LYS. The ICER was more than $50,000 per LYS when the drug costs were 200% of the baseline value ($25,300). When the cirrhosis rate was decreased to 1% (25% of the baseline value), the ICER was almost $100,000 per LYS.

**Authors' conclusions**

The results supported the authors’ hypothesis that antiviral therapy for post-orthotopic liver transplantation (OLT) patients with recurrent hepatitis C virus (HCV) is both efficacious and cost-effective.

**CRD COMMENTARY - Selection of comparators**

The reason for the choice of the comparator, no antiviral treatment, was clear.

**Validity of estimate of measure of effectiveness**

The principal input parameters for the model were derived from published studies. It was unclear whether the review was conducted systematically to identify relevant research and minimise biases. The authors did not report the methods used to judge the relevance of the data or to combine the primary studies. However, the annual rates were investigated in a sensitivity analysis. The authors needed to have been certain that IFN-alpha was used in this study since, at that time, another IFN (IFN pegyle) being used to treat HCV infection had better effectiveness in combination.
with RIB than IFN alpha.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The decision analysis model used to derive the measure of health benefit was appropriate, even though the authors made several model assumptions. The method used to derive the life expectancy was appropriate. The benefits were not discounted, although the costs were.

Validity of estimate of costs
The perspective of the health service provider was used and only the direct costs were included. The authors included a cost of dying, which was not explained. The cost of dying was very high at $65,000 per death and a cost-to-charge ratio of 0.65 was applied. This should make a big difference to the results and, as there was no explanation, it is hard to judge the validity of the results. The costs and the quantities were not reported separately and few details of the cost quantities were given. The authors made some assumptions. The dates to which the cost data related were not reported, which will hinder the reproducibility of results in other settings. The price year was reported, thus aiding reflation exercises. The cost estimates were treated deterministically. The source of the cost data was reported. Sensitivity analyses were performed. An appropriate discount rate was used.

Other issues
The generalisability of the results was discussed a little. The findings were not compared with those from other studies. The authors indicated that this was the first cost-effectiveness analysis on this subject. The authors reported further limitations of their study, in particular, assumptions made about the long-term efficacy of treatment and the absence of data on genotype. The authors do not appear to have reported the results selectively.

Implications of the study
The authors recommended that further models should be able to incorporate the impact of genotype on predicting sustained viral response.

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None stated.

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Other publications of related interest


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