Cost-effectiveness of treatment for hepatitis C in an urban cohort co-infected with HIV


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 study examined three treatments for chronic infection with hepatitis C virus (HCV) in patients co-infected with the human immunodeficiency virus (HIV). The treatments were:

- combination therapy with interferon-alpha-2a and ribavirin (IFN-RIB);
- monotherapy with pegylated interferon-alpha-2a (pegIFN); and
- combination therapy with pegylated interferon-alpha-2a and ribavirin (pegIFN-RIB).

IFN given at 3 million IU 3 times per week, RIB at 800 mg/day, and pegIFN at 180 microg subcutaneously weekly.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of patients with HCV and HIV. The characteristics of the eligible patients came from a clinical trial. The eligible patients had a mean age of 44 years, 66% had genotype I HCV, 16% had cirrhosis, and 98% had CD4 cell counts greater than 200 cells/mm3. Several exclusion criteria were reported, such as active psychiatric and medical illness, decompensated liver disease and advance HIV disease (defined as a CD4 cell count of less than 100 cells/mm3).

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1997 and 2004. The costs and most resource use data came from studies published between 1997 and 2005. The price year was 2004.

Source of effectiveness data
The clinical data used in the model were HCV natural history parameters stratified by gender and age (fibrosis progression, transition rates among other health states, and mortality rates due to HCV complications) and response rates with the three therapies under investigation.

Modelling
A published deterministic state-transition decision model was used (and updated) to simulate the natural history of HCV infection in patients co-infected with HIV. An extensive description of health states and transition patterns was provided. A simplified schematic of the model was reported. The cycle length was 1 month and a lifetime horizon was considered. The analysis assumed 48 weeks of HCV therapy for all patients.

Sources searched to identify primary studies
The clinical data came from several sources, although only some of these were described in detail. Treatment effectiveness came from a clinical trial (APRICOT) that involved 868 individuals in 19 countries. Excess mortality due to HIV came from the Multicenter AIDS Cohort Study. Little information on the other primary studies was provided.

Methods used to judge relevance and validity, and for extracting data
It was unclear whether a systematic review of the literature was undertaken to identify the primary studies. However, the authors chose the most recent clinical trial (APRICOT) to obtain clinical effectiveness with the different treatments analysed, which this should have ensured high internal and external validity (multi-country). Some assumptions based on published data were also made.

Measure of benefits used in the economic analysis
The summary benefit measure used was the life-years (LYs). These were estimated using the decision model. The benefits were discounted at an annual rate of 3%.

Direct costs
The analysis of the costs included only direct medical costs, despite the fact that the authors stated that a societal perspective had been adopted. The analysis included the costs of drugs and annual HCV/HIV care (compensated cirrhosis, ascites, variceal haemorrhage, hepatic encephalopathy, hepatocellular carcinoma and liver transplant). The cost categories included hospitalisations, outpatient visits, laboratory tests, medications and interventions. A detailed breakdown of the cost items was not given, but the costs were presented as macro-categories. The unit costs and the quantities of resources used were not presented separately. The costs and quantities of resources used were derived from average wholesale prices for drugs and from published studies for the other items. Discounting was relevant, as the long-term costs were evaluated, and an annual rate of 3% was used. The price year was 2004.

Statistical analysis of costs
The costs and quantities were treated deterministically.

Indirect Costs
Productivity costs were not explicitly included, despite the perspective of the study.

Currency
US dollars ($).

Sensitivity analysis
Univariate and two-way sensitivity analyses were carried out to assess the robustness of the results of the analysis to variations in the clinical and economic inputs of the model around plausible ranges. The ranges were presumably derived from the literature. In an exploratory analysis, it was assumed that treatment would cease if no early virological response occurred.

Estimated benefits used in the economic analysis
In the sub-group of men with genotype I, the expected LYs were 11.63 with no treatment, 11.71 with IFN-RIB, 11.83 with pegIFN and 12.06 with pegIFN-RIB.

In the sub-group of men with non-genotype I, the expected LYs were 11.63 with no treatment, 11.88 with IFN-RIB, 12.09 with pegIFN and 12.52 with pegIFN-RIB.

In the sub-group of women with genotype I, the expected LYs were 12.28 with no treatment, 12.37 with IFN-RIB, 12.48 with pegIFN and 12.73 with pegIFN-RIB.

In the sub-group of women with non-genotype I, the expected LYs were 12.28 with no treatment, 12.55 with IFN-RIB, 12.76 with pegIFN and 13.20 with pegIFN-RIB.

Cost results
In the sub-group of men with genotype I, the expected costs were $240,300 with no treatment, $256,400 with IFN-RIB, $261,100 with pegIFN and $271,700 with pegIFN-RIB.

In the sub-group of men with non-genotype I, the expected costs were $240,300 with no treatment, $257,900 with IFN-RIB, $263,400 with pegIFN and $275,600 with pegIFN-RIB.

In the sub-group of women with genotype I, the expected costs were $252,200 with no treatment, $268,400 with IFN-RIB, $273,200 with pegIFN and $284,000 with pegIFN-RIB.

In the sub-group of women with non-genotype I, the expected costs were $252,200 with no treatment, $270,000 with IFN-RIB, $275,700 with pegIFN and $288,400 with pegIFN-RIB.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios (i.e. the incremental cost per LY gained) were calculated in order to combine the costs and benefits.

Regardless of genotype and gender, combination therapy with pegIFN-RIB was the most effective option, whilst IFN-RIB and pegIFN alone were extended dominated strategies.

The incremental cost per LY gained for pegIFN-RIB compared with no treatment was $73,000 in men with genotype 1, $39,700 in men with non-genotype 1, $70,700 in women with genotype 1 and $39,300 in women with non-genotype 1.

Similar results were achieved in an exploratory analysis in which it was assumed that treatment was ceased when no early virological response occurred.

The sensitivity analysis showed that the results were insensitive to varying parameters across plausible ranges. The cost-effectiveness ratios were slightly sensitive to variations in the annual excess death rate due to HIV, fibrosis progression rates, and treatment efficacies in non-cirrhotic patients.

In a two-way sensitivity analysis, when treatment effectiveness exceeded 50%, the cost-effectiveness ratios were consistently less than $50,000, regardless of the relative risk of fibrosis progression. When treatment effectiveness exceeded 50%, the cost-effectiveness ratio was always lower than $100,000.

The discount rate strongly affected the conclusions of the analysis. With no discounting, the incremental cost-effectiveness ratio was approximately 60% lower than in the base-case analysis. With a 5% discount rate, the ratio was about 140% higher than in the base-case.

Authors’ conclusions
Combination therapy with pegylated interferon and ribavirin (pegIFN-RIB) would appear to be cost-effective for hepatitis C virus (HCV) in eligible patients co-infected with stable human immunodeficiency virus (HIV) disease. The
treatment was more effective and cost-effective in non-genotype 1 patients than in genotype 1 patients.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear since all available treatments for HCV patients co-infected with HIV were considered. Dosages were reported. You should decide whether they are valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
Most of the clinical data were derived from the published model. It was not stated whether a systematic review of the literature was undertaken to identify the primary studies, which might therefore have been identified selectively. However, treatment effectiveness was taken from a recent, multi-centre, multi-national, double-blind, randomised controlled trial with a large sample size. This enhances the internal validity of the study. Limited information on the primary studies was provided. A sensitivity analysis was carried out to address the issue of uncertainty and variability in the data.

**Validity of estimate of measure of benefit**
Survival was an appropriate benefit measure since this represents the key dimension of health for patients with HCV and HIV. The LYs were estimated using a modelling approach. The impact of discounting was investigated. Aspects related to quality of life were not considered, although, as the authors acknowledged, they might have been relevant.

**Validity of estimate of costs**
The analysis of the costs was carried out from a societal perspective, but the indirect costs were not considered. The costs were presented as macro-categories and a breakdown of the cost items was not provided. It will be difficult to replicate the analysis in other settings since there were few details of the sources of the costs and resource use data. The costs were treated deterministically but sensitivity analyses were carried out on the key cost estimates; these had a very limited impact on the results of the analysis. The price year was reported, which will assist in reflating the analysis in other time periods.

**Other issues**
The authors stated that their findings differed from those from other published studies that had found that monotherapy is cost-effective. The main reason for this difference was the availability of more recent clinical data. The issue of the generalisability of the study results to other settings was addressed in the sensitivity analysis, in which all model inputs were varied. It was pointed out that the analysis should be restricted to a specific target population of treatment-eligible patients with stable HIV disease and stable CD4 cell counts between 200 and 500 cells/mm3.

**Implications of the study**
The study results support the use of the combination therapy pegIFN-RIB for HCV in eligible patients co-infected with stable HIV disease. The authors noted that further studies should be performed to establish the effectiveness of combination HCV therapy in populations with low eligibility for treatment.

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**Bibliographic details**
Other publications of related interest
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