Cost-benefit analysis of a nationwide infant immunization programme against hepatitis A in an area of intermediate endemicity

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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 implementation of a nationwide infant immunisation programme against hepatitis A in an area of intermediate endemicity.

Type of intervention
Primary prevention.

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

Study population
The study population comprised the whole Israeli population.

Setting
The setting was society. The economic analysis was carried out in Israel.

Dates to which data relate
The effectiveness and resource use data were collected from studies published between 1987 and 1997. The cost data were obtained from sources relating to the years 1987 to 1996. The price year was 1997.

Source of effectiveness data
The effectiveness data were derived from a review of the literature and personal communications. In addition, the authors made assumptions about the effectiveness.

Modelling
A negative exponential model was used to determine the age-specific incidence rates of the reported and unreported symptomatic cases of HAV. These took into consideration the indirect force of infection effects or herd effects.

Outcomes assessed in the review
The review assessed HAV case rates, reporting rates, case fatality rates, compliance rates, vaccine efficacy, and adverse events.

Study designs and other criteria for inclusion in the review
Not stated.
Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

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

Number of primary studies included
Eight primary studies were included in the review.

Methods of combining primary studies
The effectiveness data were taken from primary studies and were not combined.

Investigation of differences between primary studies
Not stated.

Results of the review
The proportion of HAV cases was 94.7%.

The reported incidence rate of HAV was 54 per 100,000.

The case fatality rate for the period 1985 to 1994 was 0.0071%.

The case fatality rate for the fulminant form was 58.3% for the period 1987 to 1988.

The rate of compliance was 95% for the first vaccination (15 months), and 92% for the second vaccination (24 months).

The rate of minor reactions was 1.25% with the first vaccination (15 months), and 2.50% with the second vaccination (24 months).

Methods used to derive estimates of effectiveness
The authors received data from personal communications on the reporting rates, the case fatality rate for 1994 to 1996, and the fulminant fatal and nonfatal rates. They also made the assumption that the vaccine efficacy would fall annually.

Estimates of effectiveness and key assumptions
The authors made the following assumptions.

The reporting rate was 58.9%.

The case fatality rate for the fulminant form was 29.5% for the period 1994 to 1996.

The fulminant fatal rate was 0.0359% and the nonfatal rate was 0.0857%.
Vaccine protective efficacy would last for ten years and would fall by 2% for each year thereafter.

**Measure of benefits used in the economic analysis**
The benefit measure used by the authors in the cost-benefit analysis was the monetary value of savings in health service resources, and averted work absences, transport costs and premature mortality. However, this database stipulates that the benefit should be directly associated with health gain. Thus, in this instance, only the benefit due to reduced mortality should be included.

The value of a life-year lost was equivalent to the per capita GNP of $15,085 in 1997, increasing at a rate of 2.08% per annum.

The summary measures of benefit in the cost-effectiveness analysis were the number of cases averted, the number of person-lives saved and the number of life-years gained.

**Direct costs**
The direct costs were discounted at an annual rate of 4%. Some of the quantities and unit costs were reported separately for some HAV consequences. For example, the number of days in hospital were estimated and given separately for relapsing or severe forms, but not for cases where there was a liver transplant. The direct costs were for the vaccines, labour, training and health education, transportation of the vaccine and nurses, cold-chain costs, and adverse reactions. The quantity/cost boundary adopted was that of the health service. The cost estimates were gathered from a mixture of published sources, personal communications, authors' assumptions and unattributed sources. The price year was 1997.

**Statistical analysis of costs**
No statistical analysis of costs was reported.

**Indirect Costs**
The indirect costs included were the monetary benefits of vaccination arising from decreased work absences and the number of averted potential life-years lost. Work absence costs were derived from published age- and gender-specific employment costs, adjusted for the unemployment rate and the number of days lost.

**Currency**
US dollars ($). The exchange rate was 3.50 Israeli shekels to the US dollar.

**Sensitivity analysis**
One-way sensitivity analyses were conducted on the discount rate, vaccine efficacy, vaccine efficacy decay rate, and the incidence rate.

**Estimated benefits used in the economic analysis**
From the cost-effectiveness analysis, a nationwide vaccination policy would reduce the expected number of symptomatic cases per year from 4,880 to 4,319 in 1997, from 4,248 to 380 in 2014, and from 3,435 to 1,060 in 2041.

The number of symptomatic HAV cases in the population would be reduced from 181,000 to 47,000 during the 45 years from 1997 to 2041.

The proportion of cases in people aged over 40 years would increase from 2.4% in 1997 to 3.4% in 2014.

The proportion of cases in the under-fives would decrease from 23.7% in 1997 to 17.7% in 2014.
The number of person-lives saved would be approximately 0.2 in 1997, 1.4 in 2014, and 0.9 in 2040.

The number of averted potential life-years lost was 54 years per person in 1997, 55.1 years per person in 2014, and 60.3 years per person in 2040.

These saved life-years lost produced mortality benefits amounting to $0.1 million for 1997, $1.1 million for 2014, and $1.1 million for 2040. This represented an increase in the total benefit to $108.6 million for the 45-year period.

Cost results
Over the 45-year period, the cost of the vaccination programme in terms of resource use was $32.0 million to the health services, and $42.1 million to the health services and society.

The reduced HAV incidence produced savings of $59 million due to reduced health service costs, and $91 million when the costs due to lost work and transportation were included.

Synthesis of costs and benefits
When the benefit due to averted mortality was included, the savings to society were $108.6 million. This was calculated by the saving ($108.6 million) minus the cost of vaccination resource use ($42.1 million).

The costs and benefits relating to the health services were expressed as the health service benefit to cost ratio, 1.80:1.

The costs and benefits relating to health services, travelling, and absence from work were expressed as the resource benefit to cost ratio, 2.13:1.

The costs and benefits relating to health services, travelling, absence from work, and mortality were expressed as the societal benefit to cost ratio, 2.54:1.

The benefit to cost ratio was sensitive to the choice of discount rate. The health service benefit to cost ratio fell from 1.80:1 to 1.66:1 when using a 5% discount rate, and to 1.24:1 when using a 10% rate. The societal benefit to cost ratio fell from 2.58:1 to 2.27:1 when using a 5% discount rate, and to 1.57:1 when using a 10% rate.

Authors' conclusions
The results suggested that the recent adoption of a nationwide infant hepatitis A immunisation policy in Israel was both medically and economically justifiable.

CRD COMMENTARY - Selection of comparators
The comparator of 'no vaccination' was justified since it represented current practice in Israel. You should decide if these health technologies are relevant to your setting.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken and more information about the design of the review could have been reported. In particular, there were no details on how the primary studies were identified, and the criteria on which they were selected and assessed. The authors made several assumptions, and justified some of these by the lack of published data. There was also extensive use of personal communications.

The authors carried out sensitivity analyses to account for uncertainty regarding effectiveness estimates, but only investigated a small number of parameters. The complexity of the model does not enable evaluation, except by sophisticated computer-aided means.
Validity of estimate of measure of benefit
The benefits were estimated directly from the effectiveness analysis in two ways. Firstly, by a summary in terms of health consequences, i.e. the number of cases avoided and the life-years gained. Secondly, by a monetary valuation of the life-years gained.

Both methods had their pros and cons, but neither accounted for morbidity and the consequent quality of life effects. Also, the monetary method, whilst producing an easy to manage single measure of net benefit, required additional assumptions, for example, the value of life-years gained is entirely captured by an average rate of pay.

Validity of estimate of costs
positive features of the cost analysis were that all relevant direct and indirect cost categories seem to have been included, and the price year was reported. In addition, some of the quantities and costs were reported separately, which made it easier to test the applicability of the cost results in other settings. However, no statistical or sensitivity analyses were reported on costs, thus limiting the generalisability of the results.

Other issues
The authors made appropriate comparisons of their findings with those from other studies, and addressed the issue of generalisability to other settings. They suggested that, if the incidence of HAV were to fall, then for some wealthy countries, the cost to benefit ratio might be less than 1. They also stated that although poorer countries would have a cost to benefit ratio of greater than 1, they might not have the budget for the vaccination programme. The authors did not seem to have presented their results selectively. The study considered children aged 15 months and this was reflected in the authors’ conclusions. The authors stated that the benefit to cost ratios were biased downwards. This was not only because of deviations from linearity of herd effects, but also because the authors did not attempt to account for the considerable decrease in asymptomatic cases and morbidity that would occur.

Implications of the study
The authors did not state any further conclusions or recommendations. This study provided a very useful model for application to other settings, but, as the authors stated, it must be used with caution in terms of the specific values of parameter estimates.

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