Screening and early treatment of migrants for chronic hepatitis B virus infection is cost-effective

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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
This study assessed the cost-effectiveness of systematic screening and early treatment for chronic hepatitis B virus infection, in the Netherlands, in immigrants from intermediate- and high-endemic countries. The authors concluded that systematic screening for chronic hepatitis B infection was likely to be cost-effective. Despite some limitations in the data transparency, the methods appear to have been appropriate. The conclusions reached by the authors seem valid, but uncertainties remain.

Type of economic evaluation
Cost-utility analysis

Study objective
This study assessed the cost-effectiveness of systematic screening and early treatment for chronic hepatitis B virus infection among immigrants, in the Netherlands, from intermediate- and high-endemic countries.

Interventions
Screening once for chronic hepatitis B infection and subsequent treatment for identified eligible patients was compared with the status quo, which was no screening.

Location/setting
Netherlands/primary care and secondary care.

Methods
Analytical approach:
A published Markov model (Toy, et al 2009, see ‘Other Publications of Related Interest’ below for bibliographic details) was used to simulate the disease progression of hepatitis B virus infection and to assess the impact of screening and subsequent referral for early antiviral treatment. The time horizon was lifetime and the authors stated that a health care perspective was adopted.

Effectiveness data:
The authors selected the most appropriate estimates from the limited evidence available in the literature, for example for the progression probabilities for the natural history of active chronic hepatitis B and for the treatment-related transitions. The baseline prevalence of hepatitis B surface antigen (HBsAg), the detection rate (HBsAg positive), new cases (hepatitis B e antigen positive or elevated serum alanine aminotransferase), referral to specialist care, eligibility for the antiviral drug entecavir, and the rate of eligible patients starting treatment came mostly from Dutch studies. The target population was based on data from the World Health Organization, a Dutch HBsAg prevalence study, and a municipal population registry. Some assumptions were needed, particularly for screening participation, treatment take-up, and treatment adherence. The sustained virologic response to antiviral treatment was from recent clinical trials.

Monetary benefit and utility valuations:
The utility values were from a multinational study on chronic hepatitis B (Levy, et al. 2008, see ‘Other Publications of Related Interest’ below for bibliographic details).

Measure of benefit:
The summary benefit measure was quality-adjusted life-years (QALYs), which were discounted at 3% per year.

Cost data:
The direct health care costs were presented per event or state. These were the screening programme (campaign, personnel, invitation, and reminder), consultations, diagnostic tests, source and contact tracing, referral to specialist care, general practitioner follow-up, disease monitoring, and entecavir therapy. The estimates were from Dutch sources, such as the Dutch Healthcare Authority and the Dutch Health Care Insurance Board, or they were estimated by the authors. They were reported in Euros (EUR) and discounted at 3% per year.

Analysis of uncertainty:
To assess if the cost-effectiveness results were robust, one-way sensitivity analyses were performed on inputs, such as the chronic hepatitis B prevalence in the target population, the overall programme costs, the screening participation, the percentage of successful referrals, and the treatment adherence. Multivariate sensitivity analyses were performed on variables describing the treatment effectiveness, the disease progression, and the utilities. The ranges of values and the sources for the assumptions tested were reported. A probabilistic sensitivity analysis, using Monte Carlo simulation, was conducted to assess the simultaneous impact of parameter uncertainty. The impact of discounting costs at 4% and effects at 1.5%, according to Dutch guidelines, was assessed.

Results
In the base case, without screening, the total costs amounted to EUR 109.2 million and 113,411 QALYs were generated. With screening once, the total costs amounted to EUR 168.5 million and 120,025 QALYs were generated. Screening generated an incremental cost of EUR 59.3 million and an incremental gain of 6,614 QALYs, resulting in an incremental cost-effectiveness ratio (ICER) of EUR 8,966 per QALY gained.

In the univariate sensitivity analysis, the ICERs ranged from EUR 7,936 to EUR 11,705 per QALY gained and the proportion of eligible patients who actually started treatment was the most influential parameter. In the multivariate sensitivity analysis, the ICERs ranged from EUR 5,568 to EUR 60,418 per QALY gained and the highest estimate assumed a relatively slow disease progression for the natural history. The probabilistic sensitivity analysis indicated that there was a 72% chance of the ICER for screening being less than EUR 20,000 per QALY gained, the commonly accepted threshold in the Netherlands.

Authors' conclusions
The authors concluded that systematic screening for chronic hepatitis B infection among immigrants was likely to be cost-effective.

CRD commentary
Interventions:
The interventions were clearly reported and defined. The selection of the comparators, namely screening versus the usual care of no screening, was appropriate and reflected the situation in the authors' setting.

Effectiveness/benefits:
: No systematic review to identify the primary studies was conducted. The authors used Dutch data sources, where possible, but no study details nor quality assessment were provided. This makes it difficult to ascertain if the best available evidence was used. Some clinical estimates relied on assumptions, particularly treatment adherence. The model transition probabilities and the effectiveness inputs were generally well reported. The QALYs were discounted and the source for the utility data was referenced, but the data were poorly described; neither the population nor the method used to elicit them were given.

Costs:
The categories of costs were consistent with the perspective. The cost data were from published studies, but the resource use data and the price year were not reported. Sensitivity analyses were conducted on the overall programme costs, but these excluded the test and follow-up costs and the annual chronic hepatitis B medical management costs. These aspects may limit the generalisability of the findings. The time horizon and discount rate were reported. It was unclear why the authors used the 3% discount rate and not the Dutch guideline rates (costs at 4% and effects at 1.5%).
but these were tested in the sensitivity analysis producing a slightly lower ICER.

**Analysis and results:**
The model structure was not described and no diagram was given, but the authors referred to a published cost-effectiveness study for the full description (Spackman, et al. 2008). They conducted an incremental analysis and the results were presented for each strategy separately as well as incrementally. The sensitivity analyses included one-way, multivariante, and probabilistic analyses, but no cost-effectiveness acceptability curves nor scatter plots were provided and the distributions applied to the parameters were not reported. These factors reduce the generalisability of the findings and results to other settings. The authors provided a generally balanced discussion on the limitations of their study, including the lack of data to support assumptions on participation in the screening programme and on the proportion of eligible patients who started treatment.

**Concluding remarks:**
Despite some limitations in the data transparency, the methods appear to have been appropriate. The conclusions reached by the authors seem appropriate, but uncertainties remain.

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**Other publications of related interest**


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