Cost effectiveness of interferon alpha 2b combined with ribavirin for the treatment of chronic hepatitis C

Younossi Z M, Singer M E, McHutchison J G, Shermock K M

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 interferon (IFN) alpha2b combined with ribavirin for the treatment of chronic hepatitis C.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population was a hypothetical cohort of 45-year-old men with chronic hepatitis C without cirrhosis or liver cancer.

Setting
The study setting was a hospital. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were collected from studies published between 1987 and 1999. The cost data were taken from a 1998 source. The price year was 1998.

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

Modelling
A Markov decision analytic model was used to determine the cost-effectiveness of the six treatment strategies.

Outcomes assessed in the review
The review assessed response rates and annual transition probabilities. The response was categorised as either a sustained viral response (SVR) or an end of treatment viral response (ETR). The patient was considered to have a SVR if the HCV was negative after 24 weeks’ follow-up. The patient was considered to have an ETR if the HCV was negative at the end of the treatment, but positive during the follow-up. The ETR and SVR rates were presented according to the treatment strategy.

Study designs and other criteria for inclusion in the review
The effectiveness estimates were derived from recently published, large clinical trials using IFN alpha2b alone or in combination with ribavirin.

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
Summary statistics (point estimate and range) from individual studies were used.

Number of primary studies included
Fifteen primary studies were included in the review.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
The response rates for each strategy were reported as point estimates.

IFN alone: ETR 24% (95% confidence interval, CI: 18 - 30), SVR 13% (95% CI: 9 - 17).

Combined therapy for IFN-naive patients: ETR 53% (95% CI: 47 - 60), SVR 31% (95% CI: 25 - 37).

IFN followed by combined therapy for relapsers: ETR 82% (95% CI: 76 - 88), SVR 49% (95% CI: 45 - 52).

IFN followed by combined therapy for relapsers and nonresponders: ETR 29% (95% CI: 17 - 42), SVR 17.5% (95% CI: 10 - 25).

HCV genotyping followed by 48 weeks’ combined therapy (genotype 1): ETR 37% (95% CI: 29 - 44), SVR 28% (95% CI: 21 - 35).

HCV genotyping followed by 24 weeks’ combined therapy (non-genotype 1): ETR 89% (95% CI: 79 - 100), SVR 68% (95% CI: 60 - 76).

The annual transition probability from chronic hepatitis C to compensated cirrhosis was 7.3%.

The annual transition probabilities were 3.9% from compensated cirrhosis to decompensated cirrhosis, and 1.4% from compensated cirrhosis to hepatocellular carcinoma.

The annual transition probabilities were 1.4% from decompensated cirrhosis to hepatocellular carcinoma, 3.1% from decompensated cirrhosis to liver transplantation, and 12.9% from decompensated cirrhosis to death.

The annual transition probability from hepatocellular carcinoma to death was 42.7%.
The annual transition probabilities from liver transplantation to death were 21% in the first year or 5.7% in successive years.

The incidence of hepatocellular carcinoma in non-cirrhotic patients was 1 to 4% over 20 years.

The utility values varied between 0.25 for hepatocellular carcinoma and 0.82 for chronic hepatitis C.

**Measure of benefits used in the economic analysis**
The measure of benefits was the number of quality-adjusted life-years (QALYs). The utilities were derived from actual patients’ utilities using the Health Utility Index (Mark III), and were obtained directly from patients with different stages of liver disease. The benefits were discounted at an annual rate of 3%.

**Direct costs**
The direct costs were discounted at an annual rate of 3%. The quantities and costs were reported separately. The direct costs were the costs of the drugs and the monitoring or treatment. The monitoring and treatment costs included office visits and tests such as blood count, liver profile and HCV genotyping. The quantity/cost boundary adopted was that of the hospital. The source from which the quantities were estimated was not reported. The unit costs were obtained from the published wholesale prices and from the Medicare fee schedule. The price year was 1998.

**Statistical analysis of costs**
The authors reported total costs.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way and multi-way sensitivity analyses were conducted on effectiveness estimates, cost estimates, utility values, and the discount rate. The ranges reported were stated to be 95% CIs.

**Estimated benefits used in the economic analysis**
Strategy 6 (combined therapy assigned according to the patient’s genotype) produced the highest benefit with 15.89 QALYs gained. The number of QALYs gained with the other strategies ranged from 13.10 with strategy 1 (no treatment) to 15.53 with strategy 5 (IFN followed by combination therapy for relapsers and nonresponders).

**Cost results**
Strategy 5 had the lowest cost at $34,561. The costs for the other strategies ranged from $34,758 for strategy 4 (IFN followed by combination therapy for relapsers) to $38,747 for strategy 1 (no treatment).

**Synthesis of costs and benefits**
The incremental cost-effectiveness ratio of strategy 6 over strategy 5 was $7,500 per QALY gained. All the other strategies were dominated. The sensitivity analyses confirmed the robustness of these results, with the incremental cost-effectiveness ratio only above $50,000 per QALY when the ETR went from 37 to 29%. There was a 3% probability of this occurring.
Authors’ conclusions
The use of interferon (IFN) combined with ribavirin, where the duration of therapy was established according to the viral genotype, was a cost-effective approach in treating patients with chronic hepatitis C.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparators used. You should decide if these health technologies are relevant to your setting.

Validity of estimate of measure of effectiveness
The authors undertook a review of the literature to derive the effectiveness estimates. This seems to have been appropriate, although they did not state whether a systematic review of the literature had been undertaken. Further details of the methods underlying the literature review could have been provided. The validity of the results was enhanced by conducting sensitivity analyses to account for the variability in the estimates. However, the source of the point estimates and confidence intervals was not reported. In addition, it was not stated whether any meta-analysis was carried out.

Validity of estimate of measure of benefit
The estimation of benefits was modelled. The instrument used to derive a measure of health benefit, the health utility index, seems to have been appropriate. It was appropriate that the estimates were derived from individuals with liver conditions rather than, for example, by experts or via an intermediate instrument.

Validity of estimate of costs
There were several positive features of the cost analysis. First, all the relevant direct cost categories were included. Second, the validity of the cost results was enhanced by performing appropriate sensitivity analyses. Third, the quantities and costs were reported separately, thus improving the generalisability of the results. In addition, the price year was reported, which would make reflation exercises in other settings feasible. However, the charges were used to estimate the costs, making attribution to resource quantities impossible, and the source of the quantities was not given. Also, the source of the ranges for the sensitivity analysis was not given.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, and addressed the issue of generalisability to other settings via a sensitivity analysis. The authors did not seem to have presented their results selectively. The study considered 45-year-old men with chronic hepatitis C without cirrhosis or liver cancer, and this was reflected in the authors’ conclusions. The authors noted several limitations. For example, the rates of progression to different states of health were obtained from retrospective data. Moreover, although indirect costs were negligible during therapy, they may be substantial during the entire illness. The authors also acknowledged that they did not compare those strategies based on IFN alpha2a or IFN alfacon-1.

Implications of the study
The authors did not draw any further conclusions or make any recommendations. Given the use of a sensitivity analysis, the results seem to support the conclusion that the combined IFN and ribavirin therapy, adjusted according to the viral genotype, was a cost-effective approach. This should be viewed in the context of the cost-effectiveness of other technologies, for which the authors provided some evidence.

Source of funding
None stated.
Bibliographic details

PubMedID
10534357

DOI
10.1002/hep.510300518

Indexing Status
Subject indexing assigned by NLM

MeSH
Antiviral Agents /economics /therapeutic use; Cost-Benefit Analysis; Decision Trees; Drug Therapy, Combination; Hepatitis C, Chronic /drug therapy /economics; Humans; Interferon-alpha /economics /therapeutic use; Male; Markov Chains; Middle Aged; Models, Statistical; Probability; Quality of Life; Recombinant Proteins; Ribavirin /economics /therapeutic use; Sensitivity and Specificity; Time Factors; United States

AccessionNumber
21999002050

Date bibliographic record published
30/04/2002

Date abstract record published
30/04/2002