Cost-effectiveness of combination peginterferon alpha-2a and ribavirin compared with interferon alpha-2b and ribavirin in patients with chronic hepatitis C


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
This study compared peginterferon alpha-2a (PegIFN2a) plus ribavirin (RIB) and interferon alpha-2b (IFN2b) plus RIB for the treatment of chronic hepatitis C virus (CHV). RIB dose and treatment duration was determined by genotype. Patients with genotype 1 received 1,000 - 1,200 mg for 48 weeks, while patients with genotype 2/3 received 800 mg for 24 weeks. Patients with genotype 1 were given a predictive test and treatment ceased if no treatment response was identified. Patients receiving PegIFN2a were given the predictive test after 12 weeks, while those taking IFN2b were tested 24 weeks after starting treatment.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of treatment-naive male patients with CHV, with an average age of 45 years.

Setting
The setting appears to have been secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were taken from papers published between 1996 and 2004. The dates to which the resource use data related were not reported. The price year was 2003.

Source of effectiveness data
The effectiveness data were derived from a review or synthesis of completed studies.

Modelling
A Markov model was used to determine the costs and benefits of the treatment of CHV in a hypothetical cohort of treatment-naive patients aged 45 years. There were two treatment groups, PegIFN2a plus RIB and IFN2b plus RIB. The model considered seven states. More specifically, sustained virological response, chronic hepatitis C, compensated cirrhosis, decompensated cirrhosis, hepatocellular carcinoma, liver transplant and death. The time span of the model was the lifetime of the patients.
Outcomes assessed in the review
The model parameters estimated from the literature were:

- the rate of sustained viral response;
- the rate of treatment discontinuation following the treatment response test (for patients with genotype 1 only); and
- the probabilities of progressing from one health state to another.

Study designs and other criteria for inclusion in the review
The estimates of sustained viral response were taken from a randomised controlled trial. The designs of the sources of the other model parameters were not reported.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

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

Number of primary studies included
Eleven studies were used to derive the measures of effectiveness.

Methods of combining primary studies
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The rate of sustained viral response for patients taking PegIFN2a was 46% for patients with genotype 1 and 76% for patients with genotype 2/3.

Sustained viral response among patients taking IFN2b was 36% for patients with genotype 1 and 61% for patients with genotype 2/3.

Treatment was discontinued following a treatment response test for 19% of genotype 1 patients taking PegIFN2a and 49.9% of genotype 1 patients taking IFN2b.

The following annual health state progression probabilities were identified:

- chronic hepatitis C to compensated cirrhosis, 0.073;
- compensated cirrhosis to decompensated cirrhosis, 0.039;
- compensated cirrhosis to hepatocellular carcinoma, 0.014;
decompensated cirrhosis to hepatocellular carcinoma, 0.014;
decompensated cirrhosis to liver transplantation, 0.031;
decompensated cirrhosis to death, 0.129;
hepatocellular carcinoma to death, 0.427;
liver transplant (year 1) to death, 0.210; and
liver transplant (year 2+) to death, 0.057.

**Measure of benefits used in the economic analysis**
The measure of health benefit used was the quality-adjusted life-years (QALYs). Estimates of the quality of life for each of the health states were taken from a published study that used the Health Utility Index (HUI Mark III). The QALYs were discounted at a rate of 3% per annum.

**Direct costs**
The costs to a health care purchaser were included in this study. The costs of medical care including inpatient, outpatient, diagnostic and procedure costs were taken from published studies. There were no details of how the costs were calculated. The costs of drugs were based on wholesale acquisition costs. Resource use and, therefore, total costs were estimated using modelling. The price year was 2003 and future costs were discounted at a rate of 3% per annum.

**Statistical analysis of costs**
The cost data were treated deterministically.

**Indirect Costs**
No indirect costs were included in this study.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way and sub-group sensitivity analyses were performed to investigate uncertainty in the model parameters. The sources of the ranges used in the sensitivity analyses were unclear.

**Estimated benefits used in the economic analysis**
The estimated incremental benefit for genotype 1 patients treated with PegIFN2a plus RIB compared with IFN2b plus RIB was 0.7 QALYs over the patients' lifetime.

For patients with genotype 2/3 the incremental benefit of treatment with PegIFN2a plus RIB compared with IFN2b was 1.05 QALYs over the patients' lifetime.

**Cost results**
The cost results were not reported in a non synthesised manner.

**Synthesis of costs and benefits**
For patients with genotype 1 the incremental cost of treatment with PegIFN2a plus RIB compared with IFN2b plus RIB was $2,600 per QALY.

Treatment with PegIFN2a plus RIB for patients with genotype 2/3 was dominant (i.e. it was more effective and had lower costs) treatment with IFN2b plus RIB.

The authors also reported that, if 75% of patients had genotype 1 and 25% had genotype 2/3, treatment with PegIFN2a plus RIB was dominant.

The authors reported that in all of the sensitivity analyses, the incremental cost-effectiveness remained below $16,500 per QALY.

**Authors’ conclusions**

Peginterferon alpha-2a (PegIFN2a) plus ribavirin (RIB) was more cost-effective than interferon alpha 2-b (IFN2b) plus RIB for the treatment of naive adults with chronic hepatitis C.

**CRD COMMENTARY - Selection of comparators**

Two treatment strategies were evaluated. One was the strategy recommended by the National Institutes of Health Consensus Development Conference Statement of the Management of Hepatitis C. The other, more effective strategy was also approved by the same body. These are not the only possible strategies. You should consider whether these treatments are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness data used in the model came from completed studies. However, it was unclear whether a systematic review was carried out and limited information on the primary studies was reported in this paper. This means that it was not possible to assess the validity of the sources used. Some of the evidence was taken from a randomised controlled trial.

**Validity of estimate of measure of benefit**

The measure of health benefit (QALYs) was appropriate to determine the impact of the interventions on the patient health. In addition, it is a measure that is widely used in similar studies and therefore allows clear comparisons to be made. The valuations of the different health states were taken from a published study. Unfortunately, the present paper did not report the valuation methods used in the original study, thus it is not possible to comment on the validity of these estimates. The future health benefits were discounted.

**Validity of estimate of costs**

The authors explicitly stated the perspective adopted in the study. As such, it appears that all the costs appropriate to that perspective have been included in the study. The unit costs and resource use were taken from published studies, but the methods used were not reported. This limits the generalisability of the study results. The price year was clearly stated, thus making reflation exercises possible. The costs were treated deterministically in the base-case but were varied in the sensitivity analyses. The future costs were discounted and undiscounted data were included in the sensitivity analysis.

**Other issues**

The authors compared their study with similar studies and commented on possible reasons for differing results. They did not consider how their study findings could be applied to other settings. However, sensitivity analyses were conducted, thus increasing the external validity of the study results. The authors' conclusions reflected the scope of their analysis.
Implications of the study
The authors did not make any direct recommendations for changes to practice or further research.

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