Cost-utility analysis of hepatitis A prevention among health-care workers in Israel

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
Three different strategies to prevent hepatitis A (HA) amongst day care centre employees were considered in the analysis.

Strategy one was the status quo passive immunisation strategy. Immunoglobulin was administered after an outbreak in the hospital.

Strategy two was the selective vaccination strategy. After screening for HA virus (HAV)-immunoglobulin G (IgG) status, employees with negative results would then be offered an active vaccine.

Strategy three was the mass vaccination strategy. The active vaccine was administered to all workers without screening for HAV-IgG. In this analysis the authors assumed that the vaccine used would be the commercially available formalin-inactivated HAV vaccine (Havrix; Smith Kline Beecham Biologicals), and that the immune status of the worker would be defined using a commercially available radio immunoassay test (HAVAB; Abbot Laboratories).

Type of intervention
Primary prevention.

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

Study population
The study population comprised a cohort consisting of almost 65,000 health care workers in Israel. No inclusion or exclusion criteria were reported.

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

Dates to which data relate
The effectiveness data were derived from studies dating from 1978 to 1999. The price year was not reported.

Source of effectiveness data
The effectiveness data were obtained from a review of completed studies.

Modelling
The cost-effectiveness analysis was based on a decision tree developed using computer simulation of the epidemiological and economic consequences of HA. To predict the number of HA cases after the implementation of each of the prevention campaigns, a Markov model was constructed. The model scope was restricted to 20 years, which
was the minimal predicted period of immunity induced by an HA active vaccine. Further details of the Markov model were not reported.

**Outcomes assessed in the review**
The outcomes assessed included:

- the relapse rate of HA cases;
- the seroconversion rate of an HAV-IgG seronegative person;
- the case fatality rate for HA;
- the severe hospitalisation rate;
- the rate of fulminant hepatitis resulting in liver transplantation;
- the age-occupation-specific incidence rates of HA, from which the annual hepatitis A attack rates were calculated as the incidence divided by (1 - incidence);
- the effectiveness of the vaccine;
- the validity (sensitivity and specificity) of the HAV IgG antibody blood tests, and its population-specific positive predictive value; and
- the rate of compliance with the blood test and vaccine administration.

**Study designs and other criteria for inclusion in the review**
The age-occupation-specific incidence rates were obtained from a nationwide survey of clinical hepatitis A cases in Israel that had been conducted by the authors of the present study. No further details of the designs of the other studies included in the review were given.

**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**
Approximately 10 primary studies were included in the review.

**Methods of combining primary studies**
Three studies providing evidence on the effectiveness of the HA vaccine were reviewed. These reported effectiveness ranging from 90 to 100%. It was unclear which estimates were chosen for the base-case scenario. For all other measures of outcomes, only one study was used to derive each.
Investigation of differences between primary studies
The authors did not provide any information on possible differences between the three studies reporting the effectiveness of the HA vaccine.

Results of the review
The relapse rate of HA cases was 10%.

The seroconversion of an HAV-IgG seronegative person was 1.10 times the clinical manifested incidence rate in 18- to 39-year-old employees and 1.30 times in older employees.

The case fatality rate for HA was determined as 0.3% for 18- to 39-year-old patients and 2.1% for older patients.

Severe hospitalisation was required for 20% of patients under age 40 years and 41.6% for those older than 40.

Fulminant hepatitis resulting in liver transplantation occurred in 1% of all cases.

The average annual number of cases was 4.5 for physicians aged younger than 39 years and 2.5 for those over 39 years, among a susceptible population of 4,346 or 4,605 physicians, respectively. The attack rates per 100,000 were 103.55 (age 18 - 39) and 54.28 (age >39), respectively.

The average annual number of cases was 4.5 for nurses aged younger than 39 years and 2.0 for those over 39 years, among a susceptible population of 3,073 or 2,418 nurses, respectively. The attack rates per 100,000 were 65.98 (age 18 - 39) and 90.00 (age >39), respectively.

The average annual number of cases was 3.5 for paramedical workers aged younger than 39 years and 5.5 for those over 39 years, among a susceptible population of 6,820 or 2,222 paramedical workers, respectively. The attack rates per 100,000 were 113.90 (age 18 - 39) and 222.49 (age >39), respectively.

The effectiveness of the vaccine when administered in two doses ranged from 90 to 100%.

The validity of the HAV IgG antibody blood test was 99%, and the calculated population-specific positive predictive value was 91.67%.

Measure of benefits used in the economic analysis
The measures of benefit used were the number of HA cases prevented and the quality-adjusted life-years (QALYs) gained. The utility values used to derive the QALYs were obtained from a study assessing utility loss due to gallstone, using the Health and Activity Limitation Index (HALex).

Direct costs
The direct costs included in the analysis were those of the health service, which included the cost of the vaccination programme and the medical costs of treating HA. The vaccination programme costs covered manpower, administration, transportation, the serological HAV-IgG test and vaccination. The medical treatment costs for HA were derived from a study evaluating the cost of treating HA in Israel. The resource quantities and the costs were not reported separately. As the costs were incurred during 20 years, they were appropriately discounted at a rate of 3% per annum. The study reported the average costs. The price year was not reported.

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

Indirect Costs
The indirect costs were not included in the analysis.
Currency
US dollars ($). The authors did not report the costs in the original national currency.

Sensitivity analysis
One-way sensitivity analyses were performed in which the total cost of two doses of vaccine, the cost of the serological test for the antibody to HAV, and the quality of life adjustment values, were varied.

Estimated benefits used in the economic analysis
For physicians, the expected number of HA cases for the younger (18 - 39 years) and older (40+ years) populations were, respectively, 89.03 and 49.72 with passive vaccination, 20.72 and 12.39 with selective vaccination, and 12.91 and 7.21 with mass vaccination. The corresponding number of QALYs gained for the two populations (18 - 39 years and 40+ years, respectively) were 13.6371 and 13.6374 with passive vaccination, 13.6379 and 13.6380 with selective vaccination, and 13.6380 and 13.6381 with mass vaccination.

For nurses, the expected number of HA cases for the younger (18 - 39 years) and older (40+ years) populations were, respectively, 89.38 and 23.99 with passive vaccination, 33.06 and 6.91 with selective vaccination, and 12.96 and 3.48 with mass vaccination. The corresponding number of QALYs gained for the two populations (18 - 39 years and 40+ years, respectively) were 13.6377 and 13.6379 with passive vaccination, 13.6380 and 13.6381 with selective vaccination, and 13.6381 and 13.6381 with mass vaccination.

For paramedical workers, the expected number of HA cases for the younger (18 - 39 years) and older (40+ years) populations were, respectively, 69.17 and 26.10 with passive vaccination, 16.38 and 6.51 with selective vaccination, and 10.03 and 3.78 with mass vaccination. The corresponding number of QALYs gained for the two populations (18 - 39 years and 40+ years, respectively) were 13.6373 and 13.6374 with passive vaccination, 13.6380 and 13.6381 with selective vaccination, and 13.6381 and 13.6381 with mass vaccination.

Cost results
The costs per physician in the younger and older populations were, respectively, $11.47 and $0.22 with passive vaccination, $76.80 and $33.56 with selective vaccination, and $86.93 and $70.79 with mass vaccination.

The costs per nurse in the younger and older populations were, respectively, $5.38 and $33.56 with passive vaccination, $51.84 and $23.26 with selective vaccination, and $74.27 and $70.73 with mass vaccination.

The costs per paramedical worker in the younger and older populations were, respectively, $15.16 and $9.09 with passive vaccination, $65.39 and $42.35 with selective vaccination, and $87.99 and $80.11 with mass vaccination.

Synthesis of costs and benefits
The costs and benefits were combined as the cost per prevented HA case compared with the passive vaccination strategy, and by calculating a cost-utility ratio (i.e. the additional cost required per QALY gained when compared with the passive vaccination strategy).

Using the selective vaccination strategy as opposed to the passive strategy, the cost per prevented HA cases in the younger and older populations were, respectively, $6,240 and $13,712 for physicians, $10,843 and $24,411 for nurses, and, $6,733 and $17,363 for paramedical workers. The corresponding cost-utility ratios for both age populations were, respectively, $56,532 and $39,619 per QALY for physicians, $98,317 and $70,531 per QALY for nurses, and $61,350 and $50,166 per QALY for paramedical workers.

Using the mass vaccination strategy as opposed to the passive strategy, the cost per prevented HA cases in the younger and older populations were, respectively, $6,399 and $25,477 for physicians, $11,509 and $61,858 for nurses, and, $8,196 and $28,898 for paramedical workers. The corresponding cost-utility ratios for both age populations were,
respectively, $70,604 and $318,418 per QALY for physicians, $121,162 and $717,056 per QALY for nurses, and $181,407 and $323,283 per QALY for paramedical workers.

The one-way sensitivity analyses showed that variations in the total cost of two doses of vaccine, the cost of the serological test for the antibody to HAV, and the quality of life adjustment values, altered the cost-effectiveness analysis. The break-even direct cost of treating HA in which vaccination was cost-beneficial was $28,060 for 18- to 39-year-old patients and $57,660 for patients aged 40+ years.

Authors' conclusions
The authors concluded that, in view of their study and taking $60,000 as the limit cost per saved quality-adjusted life-year (QALY), selective vaccination was cost-effective for physicians and paramedical workers. They also concluded that mass vaccination for all health care workers, aside from older nurses, would be cost-effective if the vaccine price was reduced to $23.

CRD COMMENTARY - Selection of comparators
A justification was given for using the passive vaccination strategy (i.e. routine HA vaccination only given to individuals aged 18 and 24 months in Israel). You should decide if this is a widely used health intervention in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken to identify all relevant research and minimise biases. Where it was relevant (e.g. to derive the effectiveness of the vaccine), the authors did not report how the estimates of effectiveness from the different primary studies were combined, nor did they report if they had investigated any differences between these studies. To obtain estimates on the incidence of HA among different groups of health care workers, the authors used results from a study they had already conducted because of the low validity of official data on HA in Israel. The lack of detail about the methods used to identify the data makes it difficult to ascertain whether the best available evidence was used.

Validity of estimate of measure of benefit
The estimation of benefits was derived through the authors’ model. The QALYs were derived using utility values obtained in a study conducted to determine the loss due to gallstones. However, the authors reported no study or expert opinion reporting similarities between the two diseases in terms of quality of life.

Validity of estimate of costs
All the categories of cost relevant to the perspective adopted were included in the analysis. In addition, all relevant costs appear to have been included. The costs and the quantities were not reported separately, which will limit the generalisability of the authors' results. The costs of HA treatment were derived from a study evaluating the cost of treating HA in Israel. However, the authors did not report the sources from which they estimated the costs of the vaccination programme. A sensitivity analysis of the costs was conducted, using ranges that appear to have been appropriate. The authors converted all of the costs into US dollars, but they did not report the exchange rate used or the costs in national currency units. The price year was not reported, which will hamper any possible inflation exercises.

Other issues
The authors compared their findings with those from other studies that had found that HA vaccination was cost-effective in high-risk groups. The issue of generalisability to other settings was addressed in the sensitivity analysis. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors reported a limitation to their study in that it assumed a constant power of infection, and that improvements in hygienic conditions and awareness of infection risks might have led to a declined power of infection, hence, higher cost-effectiveness ratios. However, because no externalities of the vaccine were considered (such as herd immunity),
the cost-effectiveness ratios were higher than they would otherwise have been.

**Implications of the study**
The authors recommended selective vaccination for HA for physicians and paramedical workers only. Mass vaccination of virtually all health workers is only recommended when its unit price falls below $23.

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**Other publications of related interest**


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