Cost-effectiveness analysis of hepatitis A vaccination strategies for adults
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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 compares the effectiveness of different Hepatitis A vaccination strategies for adults. The strategies compared were: no intervention;

vaccination against hepatitis A (vaccination strategy); and

testing for antibodies to hepatitis A and vaccinating those without antibodies (test strategy).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of healthy patients’ aged 50 at the start of the evaluation. No inclusion or exclusion criteria were reported. The data for the hypothetical cohort were derived from published literature. No details about the study population or study samples used in the published evaluations were reported.

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

Dates to which data relate
The effectiveness and probability data relate to literature published between 1976 and 1997. The price year was 1997.

Source of effectiveness data
The effectiveness data were derived from a review/synthesis of completed studies.

Modelling
The authors used a Markov decision-analytical model to simulate the costs and health consequences of the hepatitis A prevention strategies.

Outcomes assessed in the review
The outcomes used as input parameters to the model can be divided into 2 categories: hepatitis parameters and vaccine parameters. The hepatitis parameters were:

the annual incidence of hepatitis A in patients aged over 50.
the prevalence of antibodies to hepatitis A in patients aged over 50;

the sensitivity and specificity of antibody testing;

the severity of hepatitis A; and

the number of workdays lost from hepatitis A.

The vaccine parameters were:

compliance with vaccine;

duration of prevention from the vaccine; and

vaccine efficacy.

Study designs and other criteria for inclusion in the review

The design of studies included in the review was not stated and the authors did not report whether any inclusion or exclusion criteria were used to select studies for review.

Sources searched to identify primary studies

The authors did not report the sources searched to identify primary studies.

Criteria used to ensure the validity of primary studies

No criteria used to ensure the validity of the primary data sources were reported.

Methods used to judge relevance and validity, and for extracting data

No criteria used to judge the relevance and validity of the data or methods to extract data were reported.

Number of primary studies included

The authors referenced 16 published primary data sources as sources of the effectiveness and probability data. The authors also used expert opinion to estimate the sensitivity and specificity of ELISA antibody testing for hepatitis A.

Methods of combining primary studies

The authors did not report the method used to combine primary data sources to derive estimates of individual parameters.

Investigation of differences between primary studies

Any differences between primary data sources, in terms of participants, intervention or outcome measures, were not reported or explained by the authors.

Results of the review

The results of the outcomes used as input parameters to the model were as follows:

HEPATITIS PARAMETERS:

annual incidence of hepatitis A = 5/100,000 (range; 3.30/100,000);
prevalence of antibodies to hepatitis A = 0.63 (range: 0.3 - 0.73);
sensitivity and specificity of antibody testing = 0.99 (range: 0.97 - 1.0);
severity of hepatitis A: asymptomatic = 10% (range: 5 - 20%), symptomatic hospitalised = 16% (range: 10 - 20%),
symptomatic fatal = 2.7% (range: 0.5 - 3.0%);
number of workdays lost from hepatitis A: symptomatic not hospitalised = 10, symptomatic hospitalised = 40.

VACCINE PARAMETERS:
compliance with vaccine: receive vaccine = 1 (range: 0.8 - 1.0), receive second dose = 0.8 (range: 0.6 - 1.0);
duration of protection from the vaccine: one dose = 3 years, two doses = 20 years (range: 10 years - lifetime);
vaccine efficacy: one dose = 0.94 (range: 0.9 - 0.99), two doses = 0.99 (range: 0.84 - 1.0).

Methods used to derive estimates of effectiveness
The opinion of hepatologists practising in a tertiary care hospital was used to estimate the sensitivity and specificity of ELISA antibody tests for hepatitis A and compliance with vaccine.

Estimates of effectiveness and key assumptions
The effectiveness of antibody testing was estimated as 0.99 sensitivity and 0.97 - 1.0 specificity.

Measure of benefits used in the economic analysis
The measure of benefit used in the economic analysis was extra life years saved.

Direct costs
The authors did not report resource use and unit costs separately. The authors reported that the direct costs included those associated with the intervention (cost of serology test and the vaccine) and the costs of treating patients who contracted hepatitis A. Where costs were not available, the authors used hospital charges adjusted by Medicare average cost-to-charge ratio multiplier of 0.53. Discounting was undertaken at a rate of 3% per annum. The price year was 1997 and costs were adjusted to that year using the medical services component of the consumer price index for the United States. The following direct costs were included in the analysis:

vaccine cost (per dose) = $57 (range: 5 - 57).
serology test = $17.50 (range: 17.50 - 60.0).

cost of medical care for symptomatic hepatitis A: not hospitalised = $142 (range: 100 - 300), hospitalised = $7,138 (range: 3,000 - 9,000), fatal = $19,603 (range: 15,000 - 60,000).

The authors assumed that there were no additional costs for asymptomatic hepatitis or for the administration of the vaccine. This latter assumption was justified on the basis that people around the age of 50 were likely to visit their physician for other medical problems.

Statistical analysis of costs
No statistical analysis of costs was conducted.

Indirect Costs
The indirect costs of time lost from work due to hepatitis were included in the analysis. The time lost from work was estimated from 2 published studies. The value of time lost from work was proxied by a national hourly wage rate ($11.67, range: 5 - 20), which was estimated from governmental statistics. The authors indicated that the severity of disease, and therefore time lost from work, is higher in older than younger people. The authors reported no other information about the estimation of indirect costs.

**Currency**

US dollars ($). No currency conversions were reported.

**Sensitivity analysis**

The authors performed one-way sensitivity analysis on all variables. In the one-way sensitivity analysis the probability and cost estimates were varied for 1 variable at a time while observing the impact on the model. Two-way sensitivity analyses were done to identify scenarios in which simultaneous variations in 2 variables impacted the model. The authors reported that wide ranges for sensitivity analyses were used and in some instances ranges that would apply to population-based, mass vaccination programmes were used. The authors did not report whether explicit criteria or methods were defined to select the ranges for the sensitivity analysis.

**Estimated benefits used in the economic analysis**

The outcomes of each of the different strategies, over the lifetime of the cohort were:

- no intervention = 17.984456 life years;
- test = 17.984704 life years and 0.0002476 life years gained versus no intervention;
- vaccinate = 17.984706 life years and 0.0000025 life years gained versus the test intervention.

The side effects of the vaccine were assumed to be rare and mild and so were not included in the measure of benefits. The benefits were discounted at a rate of 3%.

**Cost results**

The total (direct plus indirect) costs of each of the three strategies were:

- no intervention = $1.12 per person;
- test = $58.09 per person and an incremental cost of $56.97 versus no intervention; and
- vaccinate = $108.41 per person and an incremental cost of $50.32 versus the test intervention.

The time horizon used was from the initial assignment in the model to death, and included the costs of initial treatment for hepatitis A and relapses occurring within 1 year. The costs of side effects from the vaccine were not included.

**Synthesis of costs and benefits**

A synthesis of costs and benefits was carried out by calculating an incremental cost-effectiveness ratio (additional cost per additional life year gained). Compared with the no intervention strategy the test strategy saved an additional 1-year of life at a cost of $230,113. However, compared with the test strategy the vaccination strategy saved an additional year of life at a cost of $20.1 million. For the one-way sensitivity analysis the authors reported that the model was most sensitive to changes in the annual incidence rate of hepatitis A. When the hepatitis A incidence rate was as high as 30/100,000 and all other variables remained the same, the test strategy cost $182,000 per year of life saved. When the cost of a vaccine fell to $7, the vaccination strategy was preferred and cost $48,928 per year of life saved compared with no intervention. The authors stated that the case fatality rate would have to increase to 17% for the test strategy to reach $50,000 per life-years saved, a commonly accepted benchmark value. The authors reported that, when the starting
age was lowered to 30 years, the test strategy cost $290,000 per year of life saved compared with $230,113 per year of life saved at baseline (age 50). Between ages 30 and 50 the cost-effectiveness of neither of the interventions approached the accepted benchmark of $50,000 per life year saved. The authors stated that, when decreased quality of life associated with hepatitis A was included in the analysis, the incremental cost-effectiveness of the test and the vaccination strategies were $225,000 and $19.65 million per quality-adjusted-life-year, thus showing results similar to the baseline analysis. The model was not sensitive to changes in any other variables in one-way sensitivity analysis within a reasonable range. In relation to the two-way sensitivity analysis the authors stated that, when the annual incidence rate was 30/100,000 and the cost of the vaccine was $41, the vaccination strategy cost an additional $50,000 per-life-year saved compared with no intervention.

Authors’ conclusions
The authors concluded that, for middle-aged adults in the United States, testing for immunity and vaccinating non-immune persons or vaccination without earlier testing is cost-effective. The authors stated that these vaccines only become cost-effective when the vaccine costs less than $7, or when the hepatitis A case fatality rate exceeds 17%.

CRD COMMENTARY - Selection of comparators
A justification was given for the choice of comparator used, namely that it represented current practice in the authors setting. You, as a user of this database, should decide if this is a widely used health technology in your own setting.

Validity of estimate of measure of effectiveness
The authors did not report sufficient information about the literature used to estimate input parameters to assess whether a systematic search and review had been undertaken or whether the authors used data from the available studies selectively. The authors did not report the methods used to combine data from different sources or investigate the impact of differences between primary studies when estimating effectiveness. The authors used expert opinion to estimate the sensitivity and specificity of the hepatitis vaccine. These factors mean that it is not possible to assess the validity of the sources of data used as probability inputs to the model. The authors did not report whether, or how, the structure of the decision model was validated.

The authors reported a number of limitations to their study, one of which is that, because of suspected underreporting of hepatitis A, it is difficult to get an accurate measure of its true incidence. Furthermore the authors also reported that the hepatitis A incidence and mortality rates reported in the literature refer to the entire cohort of persons aged 50 and older, with no breakdown available for each year of age. The authors applied published cohort rates to each year of life over 50 years, thus biasing the study against both intervention strategies. The authors reported that, in cases of uncertainty, they usually adopted a conservative approach, which biased the model against any intervention.

The authors conducted sensitivity analysis on all the model parameters, and reported using wide ranges for each variable. The model was not sensitive to change in the values of the input variables, suggesting that the conclusions drawn from the data were likely to be robust.

Validity of estimate of measure of benefit
The authors reported life years and life years gained as summary measures of benefit. These were derived from the decision model. The validity of the measures is subject to the limitations noted above. The authors assumed that side effects of the vaccine were rare, non-fatal and mild. They also assumed that hepatitis is a short-lived illness when treated, and that relapses after initial treatment for hepatitis would be short and mild. On the basis of these assumptions, the authors suggested that decreases in quality of life for those who survived were unlikely. This was tested in the sensitivity analysis, and increased the incremental cost effectiveness ratios of the test and vaccination strategies still further. The measure of benefit used did not include any value to patients of the test or vaccination per se, or the value of any effects on the risk of infection to the general population.

Validity of estimate of costs
All categories of cost relevant to the perspective adopted were included in the analysis. Although some costs were excluded from the analysis, these are unlikely to have affected the authors’ conclusions. Costs and quantities were not reported separately and no statistical analysis of prices or quantities was performed. However, sensitivity analysis of costs was performed and the ranges used appeared appropriate. Discounting was undertaken at a rate of 3% per annum. No currency conversions were reported.

Other issues
The authors made appropriate comparisons of their findings with those from other studies and the reasons for differences in the overall estimates of cost effectiveness. The issue of generalisability to other settings was addressed.

Implications of the study
The authors conclude that, for middle-aged adults in the United States, neither testing for immunity and vaccinating non-immune persons, nor vaccination without earlier testing is a cost-effective strategy. The authors state that these vaccines only become cost-effective when the vaccine costs less than $7, or when a hepatitis A case fatality rate exceeds 17%. The authors propose that further studies of the cost-effectiveness of hepatitis A vaccine should include the evaluation of the cost-effectiveness of vaccinating patients with chronic liver diseases.

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