Cost-effectiveness of peginterferon alfa-2b in combination with ribavirin as initial treatment for chronic hepatitis C in Sweden

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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
The study examined the use of peginterferon alpha-2b (pegIFN) in combination with ribavirin as initial therapy for chronic hepatitis C virus (HCV). The regimen examined was 48 weeks of therapy, with pegIFN administered at 1.5 microg/kg per week and ribavirin at 800 mg/day.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis

Study population
The modelled population comprised a cohort of HCV patients, modelled from the age of 43 years. The reference patient was previously untreated for HCV, had mild or moderate hepatitis with genotype 1 (GT1) or 2/3 (GT2/3). The analysis was performed separately for GT1 and GT2/3 patients.

Setting
The setting was primary care. The economic analysis was set in Sweden.

Dates to which data relate
The effectiveness and epidemiological data were drawn from articles published between 1989 and 2003. The cost data were drawn from local hospital price lists in an unreported year. The price year was 2005.

Modelling
A computer-based Markov model was adapted to describe the natural history of HCV and to assess the costs and outcomes. The model had been published in another paper (Sennfalt et al. 2001, see ‘Other Publications of Related Interest’ below for bibliographic details). Eleven health states were present: viral negative, mild hepatitis, moderate hepatitis, cirrhosis, diuretic-sensitive ascites, refractory ascites, variceal haemorrhage, hepatic encephalopathy, liver cancer, liver failure and death. The Markov cycle length was 1 year and half-cycle corrections were applied. A lifetime horizon was examined, over which the model estimated average life expectancy, quality-adjusted life expectancy and lifetime costs for identical cohorts receiving the two different treatments.

Study designs and other criteria for inclusion in the review
Sustained virological response rates were the principal measures of treatment efficacy. Transitions between the 11 health states represented the natural history of the disease. An early stopping rule was implemented, whereby early virological response rates were evaluated at 12 weeks and treatment was discontinued if no response was shown.

Sources searched to identify primary studies
Data informing the natural history of the disease (transition probabilities) were obtained from the literature (9 publications), supplemented by Swedish clinical expert opinion. A single randomised controlled trial provided the virological response data.

Methods used to derive estimates of effectiveness
The methods used for the data search, selection, extraction and synthesis were not reported.

**Measure of benefits used in the economic analysis**
The summary measure of benefit was the quality-adjusted life-year (QALY). Utility weights for the different health states in the model were drawn from a single study and authors’ assumptions. The authors assumed a lower quality of life during pegIFN treatment than during IFN treatment, i.e. they weighted the analysis against the intervention under study. The QALYs were discounted at a rate of 3% per year.

**Direct costs**
Health care resources consumed by patients at different stages of chronic HCV infection were evaluated. Estimates of resource use were based on Swedish clinical practice, as reported by Swedish clinical experts. The unit costs were obtained from the internal price lists of various health care providers in Sweden. The costs were discounted at a rate of 3% per year. The price year was 2005.

**Statistical analysis of costs**
The costs were treated deterministically and were not examined in the sensitivity analysis.

**Indirect Costs**
Productivity costs were not relevant to the perspective chosen.

**Currency**
Euros (EUR). The exchange rate used to convert Swedish kroner was not reported.

**Sensitivity analysis**
Probabilistic sensitivity analysis was performed to examine the stability of the results (Monte Carlo simulations with 1,000 samples, 100 trials per sample). Beta-distributions were applied to response rates, probabilities of disease progression and quality of life weights. Cost-effectiveness acceptability curves (CEACs) were presented for each genotype group.

**Estimated benefits used in the economic analysis**
In GT1 patients, pegIFN generated 19.02 QALYs and IFN generated 18.73 QALYs.

In GT2/3 patients, pegIFN generated 20.64 QALYs and IFN generated 20.55 QALYs.

Thus, pegIFN generated 0.29 additional QALYs in the GT1 group and 0.09 QALYs in the GT2/3 group.

**Cost results**
The average costs for pegIFN were EUR 29,722 in GT1 patients and EUR 20,201 in GT2/3 patients, whereas those for IFN were EUR 29,926 in GT1 patients and EUR 19,260 in GT2/3 patients. Thus, pegIFN was cost-saving (EUR 204) in GT1 patients.

The incremental cost of pegIFN in GT2/3 patients was EUR 941.

**Synthesis of costs and benefits**
In the base-case, pegIFN was the dominant strategy for GT1 patients (pegIFN improved outcomes and at a lower cost than IFN).

The incremental cost-effectiveness ratio for pegIFN in GT2/3 patients was EUR 10,500 per incremental QALY.

The CEAC for GT1 showed that at a willingness-to-pay (WTP) of EUR 1,000 per QALY, the probability that pegIFN was cost-effective was 70%, increasing to 85% at a WTP of EUR 16,000. However, the CEAC for GT2/3 showed that the probability that pegIFN was cost-effective reached a plateau of approximately 50% at a WTP of approximately EUR 10,000.
Authors' conclusions
The authors concluded that peginterferon-alpha2b (pegIFN) was cost-effective in GT1 patients, but that its cost-effectiveness in GT2/3 patients was uncertain.

CRD COMMENTARY - Selection of comparators
A justification was given for the comparator. IFN represented current treatment practice for HCV. You should decide if it represents a relevant comparator in your own setting.

Validity of estimate of measure of effectiveness
The parameters were derived from published research and some expert opinion. Treatment response rates were assumed to be the same for mild and moderate disease, but no supportive evidence for this assumption was presented. The authors did not present any search methods or inclusion criteria, nor did they provide justification for their selection of estimates. A randomised controlled trial, a study design which can have a high level of validity, provided the response rates. No detail was provided of the other studies that informed the natural history parameters.

Validity of estimate of measure of benefit
The estimation of benefit was appropriately derived using a Markov model and was appropriately discounted. The utility weights were taken from a single study which was not described, i.e. the methods used to calculate the weights were not reported. Although the study was German, the authors did not discuss the transferability of the estimates to the Swedish population. Confidence intervals for the weights were authors' assumptions.

Validity of estimate of costs
All relevant categories and types of costs for the perspective chosen were included. The quantities and the unit costs were reported separately, in detail, thus facilitating transferability. The unit costs were obtained from an unspecified number of providers in the authors' setting, but it was unclear whether charges had been used to proxy costs and whether the values were representative of the Swedish setting. The exchange rate was not provided for the conversion from Swedish kroner to euros. Prices were presented in 2005 prices; it was not clear whether indexing had been performed. The costs were appropriately discounted. The authors did not investigate any uncertainty in the cost estimates. The quality and detail of the cost reporting was high, thus enhancing the generalisability of the study.

Other issues
The authors compared their findings with those from other studies and found them to be in agreement. The study examined 43-year-old patients with novel mild and moderate disease and this was reflected in the authors' conclusions. The authors did not present their results selectively. However, the reader should bear in mind that the study results are driven by efficacy parameters from only one randomised controlled trial, as well as an assumption of equivalent efficacy in mild and moderate disease. The authors noted other limitations to their study. First, only direct health care costs were included, although indirect costs may be substantial in this population. Second, the analysis was intended to reflect Swedish clinical practice but GT2/3 patients in Sweden receive only 24 weeks of treatment, rather than the 48 used in the model. Finally, transition probabilities may be age- and gender-dependent, but this was not taken into account in the model.

Implications of the study
The authors did not make any policy recommendations.

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Other publications of related interest
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MeSH
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