Cost-effectiveness of hepatitis A-B vaccine versus hepatitis B vaccine for healthcare and public safety workers in the western United States

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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 hepatitis A-B vaccine instead of hepatitis B vaccine among health care and public safety workers.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 100,000 health care and public safety workers from 11 western states with hepatitis A rates twice the national average. Vaccination candidates were assumed to be 25 years old and not to have been immunised against hepatitis A or B.

Setting
The setting appears to have been community care. The economic study was carried out in 11 western states of the USA.

Dates to which data relate
The effectiveness and resource use data were obtained from studies published between 2000 and 2002. The price year was 2002.

Source of effectiveness data
The effectiveness data were derived from a review of completed studies and authors' assumptions.

Modelling
A Markov model was developed to predict the lifetime hepatitis A outcomes. The model had annual cycles through to 85 years of age, or death due to any cause. The health states considered in the model were uninfected but susceptible to hepatitis A, uninfected and immune to hepatitis A, infected with hepatitis A, or deceased. Hepatitis B outcomes were not considered, under the assumption that monovalent and bivalent vaccines provide equal protection against hepatitis B.

Outcomes assessed in the review
The outcomes derived from the review of the literature were:
the hepatitis A incidence;
the vaccination efficacy; and
rates of hospitalisation, liver transplant and mortality for those with hepatitis A infection.

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

Sources searched to identify primary studies
The data on incidence of hepatitis A were obtained from the National Notifiable Diseases Surveillance System of the Centers for Disease Control and Prevention. No other source was 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
At least 3 studies were used to estimate the model probabilities.

Methods of combining primary studies
It appears that it was not possible to combine the primary studies, as most of the probabilities were taken from a single study.

Investigation of differences between primary studies
The authors do not seem to have investigated differences between the primary studies.

Results of the review
The rate of reported hepatitis A (per 100,000) during the period 1990 to 1998 ranged from 4.5 to 36.0. The average annual decline was 2.1%. The predicted rate of reported hepatitis A (per 100,000) for future years ranged from 1.3 for the 75 years and older group, to 29.1 for the 21- to 29-year-old group.

The age-specific reporting rates of hepatitis A ranged from 22.5% (for age group 25 to 29 years) to 24.7% (for age group >/= 40 years).

The age-specific probabilities of developing overt disease ranged from 73 to 90%.

The efficacy of the hepatitis A-B vaccine was 92% after the first dose, 98% after the second dose, and 99% after the third dose.

The hospitalisation rates for those with hepatitis A ranged from 10 to 33%.

The liver transplant rates for those with hepatitis A ranged from 0.02 to 0.08%.

The case-fatality rates for those with hepatitis A ranged from 0.18 to 2.83%.
Methods used to derive estimates of effectiveness
Some of the model parameters were obtained from experts' opinion. A Delphi method was used to combine the opinions of an expert panel because the duration of protection after an incomplete vaccination series was not well established.

Estimates of effectiveness and key assumptions
The probability of maintaining hepatitis A immunisation, given vaccination at the age of 25 years, ranged from 23% (75 years old; 1 dose) to 95% (30 years old; 3 doses).

Measure of benefits used in the economic analysis
The main measure of health benefit was the number of quality-adjusted life-years (QALYs) lost. The QALYs lost due to hepatitis A morbidity were estimated using the time trade-off method in a survey of 181 American adults. The QALYs were discounted at a rate of 3%. Other measures of health benefit were the number of cases of overt hepatitis A averted, the decrease in hepatitis A related hospitalisations, liver transplants and deaths.

Direct costs
The methodology used to estimate treatment costs for hepatitis A was reported elsewhere (see 'Other Publications of Related Interest' below for bibliographic details). The costs of liver transplant, hospitalisation and outpatient care were considered in the study. The quantities of resource consumption were not reported. Fees for professional and hospital services were based on Medicare reimbursed amounts. Other costs were derived from published studies. The wholesale prices of the drugs were reduced by 20%, and it was assumed that the lowest generic cost was used when available. Charges associated with liver transplant were reduced by 30% to reflect reimbursements. The price year was 2002. A discount rate of 3% was applied.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The value of lost work was based on the wages of the health care and public safety workers. It was assumed that the real wages would increase by 1.4% annually. The number of work-days lost for non-hospitalised and hospitalised patients were derived from a published study. A 100% employment rate through to the age of 64 years was assumed, with 0% employment thereafter. The price year was 2002. A discount rate of 3% was applied.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were performed to assess the robustness of the results. The assumptions tested were as follows:

the duration of hepatitis A protection was assumed to never exceed 20 years;
the forecast decline in hepatitis A vaccine rates was doubled;
the private vaccine price was substituted for the blended public-private price;
the predicted rates of hepatitis A hospitalisation, liver transplant and death were reduced by 50%; and,
for each of these alternatives, assumptions were made simultaneously.
The cost per QALY gained in areas of lesser hepatitis A risk was also calculated. Finally, an analysis was performed to consider the fact that most American children had complete hepatitis B immunisation as infants, and approximately half of US adolescents were fully immunised.

**Estimated benefits used in the economic analysis**
A total of 0.06 QALYs were lost per nonfatal hepatitis A infection.

The number of QALYs lost was 246 with the hepatitis B vaccine and 32 with the hepatitis A-B vaccine. Thus, the use of the hepatitis A-B vaccine would prevent the loss of 214 QALYs (63% of this gain attributable to reduced mortality and 37% to prevention of morbidity).

The substitution of a hepatitis A-B vaccine for the hepatitis B vaccine would prevent 1,735 cases of overt hepatitis A.

The number of hepatitis A-related hospitalisations, liver transplants and deaths would decline by 82%, 86% and 75%, respectively.

**Cost results**
The total hepatitis A costs per 100,000 health care and public safety workers over the study period were $9.2 million ($2.2 million direct costs and $7.0 million indirect costs) with the hepatitis B vaccine and $6.6 million ($5.4 million added vaccination costs, $292,000 direct costs and $865,000 indirect costs) with the hepatitis A-B vaccination. The difference was $2.6 million.

If the hepatitis A-B vaccine was used, the hepatitis A treatment costs would decrease by $1.9 million and the work-loss costs by $6.1 million. Much of the decline in treatment costs would be associated with hospital admissions (65%) versus outpatient treatment (27%) and liver transplants (8%).

**Synthesis of costs and benefits**
The results of the base-case scenario showed that substituting hepatitis A-B vaccine for hepatitis B vaccine is a dominant strategy since it would provide improved health outcomes and economic savings. The cost-effectiveness improved as the time horizon was extended. In the base-case scenario, the financial benefits outweighed the costs at year 11.

The findings were stable through a range of one-way sensitivity analyses, although the time until the financial benefits outweighed the costs increased. When the assumptions tested in the sensitivity analyses were simultaneously made less favourable to hepatitis A protection, the cost-effectiveness approached $25,000 per QALY gained. When the hepatitis A rates applied were 199% to less than 50% of the national average, the cost per QALY gained ranged from $1,717 to $94,100. When considering the fact that most American children complete hepatitis B immunisation as infants, the cost-effectiveness ratio was $20,635 per QALY gained.

**Authors' conclusions**
Substituting hepatitis A-B vaccine for hepatitis B vaccine would reduce morbidity, mortality and costs.

**CRD COMMENTARY - Selection of comparators**
The choice of the comparator (hepatitis B vaccine) seems to have represented current practice in the authors' setting. You should decide if this is a relevant strategy in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness evidence was derived mainly from published studies. However, a systematic review of the literature was not undertaken. Although this is common practice with models, it does not always ensure that the best data
available are used in the model. In addition, it is possible that the effectiveness data from available studies were used selectively. Moreover, the criteria used to ensure the validity of the primary studies and the methods used to judge and extract the data were not reported. Thus, it was difficult to assess the internal validity of the data used in the model. However, the authors carried out a number of sensitivity analyses relating to the efficacy estimates. These analyses improve both the internal validity and the generalisability of the study by demonstrating the robustness of the results to changes in the base-case estimates. The use of the Delphi method to estimate the parameter with higher uncertainty appears to have been reasonable.

Validity of estimate of measure of benefit
QALYs were used as the measure of benefit. The choice of this measure facilitates comparisons with other studies. The utilities were derived from a published study which used the time trade-off method in a survey conducted on a large sample. Therefore, it would appear that the quality of life evidence used in the model was appropriate.

Validity of estimate of costs
The hepatitis A treatment costs were derived from published studies. It appears that these costs have been estimated according to 1997 clinical practice (see 'Other Publications of Related Interest' below for bibliographic details). Although the inflation methods used were appropriate, the clinical practice could have changed between 1997 and the time the study was carried out. It is probable that the results are not strongly affected by this, as it seems that all the cost categories relevant to the perspective adopted have been included in the study. The unit costs were not reported. All of the costs were derived from official published sources and were appropriately adjusted to the year 2002. Discounting was applied appropriately and a sensitivity analysis was carried out to assess the robustness of the estimates used.

Other issues
The authors compared their findings with those of another study that showed different results. The authors justified this disparity on the grounds of differences between the studies in terms of their estimation of infection risks. The issue of generalisability was not explicitly assessed, although comprehensive sensitivity analyses were performed. As such, the external validity of the results was enhanced. The authors did not report any further limitations of their study.

Implications of the study
The authors did not make any explicit recommendations for changes in policy or practice, or the need for further research.

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Other publications of related interest

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Cohort Studies; Cost-Benefit Analysis; Health Personnel /statistics & numerical data; Hepatitis A Vaccines /economics; Hepatitis B Vaccines /economics; Humans; Markov Chains; Models, Statistical; Occupational Diseases /economics /epidemiology /prevention & control; Occupational Exposure /economics /prevention & control /statistics & numerical data; Quality of Life; United States /epidemiology; Vaccines, Combined

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