Cost-effectiveness of hepatitis A/B vaccine versus hepatitis B vaccine in public sexually transmitted disease clinics

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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
A hepatitis B vaccination course and a new compound regimen vaccination called hepatitis A/B were under assessment for the prevention of hepatitis A or B. Both regimens were administered in three doses at three follow-ups.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness and cost-utility analyses.

Study population
The study population comprised a hypothetical cohort of one million adults seen at public STD clinics in 2002. The cohort was assumed to be equally divided among the participants at ages 18, 22, 26 and 30 years.

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

Dates to which data relate
The effectiveness data were obtained from published studies dating from 1994 to 2003. The costs were extracted from published studies dating from 1999 to 2003. The costs were expressed in 2002 prices.

Source of effectiveness data
The effectiveness data were derived from a review of published studies and from an expert panel.

Modelling
A Markov model was developed to predict the impact of hepatitis A. The model started at the year of presentation and continued in annual cycles for 50 years, or until hepatitis A infection occurred. The model provided hepatitis A protection at one point in time and modelled the behaviour of immunisation on a single cohort over the next 50 years.

Outcomes assessed in the review
Several outcomes were reviewed from the literature to construct the model. The outcomes assessed included:

- the incidence of hepatitis A,
- the protective levels of hepatitis A antibodies,
the hospitalisation rates and fatality for those with overt disease,

the life-years lost, and

the quality-adjusted life years (QALYs).

**Study designs and other criteria for inclusion in the review**
Not reported.

**Sources searched to identify primary studies**
Not reported.

**Criteria used to ensure the validity of primary studies**
Not reported.

**Methods used to judge relevance and validity, and for extracting data**
Not reported.

**Number of primary studies included**
The parameters for the model were derived using information collected from 9 published studies. In addition, expert opinion was elicited for one parameter of the model.

**Methods of combining primary studies**
Individual parameters were mostly taken from one source, therefore a synthesis of strategies was not possible. For those parameters for which more than one source was used, it was unclear what strategy was used to combine them.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The results of the review can be summarised as follows:

natural immunity was present in 14% of those presenting at age 19, 16% at age 22, 18% at age 26, and 20% at age 30 years;

the annual rate of reported hepatitis A (per 100,000) ranged from 11.74 to 2.87, depending on the age group;

projected future infection rates were assumed to decrease at a rate of 2.1% per year;

protective levels of hepatitis A antibodies were estimated to be 92% of adults after the first dose of hepatitis A/B vaccine, 98% after the second dose, and 99% after the third dose;

age-specific probabilities of developing overt disease ranged from 73 to 90%; and

for those with overt disease, hospitalisation rates ranged from 10 to 33%, liver transplant rates from 0.02 to 0.08%, and case-fatality rates from 0.18 to 2.83%.
Methods used to derive estimates of effectiveness
Because the duration of protection after an incomplete series was not well established, the Delphi method was applied to combine the responses of an expert panel.

Estimates of effectiveness and key assumptions
From 5 to 50 years, the probability of hepatitis A immunity ranged from 68% to 23% with 1 vaccine dose, from 83% to 44% with 2 vaccine doses, and from 95% to 74% with 3 vaccine doses.

Measure of benefits used in the economic analysis
Two outcomes were used as measures of benefits in the economic analysis. These were the life-years lost as a result of fatal hepatitis A and the QALYs. The former (life-years lost) were based on the timing of fatal infections and US life expectancies. QALYs lost to nonfatal hepatitis A were based on a survey of the general adult US population using time trade-off methods.

Direct costs
The direct costs presented in the analysis were those of the health system. The costs of treating hepatitis A were taken from a published study. These included the cost of hepatitis A treatment, inpatient and outpatient visits, prescribed items, over-the-counter medication, and liver transplants. The authors did not report detailed resource data. The unit costs of resource use were derived from figures typically reimbursed by Medicare. Prescription and over-the-counter items costs were estimated by reducing average wholesale prices by 20%, and assuming the lowest generic cost was used when available. Liver transplant costs were taken from a published study that reported procedural costs and follow-up costs. The costs were discounted using an annual rate of 3%, as recommended by the US Public Health Service’s Panel on Cost-Effectiveness in Health and Medicine. All the costs were expressed in 2002 prices and were inflated where appropriate using the Consumer Price Index for Medical Care.

Statistical analysis of costs
The cost were treated as point estimates (i.e. the model was deterministic).

Indirect Costs
The indirect costs were not reported, but the authors acknowledged that they were unable to estimate employment rates and salaries for individuals attending STD clinics.

Currency
US dollars ($).

Sensitivity analysis
A one-way sensitivity analysis was performed on selected parameters to test the robustness of the model. Alternative discount rates of 5% and 0% were used to translate future costs and benefits to present values. The loss of vaccine immunity was increased to 100% and decreased to 50%. Future annual declines in hepatitis A incidence, hepatitis A fatality rates, and hepatitis A treatment costs were each halved and doubled. Finally, the authors assumed that individuals attending STD clinics had an elevated risk of infection, with 25 to 75% higher rates of baseline hepatitis A immunity, 25 to 75% greater infection risk among those susceptible during the 10 years after presentation, but no elevated infection risk beyond 10 years.

Estimated benefits used in the economic analysis
The number of life-years lost was 813 in the hepatitis B vaccine group and 632 in the hepatitis A/B vaccine group. The numbers of QALYs lost were 1,236 (hepatitis B arm) and 956 (hepatitis A/B vaccine group), respectively.
Cost results
The overall hepatitis A costs over a period of 50 years were $14,749,365 in the hepatitis A/B vaccine group and $10,989,831 in the hepatitis B arm. Although the overall costs of the hepatitis A/B vaccine were higher than the hepatitis B vaccine alone, some important savings were found at the end of the cycle.

Though the additional vaccine costs were substantial ($6,236,080), the model forecasted fewer costs in the hepatitis A/B vaccine group, with savings of $1,609,354 in terms of hospitalisation, savings of $664,452 in outpatient visits, and savings of $202,740 in hepatitis A-related liver transplants.

Synthesis of costs and benefits
The costs and effects were combined in an incremental analysis using the incremental cost-effectiveness ratio (ICER). The ICER was expressed as the cost per life-year saved and the cost per QALY gained. Baseline results suggested that substituting hepatitis A/B vaccine for hepatitis A/B vaccine cost $20,892 per life-year saved, or $13,397 per QALY gained. The sensitivity analysis suggested that the ICER would not exceed $42,000 per life-year saved, or $25,000 per QALY gained.

Authors’ conclusions
The substitution of the current hepatitis B vaccine by the newly available hepatitis A/B vaccine regimen appeared to reduce morbidity and mortality within the thresholds of acceptable cost-effectiveness ratios.

CRD COMMENTARY - Selection of comparators
The authors provided sufficient justification for using the hepatitis A/B vaccine as a new alternative. Having young adults at high risk of infection of hepatitis A is a good reason to vaccinate against hepatitis A/B in STD clinics. The choice of the comparator seems to have represented current practice in the authors’ setting. You should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness measures were entirely derived from published studies, although the authors did not perform a systematic review of the literature to obtain the information for the parameters of the model. Moreover, the data for each parameter were mainly taken from one source and, therefore, the primary studies were not combined. It is possible that the primary sources used by the authors represented the most up-to-date evidence available at the time of the study. However, it is widely accepted that models should summarise all the information pertaining to the parameters, otherwise we may lose the precision of the inputs of the model. This may affect the transferability of the results of the study.

Validity of estimate of measure of benefit
Quality of life and survival were used as estimates of benefits and were summarised using QALYs. The authors also reported the results using life-years saved. The use of QALYs to model benefits over the duration of the model seems to be a sensible choice, as it is quite acceptable as a standard metric in economic evaluations. In addition, it will facilitate the comparison of this analysis with similar studies. The use of time trade-off methods to derive utility weight would appear valid for the derivation of QALYs.

Validity of estimate of costs
Given the perspective adopted, all the relevant categories of cost appear to have been included in the analysis. Only the results of the costs categories were presented. It was not possible to establish what was included in each of the categories, or what unit costs were used. This made it difficult to determine how the cost estimates were calculated. The authors stated that published references had already estimated hepatitis A treatment costs (Jacobs et al., see Other Publications of Related Interest). It is difficult to determine how the results of the model can be generalised to other
settings. Discounting and inflationary methods were used appropriately.

Other issues
The authors compared the results of their study with similar studies on the cost-effectiveness of hepatitis A vaccination. The use of conservative estimates, owing to considerable uncertainty, was acknowledged as the main limitation of the analysis. Generalisability was partially addressed in the one-way sensitivity analysis and the results were not presented selectively.

Implications of the study
The study results suggested that a policy of substituting hepatitis B vaccine by hepatitis A/B vaccine would reduce morbidity and mortality in a cost-effective manner.

Source of funding
Supported by a grant from GlaxoSmithKline.

Bibliographic details

PubMedID
14603096

DOI
10.1097/01.OLQ.0000086601.18907.47

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH