Cost effectiveness of ribavirin/interferon alfa-2b after interferon relapse in chronic hepatitis C

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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
Ribavirin/interferon alfa-2b after interferon relapse in chronic hepatitis C.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
Patients with chronic hepatitis C who had a biochemical relapse after responding to interferon therapy.

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

Dates to which data relate
Effectiveness and resource use data were collected from studies published between 1981 and 1998 and were also obtained in the form of expert opinion. Cost data were taken from studies published between 1995 and 1999. The price year was 1995.

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

Modelling
A Markov decision analytic model was used to determine the cost-effectiveness of the combination of ribavirin and interferon, compared with interferon alone, for patients with chronic hepatitis C who relapsed after responding to interferon therapy.

Outcomes assessed in the review
The review assessed sustained viral-negative response, life expectancy, and quality of life.

Study designs and other criteria for inclusion in the review
Short-term effectiveness estimates were taken from a randomised controlled trial and long-term outcomes were projected using a previously published model that was based on the natural history of chronic hepatitis C.
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 from individual studies were used.

Number of primary studies included
At least 12 primary studies were included.

Methods of combining primary studies
The narrative method was used.

Investigation of differences between primary studies
Not stated.

Results of the review
With combination therapy, 78% had no evidence of hepatitis C virus in serum ("viral-negative") after 12 weeks of therapy, and 49% were viral-negative 24 weeks after stopping therapy, compared with 34% at 12 weeks and 5% at 24 weeks after interferon alone. Patients had viral testing at week 12 and therapy was discontinued in those who were viral-positive. None of the patients who were viral-positive after the first 12 weeks of treatment became sustained responders with additional therapy. Women under the age of 50 years who were treated with ribavirin had a qualitative pregnancy test before beginning therapy and every month thereafter. There was an 11% likelihood of pregnancy with condom contraception.

Methods used to derive estimates of effectiveness
Estimates of effectiveness were also derived by using an expert panel of physicians and were also based on the authors' assumptions.

Estimates of effectiveness and key assumptions
The decrease in quality of life with combination therapy was twice as great as that with interferon alone. Quality of life decreased by 24% for 1 month (or 1 week) for patients undergoing an elective abortion for an unplanned pregnancy during ribavirin treatment.

The following assumptions were also made:

- sexual partners of women would utilise contraception with condoms, continuing for six months after discontinuation of ribavirin;
- all men in the trial had partners who were potentially of child-bearing age and who would not have been using contraception otherwise;
- patients who relapsed after initial interferon treatment had a prognosis similar to those who had never been treated;
and patients who became viral-negative either spontaneously or from retreatment had a greatly reduced likelihood of developing progressive liver disease compared with those who were not treated.

**Measure of benefits used in the economic analysis**

Quality-adjusted life years (QALYs) were used as the measure of benefit. An expert panel of physicians estimated quality of life values. Benefits were discounted at an annual rate of 3%.

**Direct costs**

Direct costs were discounted at an annual rate of 3%. Quantities and costs were reported separately. Direct costs were the costs of drugs, office visits, laboratory testing, and reproductive services. The quantity/cost boundary adopted was that of the health service. Costs and quantities were obtained from the published literature, and from cost and reimbursement data. The price year was 1995.

**Statistical analysis of costs**

No statistical analyses of costs were reported.

**Indirect Costs**

Indirect costs were not included.

**Currency**

US dollars ($).

**Sensitivity analysis**

One-way sensitivity analyses were conducted on all model parameters.

**Estimated benefits used in the economic analysis**

64% of patients developed cirrhosis with interferon and 35% with combination therapy. 14% of patients developed hepatocellular carcinoma with interferon and 7% with combination therapy. 41% of patients died of liver disease with interferon and 22% with combination therapy. 14.7 QALYs were gained with interferon and 16.7 with combination therapy.

**Cost results**

Total costs were $14,200 with interferon and $14,500 with combination therapy.

**Synthesis of costs and benefits**

The incremental cost-effectiveness of combination therapy was $140 per QALY. For most subgroups of patients, combination therapy with ribavirin and interferon would be cost saving. The results changed little when the values of each model parameter were varied over a wide range of values, with the exception of the annual probability of liver progression, the annual probability of a sustained response rate, and the cost of ribavirin.

**Authors' conclusions**

A six-month course of interferon and ribavirin is indicated for patients with chronic hepatitis C who have relapsed after previously responding to interferon alone. It should reduce the cumulative incidence of liver complications and prolong life at a modest cost.
CRD COMMENTARY - Selection of comparators
A justification was given for the comparator used, namely that it represented a currently employed strategy. You, as a user of the database, should decide if these health technologies are relevant to your setting.

Validity of estimate of measure of effectiveness
Effectiveness data (model parameters) were derived partly from the literature, but the authors did not state that a systematic review of the literature had been undertaken. More information about the design of the review, identification of studies and the method of pooling primary effectiveness estimates could have been reported. The authors based their analysis on rather strong assumptions and used surrogate markers (virologic response) as a measure of benefits. The authors also assumed that virologic responders have a more benign prognosis than non-responders, although not all investigators share this assumption. These issues need to be borne in mind when considering the validity of the results.

Validity of estimate of measure of benefit
The estimation of benefits was appropriately modelled. Quality of life measures were taken from an expert panel of physicians. The estimates of physicians may be higher than estimates derived from consultation with patients or other groups.

Validity of estimate of costs
Good features of the cost analysis were that all relevant direct cost categories were included and that quantities and costs were reported separately, which enhances the generalisability of the results. The price year was reported, which would make reflation exercises in other settings possible. Charges were converted in costs and, hence, true opportunity costs were estimated. Cost estimates were based on estimates from the USA, thereby avoiding biases that may have occurred from institutional assignment. However, the authors did not consider indirect or time costs (e.g. time lost from work or non-medical costs), and the analysis did not include future liver biopsies or treatment for non-responders. Thus the future costs for the interferon-alone therapy were under-estimated.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, but the issue of generalisability to other settings was not addressed. The authors did not present their results selectively. The study considered patients with chronic hepatitis C who had relapsed after previously responding to interferon alone and this was reflected in the authors' conclusions.

Implications of the study
The authors suggested that a six-month course of interferon and ribavirin is indicated for patients with chronic hepatitis C who have relapsed after previously responding to interferon alone. It should reduce the cumulative incidence of liver complications and prolong life at a modest cost.

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