Cost-effectiveness of universal childhood hepatitis A vaccination in Chile
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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 two universal childhood hepatitis A vaccination strategies. These were vaccination at 18 and 24 months, and vaccination at 18 and 54 months.

Type of intervention
Primary prevention.

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

Study population
The study population comprised a hypothetical birth cohort of children eligible for hepatitis A vaccination.

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

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1999 and 2005. The price year was 2004.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors' opinions.

Modelling
A published Markov model was used to predict hepatitis A outcomes for children born between July 2002 and June 2003 who were potentially eligible to begin vaccination in 2004. The four health states considered were uninfected but susceptible to hepatitis A, infected with hepatitis A, immune to hepatitis A, and dead. When infection occurred, the risk of disease transmission to household and other personal contacts was considered. Infected individuals were excluded from further follow-up due to presumed lifelong immunity. Each individual was followed annually through age 50 years or until death from any cause.

Outcomes assessed in the review
The outcomes estimated from the literature were:

the rates of vaccination coverage;
the rates of vaccine protection;
the rates of reported hepatitis A;
hepatitis A seroprevalence;
the proportion of hepatitis A infection causing overt illness;
overt hepatitis A hospitalisation rates;
overt hepatitis A liver transplant rates;
overt hepatitis A case-fatality rates;
duration of hepatitis A symptoms; and
utility score while hepatitis A symptoms are present.

Study designs and other criteria for inclusion in the review
It was unclear whether a systematic review of the literature was undertaken to identify the primary studies. Details on the sources of other data were not reported. Some estimates came from unpublished data from the Chilean Ministry of Health.

Sources searched to identify primary studies
Not stated.

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

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

Number of primary studies included
Nine primary studies provided evidence.

Methods of combining primary studies
A narrative approach was used to pool the clinical estimates.

Investigation of differences between primary studies
Not stated.

Results of the review
The rate of vaccination coverage with the first dose at 18 months was 96%.

The rates of vaccine protection ranged from:
96.4% at age 2 years to 29% at age 50 with dose at 18 months;
99% at age 2 years to 75.8% at age 50 with doses at 18 and 24 months; and
96.4% to 77.7% with doses at 18 and 54 months.

The rates of reported hepatitis A per 100,000 population increased from 99.1 at ages 1 to 4 years to 259.7 at ages 5 to 9 years, and then decreased to 5.6 at ages 45 to 50 years.

The rates of hepatitis A seroprevalence increased from 10% at age 12 months to 90% at ages 45 to 50 years.

The proportion of hepatitis A infection causing overt illness increased from 7% at ages 1 to 4 years to 78% at ages 40 to 50 years.

The overt hepatitis A hospitalisation rate was 8% for case 0 to 14 years and 11% for case older than 14 years.

The overt hepatitis A liver transplant rate was 0.01% for case 0 to 14 years and 0.03% for case older than 14 years.

The overt hepatitis A case fatality rate was 0.14% for case 0 to 14 years, 0.18% for case 15 to 29 years, 0.21% for case 30 to 39 years, and 0.36% for case 40 to 50 years.

The duration of hepatitis A symptoms was 39 days.

The utility score while hepatitis A symptoms are present was 0.43.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions because of the lack of published evidence.

**Estimates of effectiveness and key assumptions**
The rate of vaccination coverage with a second dose at 24 months was 80%. The rate of vaccination coverage with a second dose at 54 months was 92.2%.

**Measure of benefits used in the economic analysis**
The summary benefit measures used were the life-years (LYs) and quality-adjusted life-years (QALYs). These were estimated using a modelling approach. The QALYs were calculated by combining life expectancy and quality of life, which were derived from the literature. An annual discount rate of 3% was applied. The overt hepatitis A cases, hospitalisations, transplants and deaths were also reported.

**Direct costs**
The analysis of the direct costs was carried out from the perspective of the health care system. It included vaccine costs (acquisition and administration), inpatient and outpatient costs due to hepatitis A, and liver transplant costs. The unit costs were presented separately from the quantities of resources used for most cost items. Resource use was estimated using data derived from published studies. The costs came from Ministry of Health sources and authors’ assumptions. Discounting was relevant, owing to the long timeframe of the model, and an annual rate of 3% was used. The price year was 2004.

**Statistical analysis of costs**
Statistical analyses of the costs were not carried out.

**Indirect Costs**
The indirect costs (i.e. productivity losses) were included in the analysis conducted from a societal perspective. The mean duration of work loss was based on published estimates, while each work day lost was valued using the median
daily wage in Chile. The unit costs were presented separately from the quantities of resources used. The price year was 2004. An annual discount rate of 3% was applied.

**Currency**
US dollars ($).

**Sensitivity analysis**
Extensive univariate sensitivity analyses were carried out to assess the robustness of the model results to variations in model inputs that made assumptions less favourable to the two vaccination strategies. The authors set most of the ranges of values used. Alternative discount rates of 0 and 5% were assumed. Two alternative scenarios were considered with respect to vaccine protection. In the first scenario, lifetime protection was conferred on all children who initially developed immunity. In the second scenario, protection waned twice as quickly as presumed by the base-case parameter estimates. The robustness of the model results to variations in vaccine price was also tested.

**Estimated benefits used in the economic analysis**
The total LYs lost due to hepatitis A were:

- 3,325 (birth cohort 1,519; personal contacts 1,806) with no vaccination,
- 488 (birth cohort 218; personal contacts 270) with vaccination at 18 and 54 months, and
- 455 (birth cohort 202; personal contacts 253) with vaccination at 18 and 24 months.

The total QALYs lost due to hepatitis A were:

- 5,435 (birth cohort 2,481; personal contacts 2,954) with no vaccination,
- 793 (birth cohort 352; personal contacts 441) with vaccination at 18 and 54 months, and
- 739 (birth cohort 326; personal contacts 413) with vaccination at 18 and 24 months.

Vaccination at 18 and 54 months reduced the numbers of hepatitis A cases among birth cohort members and their personal contacts by 84% and 86%, respectively.

Vaccination at 18 and 24 months reduced the numbers of primary and secondary cases by 85% and 87%, respectively.

Vaccination at 18 and 54 months reduced the numbers of hepatitis A-related hospitalisations by 84%, liver transplants by 83% and deaths by 83%. Vaccination at 18 and 24 months provided modestly greater reductions.

**Cost results**
The total costs were:

- $11,076,267 (vaccination costs $0; medical costs $4,733,072; indirect costs $6,343,194) with no vaccination,
- $7,188,139 (vaccination costs $5,342,106; medical costs $695,161; indirect costs $1,150,872) with vaccination at 18 and 54 months, and
- $8,164,540 (vaccination costs $6,445,194; medical costs $648,268; indirect costs $1,071,077) with vaccination at 18 and 24 months.

**Synthesis of costs and benefits**
The costs and benefits were combined by calculating the incremental cost per LY and per QALY saved.

In comparison with no vaccination and using the health care system perspective, the incremental cost per LY saved was $460 with vaccination at 18 and 54 months and $882 with vaccination at 18 and 24 months. The incremental cost per QALY saved was $281 with vaccination at 18 and 54 months and $503 with vaccination at 18 and 24 months.

When the societal perspective was adopted, both vaccination strategies dominated the no vaccination option.

In comparison with vaccination at 18 and 54 months, the incremental cost per LY saved with vaccination at 18 and 24 months was $32,006 when using the health care system perspective and $29,588 when using the societal perspective. The incremental cost per QALY saved with vaccination at 18 and 24 months over vaccination at 18 and 54 months was $19,559 when using the health care system perspective and $18,081 when using the societal perspective.

The sensitivity analysis showed that the base-case results were robust to variations in model inputs when the societal perspective was adopted. In all cases both vaccination strategies remained dominant in comparison with no vaccination.

When using the health care system perspective, the cost-utility ratios were sensitive to the discount rate, hepatitis A medical costs and vaccine price. However, the incremental cost per QALY (compared with no vaccination) never exceeded $498 for vaccination at 18 and 54 months and $720 for vaccination at 18 and 24 months.

Authors' conclusions
A strategy of universal childhood hepatitis A vaccination at 18 and 54 months was cost-effective in Chile. In all cases the incremental costs of vaccination at 18 and 54 months was lower than the annual per-capita gross domestic product in Chile (around $4,200). The incremental cost for vaccination at 18 and 24 months compared with vaccination at 18 and 54 months exceeded this threshold.

CRD COMMENTARY - Selection of comparators
The authors provided a justification for the choice of the comparators. The strategy of vaccination at 18 and 54 months was included because the Chilean system includes immunisation visits at ages 18 months and during the fifth year of life. The second strategy, vaccination at ages 18 and 24 months, required an additional visit. The strategy of no vaccination represented usual care in the authors’ setting. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence was estimated from published studies. However, it was not stated whether a systematic review of the literature was undertaken to identify the primary studies, which appear to have been included selectively. Limited information on the studies used to estimate the clinical inputs was provided. Similarly, the methods used to extract and then combine the primary estimates were not described. Some assumptions were also made. The issue of uncertainty in the data was partly addressed in the sensitivity analysis.

Validity of estimate of measure of benefit
QALYs and LYS are appropriate benefit measures because they capture the impact of the intervention on both quality of life and survival, which represent the most relevant dimensions of care. Details of the approach used to derive the utility weights were not reported. QALYs enable comparisons with the benefits of other health care interventions. Discounting was applied, as recommended in economic evaluation guidelines.

Validity of estimate of costs
The perspective adopted in the study was appropriate as all the relevant categories of costs were included in the analysis. A breakdown of the cost items was not provided and the costs were mainly presented as macro-categories. Extensive information on the unit costs and quantities of resources used was presented. This enhances the possibility of
replicating the analysis in other settings. The source of all the economic data was reported. Discounting was applied at the recommended rate. No statistical analyses of the costs were carried out, but the results of the sensitivity analyses were presented clearly. The price year was reported, which enhances the possibility of carrying out reflation exercises in other time periods. The authors noted that their analysis might have underestimated the costs associated with hepatitis A, as the medical costs were based only on governmental outlays (which might be less than costs incurred by the private sector) and the economic impact of disease outbreaks were not considered. In general, the authors pointed out that conservative estimates were used in order to bias the model assumptions against the two vaccination strategies.

**Other issues**
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. Limited sensitivity analyses were carried out, which, in part, enhance the external validity of the study. The authors noted some caveats to their analysis, which were mainly related to the uncertainty surrounding some estimates.

**Implications of the study**
The study results support the implementation of a universal childhood vaccination programme against hepatitis A in Chile.

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**Other publications of related interest**


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