Cost-effectiveness and cost-utility of the treatment of chronic hepatitis B with peginterferon alfa-2a, interferon alfa, and lamivudine in Lithuania
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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 examined the cost-effectiveness of treatments for chronic hepatitis B with peginterferon alpha-2a (PEG), interferon alpha and lamivudine. The authors concluded that chronic hepatitis B treatments improved (quality-adjusted) survival but PEG was the most effective treatment at a reasonably high treatment cost. The analysis used a conventional cost-effectiveness framework in a hypothetical cohort of patients. Information on key data sources was limited. Caution is required in interpreting the authors’ conclusions.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The study examined the cost-effectiveness of treatments for chronic hepatitis B with peginterferon alpha-2a (PEG), interferon alpha (IFN) and lamivudine.

Interventions
The three treatments under examination were PEG (subcutaneous injections at a dosage of 180μg every week for 48 weeks), interferon alpha (six million international units three times a week for 24 weeks) and lamivudine (100mg per day from 48 weeks to five years for HBeAg-positive chronic hepatitis B and 100 mg per day up to 5 years in HBeAg-negative chronic hepatitis B).

Location/setting
Lithuania/secondary care.

Methods
Analytical approach:
The analytic framework was based on a Markov model that simulated clinical and economic outcomes in a hypothetical cohort of 40-year-old patients with chronic hepatitis B. A lifetime horizon was considered. The authors stated that the analysis adopted the perspective of the National Health Insurance Fund.

Effectiveness data:
It appeared that clinical inputs for the model were taken from studies that might have been known to the authors and identified selectively. Rates of treatment response were key clinical inputs of the model. These were taken from clinical trials but it was unclear whether there was direct or indirect comparison. Other data for transition probabilities were obtained from observational studies that were not described. Some assumptions were made.

Monetary benefit and utility valuations:
Utility valuations associated with health states were taken from published sources (details not given).

Measure of benefit:
Life-years and quality-adjusted life-years (QALYs) were used as summary benefit measures and were discounted at an annual rate of 5%. Patients with complete response were reported.

Cost data:
The economic analysis included costs of drugs (acquisition and administration) and all medical costs (in-patient treatment, outpatient consultations and examinations) associated with the health states of the model (long-term virologic response, chronic hepatitis B, cirrhosis, hepatocellular carcinoma and liver transplantation). Drug dosages were estimated according to official guidelines. Drug costs were based on producer's price for Lithuania and national drug price calculation methodology for compensated drugs. Costs for other medical services were taken from official price lists and reimbursement rates. Costs were in Lithuanian currency (Lt) and some were also reported in Euros (€). A 5% annual discount rate was applied.

Analysis of uncertainty:
One-way sensitivity analyses were carried out by varying efficacy rates within confidence intervals (CI) reported in published clinical trials.

Results
Total costs, life-years and QALYs were Lt 141,166.76, 1.179 and 1.234 with PEG, Lt 114,482.41, 0.658 and 0.689 with interferon alpha, Lt 109,398.55, 0.423 and 0.442 with lamivudine for 48 weeks and Lt 123,876.51, 1.104 and 1.153 with lamivudine for five years.

In the cost-effectiveness analysis, incremental cost per life-year gained for PEG was Lt 51,256.92 (€14,845.03) compared to interferon alpha, Lt 41,993.67 (€12,162.21) compared to lamivudine for 48 weeks and Lt 230,229.69 compared to lamivudine for five years.

In the cost-utility analysis, incremental cost per QALY gained was Lt 48,980.08 (€14,185.61) with interferon alpha, Lt 40,096.19 (€11,612.66) with lamivudine for 48 weeks and Lt 214,785.71 with lamivudine for five years.

In the sensitivity analysis, incremental cost-effectiveness ratios with PEG ranged from Lt 24,412.64 to Lt 230,229.69 and incremental cost-utility ratios ranged from Lt 23,246.59 to Lt 214,785.71.

Authors’ conclusions
The authors concluded that chronic hepatitis B treatments improved (quality-adjusted) survival but PEG was the most effective treatment at a reasonably high treatment cost.

CRD commentary
Interventions:
The authors justified their selection of comparators. Interferon alpha and lamivudine were the most commonly used drugs in the setting but PEG emerged as a more effective treatment for patients with chronic hepatitis B.

Effectiveness/benefits:
Little information was provided on sources of clinical data. Treatment effect was taken from clinical trials but it was not clear whether head-to-head comparisons were available and the analysis was based on an indirect comparison with potential biases due to differences between studies. No details were given on other sources of clinical estimates so it was difficult to fully judge their validity. Only treatment effect was varied in sensitivity analysis.

Benefit measures were appropriate and enabled comparisons with other published economic evaluations. No information was given on sources of utility weights.

Costs:
The cost categories included in the analysis appeared consistent with the perspective stated by the authors, which considered only direct medical costs. Details of unit costs and quantities of resources used were not reported as most costs were presented as macro-categories and this might reduce the transparency of the economic side of the study. The price year was not reported and this precluded reflation exercises in other time periods. Some currency conversions were reported for key findings. Data sources were reported and these reflected the perspective of the third-party payer in the Lithuanian setting. Cost estimates were treated deterministically and were not subjected to analysis of uncertainty.

Analysis and results:
The study results were reported extensively. Incremental cost-effectiveness and cost-utility ratios were calculated appropriately to synthesise costs and benefits of the alternative strategies. The issue of uncertainty was partly investigated as sensitivity analyses focused exclusively on variations in treatment efficacy rates using published ranges of values. The authors stated that PEG was cost-effective assuming a threshold between $50,000 and $100,000 but this might not have been a relevant threshold for a middle-income country. The authors acknowledged some limitations of their analysis mostly related to sources of clinical data and the need for assumptions. Study results were specific to the Lithuanian setting and appeared difficult to translate to other settings.

Concluding remarks:
The analysis used a conventional cost-effectiveness framework in a hypothetical cohort of patients. Information on key data sources was limited. Caution is required in interpreting the authors’ conclusions.

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