A health economic model to assess the cost-effectiveness of PEG IFN alpha-2a and ribavirin in patients with mild 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.

CRD summary
The study aimed to determine the cost-effectiveness of immediate treatment based on pegylated interferon α-2a plus ribavirin for patients with mild chronic hepatitis C virus (HCV), compared with absence of treatment until the disease evolves to moderate HCV (monitoring alone), in Belgium. The study demonstrated the cost-effectiveness of immediate treatment and the conclusion of the analysis was robust, as shown in the sensitivity analysis. The study was well conducted in terms of methods and reporting, but most of the evidence came from a published modelling study.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective of the study was to evaluate the cost-effectiveness of treatment with pegylated interferon (PEG IFN) α-2a plus ribavirin for patients with mild chronic hepatitis C virus (HCV), characterised by no or little fibrosis, in comparison with absence of treatment until the disease evolved to moderate HCV, characterised by portal or periportal fibrosis with some septa.

Interventions
The study examined a treatment strategy versus a monitoring strategy. Under the first option, genotypes 1-4-5-6 received PEG IFN α-2a 180 μg once a week in combination with ribavirin 1,000 to 1,200 mg/day for 48 weeks; for genotypes 2 and 3, the treatment consisted of PEG IFN α-2a 180 μg once a week in combination with ribavirin 800 mg/day for 24 weeks. In the monitoring strategy, patients were treated only when they reached the state of moderate chronic HCV.

Location/setting
Belgium/secondary care.

Methods
Analytical approach:
A published Markov model representing the natural history of chronic HCV was modified and populated with published evidence in order to determine the long-term costs and benefits of the two alternatives under examination. The time horizon of the analysis was 30 years. The authors stated that the perspective of the health care payer was adopted.

Effectiveness data:
Most of the clinical data were derived from the published decision model. Response rates with the study drugs were mainly retrieved from a randomised clinical trial, while transition probabilities to populate the model were taken from other sources that were not described in detail. The key clinical parameters were early and sustained viral response with PEG IFN plus ribavirin.

Monetary benefit and utility valuations:
Utility estimates were based on published studies that were derived from a transformed visual analogue scale, EuroQoL and doctor-based estimates. The authors selected the highest utility values from amongst those found in published studies in order to adopt a conservative approach with respect to the direct treatment option.
Measure of benefit:
The summary benefit measure was the expected quality-adjusted life-years (QALYs). These were estimated using the decision model framework. An annual discount rate of 1.5% was applied.

Cost data:
The cost categories included in the analysis were those related to health services associated with chronic HCV, compensated or decompensated cirrhosis, hepatocellular carcinoma, liver transplantation and study medications. These costs were mainly derived from a published Belgian study. The costs were in euros (EUR). A single price year was not reported: treatment costs were derived from a study published in 2002, and drug costs from a national source in January 2006. The costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
Several deterministic sensitivity analyses were carried out on key model inputs such as transition probabilities, utilities, costs, response rates, time horizon, discount rate and age at the beginning of the model. Ranges of values for probability values were derived from published studies, while arbitrary variations (i.e. +/- 20%) were applied to costs and response rates. A probabilistic sensitivity analysis based on a Monte Carlo simulation was also performed by assigning stochastic distributions to model parameters.

Results
For genotypes 1-4-5-6, the expected QALYs were 20.56 with treatment and 20.32 with monitoring. The expected costs were EUR 18,045.50 with treatment and EUR 12,383.64 with monitoring. The incremental cost per QALY gained with treatment in comparison with monitoring was EUR 23,046.07.

For genotypes 2-3, the expected QALYs were 21.20 with treatment and 20.73 with monitoring. The expected costs were EUR 9,183.68 with treatment and EUR 6,981.39 with monitoring. The incremental cost per QALY gained with treatment in comparison with monitoring was EUR 4,630.56.

In the sensitivity analysis, the model results were generally quite robust to variations in key parameters. Only in implausible scenarios was the incremental cost per QALY for genotypes 1-4-5-6 higher than the commonly accepted threshold of EUR 50,000 per QALY. However, the model results were particularly sensitive to changes in health utilities.

The probabilistic sensitivity analysis showed that at a societal willingness-to-pay of EUR 50,000 per QALY, the probability that treatment is cost-effective was 98.1% for genotypes 1-4-5-6 and 100% for genotypes 2 and 3. The corresponding values for a willingness-to-pay of EUR 20,000 per QALY were 83.9% and 99.6%.

Authors’ conclusions
The authors concluded that immediate treatment based on PEG IFN α-2a in combination with ribavirin was a highly cost-effective alternative compared with monitoring for patients with mild chronic HCV in Belgium.

CRD commentary
Interventions:
The selection of the interventions under examination was appropriate for the authors’ setting and, internationally, they appear to represent the relevant strategies for patients with mild chronic HCV. The two alternative options were clearly described.

Effectiveness/benefits:
The selection of clinical data was based on the published study used as the basis for the current economic evaluation. Thus, no systematic search for data was undertaken. Some information on the primary studies was provided, in particular for the clinical trial used to derive response rate. The extensive sensitivity analysis addressed the issue of uncertainty surrounding some clinical estimates. The approach used to derive QALYs was described. The utility values obtained from each selected study were reported, and the authors justified the choice of high utility values in order to be conservative.
Costs:
The analysis of the costs appears to have been consistent with the stated perspective. The cost data were derived from
selectively identified studies and national sources, which were appropriate given the health care payer perspective
adopted. Among the available studies, conservative cost estimates were selected. The price year was not explicitly
stated, which may limit the possibility of performing reflation exercises in other time periods.

Analysis and results:
The costs and benefits were appropriately combined. The authors provided extensive information on the decision model
in terms of structure and transition patterns. The results of both the base-case analysis and the sensitivity analyses were
extensively presented. It was noted that several conservative assumptions were made about the costs, utilities and non
inclusion of liver transplantation, thus the cost-effectiveness results may have been even more favourable for the
treatment option.

Concluding remarks:
The quality of the study methodology was good and the results were well reported, although the methods relied on a
previous decision modelling analysis. The authors' conclusions are robust and appropriate.

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Other publications of related interest
Annemans L, Warie H, Nechelput M, Peraux B. A health economic model to assess the long term effects and cost-

Wong JB, Nevens F. Cost-effectiveness of peginterferon alfa-2b plus ribavirin compared to interferon alfa-2b plus

Grieve R, Roberts J, Wright M, et al. Cost effectiveness of interferon alpha or peginterferon alpha with ribavirin for

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