An economic evaluation of hepatitis A vaccination in Dutch military personnel

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
Passive immunisation of all subjects with immunoglobulin, or active immunisation of all subjects with inactivated hepatitis A vaccine consisting of 1,440 enzyme-linked immunosorbent assay (ELISA) units, or hepatitis A antibody screening and leaving inactivated vaccine for susceptible subjects only, in troops from low-prevalence countries deployed in an endemic area.

Type of intervention
Screening and primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Troops from low-prevalence countries deployed in an endemic area.

Setting
Hospital. The economic study was carried out in New York, USA.

Dates to which data relate
Data on the prevalence of hepatitis A antibodies were from troops bound for United Nations duty during 1992-1993. Other clinical data were obtained from sources published between 1987 and 1994. No dates were specified for the resource use data. The fiscal year was 1994.

Source of effectiveness data
Effectiveness data were derived from a single study, a review of the literature, and unpublished sources.

Link between effectiveness and cost data
Costing was not performed on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample consisted of a cohort of 2,325 Dutch marines and naval personnel (mean age of 28.1, range: 17-52 years) bound for United Nations duty in Cambodia during 1992-1993.

Study design
Prospective cohort study, carried out in a single centre. The duration of the follow up was until confirmation of age-specific sero-positivity. No loss to follow-up was reported.

**Analysis of effectiveness**
The principle used in the analysis of effectiveness (intention to treat or treatment completers only) was not specified. The clinical outcome measure was the prevalence of hepatitis A antibodies based on age-specific sero-positivity.

**Effectiveness results**
The study sample had a mean hepatitis A antibody prevalence of 14% with a range from 0% in 17 year olds to 83% in 51 year olds. The prevalence rates for age categories were: 17-25 years, 3.2%, 26-30 years, 9.4%, 31-35 years, 16.4%, 36-40 years, 37.4%, 41-45 years, 46.6%, and 46-52 years, 70.6%.

**Clinical conclusions**
"Specific conditions exist for the military. A single hepatitis A case in military circumstances carries the risk of an outbreak in a larger group, and key personnel may be affected."

**Modelling**
A Markov-chain model was constructed to compare the preventive strategies in terms of costs and effects.

**Outcomes assessed in the review**
The following outcomes were assessed:

- The incidence of hepatitis A in the Netherlands (annual attack rate), the hepatitis A attack rate in an endemic area, the percentage of symptomatic hepatitis A, the percentage of mild, moderate, severe, and fulminant hepatitis among the patients with symptomatic hepatitis A, the relapse rate for mild, moderate and severe hepatitis and nonoperability period (weeks, in which an individual with hepatitis A is not fit for duty) for mild, moderate, severe, and fulminant hepatitis.

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

**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**
A total of 5 studies were included in the review.

**Methods of combining primary studies**
Not reported.

Investigation of differences between primary studies
Not reported.

Results of the review
The results were as follows:

- incidence of hepatitis A in the Netherlands (annual attack rate), 0.003%;
- hepatitis A attack rate in the endemic area, 10%;
- the percentage of symptomatic hepatitis A, 90%;
- the percentage of mild hepatitis among patients with symptomatic hepatitis A was 50%, moderate hepatitis, 30%, severe hepatitis, 20% and fulminant hepatitis, 0.1%;
- relapse rate for mild hepatitis was 9%, moderate hepatitis, 7%, and severe hepatitis, 2%;

and nonoperability period for mild hepatitis was 6 weeks, moderate hepatitis, 12 weeks, severe hepatitis, 24 weeks, and fulminant hepatitis, 52 weeks.

Methods used to derive estimates of effectiveness
Effectiveness estimates were also derived from unpublished sources and assumptions made by the authors.

Estimates of effectiveness and key assumptions
Compliance rate for vaccines was 100% (99%) and for immunoglobulins, 100%.

Protection rates for vaccines was 95% (99%) and for immunoglobulins, 95%.

The duration of the protection for vaccines was 1 year (10 years) and for immunoglobulins was 73 days.

The sensitivity and specificity of the screening test were both 99%.

Measure of benefits used in the economic analysis
The benefit measure was the expected number of symptomatic hepatitis A infections for a cohort of 1,000 marines spending 6 months in an endemic area once every 3 years for a time frame of 10 years.

Direct costs
Costs were discounted. Some quantities were reported separately from the costs and cost items were reported separately. The cost analysis covered the costs of vaccines (1,440 ELISA unit vaccine and immunoglobulins), laboratory (screening test, liver function test, blood count, serology hepatitis A and B; serology hepatitis A, B, and C), consultations (general practitioner, specialist (first), and specialist (follow-up)), hospitalisation, and diagnosis and treatment (for mild, moderate, severe, and fulminant hepatitis A, relapsing hepatitis A, and liver transplantation). The perspective adopted in the cost analysis was that of the Dutch healthcare system. Treatment costs were based on available civilian data from the Dutch healthcare system. The sources of other cost data were the manufacturers, the Department of Pharmacy of the Royal Netherlands Navy, and the Laboratory of the Municipal Health Service in Amsterdam. 1994 price data were used.
Indirect Costs
Nonoperability days reported represented lost working days, but no monetary values were attributed to them.

Currency
US dollars ($). The conversion rate used was US$1=1.8 Dutch guilders.

Sensitivity analysis
A series of one-way sensitivity analyses was performed on most input data. Threshold values were calculated for the most sensitive parameters of the model.

Estimated benefits used in the economic analysis
The expected number of symptomatic hepatitis A infections for a cohort of 1,000 marines spending 6 months in an endemic area once every 3 years for a time frame of 10 years was 141.9 for the strategy of doing nothing, 7.8 for passive immunisation for all, 2.7 for inactivated vaccine for all, and 4.2 for inactivated vaccine for susceptible subjects.

Cost results
The discount rate was 5%. The expected direct costs for a cohort of 1,000 marines spending 6 months in an endemic area once every 3 years for a time frame of 10 years were $119,877 for the preventive strategy of doing nothing, $163,825 for passive immunisation for all, $70,321 for inactivated vaccine for all, and $78,424 for inactivated vaccine for susceptible subjects. The corresponding nonoperability weeks (representing lost working time) were 1,621.7 for the preventive strategy of doing nothing, 88.9 for passive immunisation for all, 30.5 for inactivated vaccine for all, and 47.6 for inactivated vaccine for susceptible subjects.

Synthesis of costs and benefits
Both active immunisation strategies were dominant strategies with better benefit outcomes and less costs relative to the doing nothing option. The incremental cost ratio (incremental cost per infection prevented) was $285 for the passive immunisation relative to the doing nothing option. The ratio of cost savings due to avoided treatment costs (due to cases of hepatitis A prevented) to intervention costs (immunisation and screening), was calculated as a measure of return on investment, resulting in values of 0.72 for the preventive strategy of passive immunisation for all, 1.72 for inactivated vaccine for all, and 1.55 for inactivated vaccine for susceptible subjects. The sensitivity analysis established that the most important parameters of the model were incidence and prevalence rates. The threshold value in terms of attack rate endemic area was 5.3% for the strategy of inactivated vaccine for all to be a cost-saving strategy.

Authors' conclusions
Overall, immunisation with inactivated hepatitis A vaccine without prior screening proved to be the optimum strategy for troops at regular risk.

CRD COMMENTARY - Selection of comparators
The reason for the choice of the comparator was clear.

Validity of estimate of measure of benefit
The internal validity of the estimates of benefit can not be objectively assessed as it is not clear whether the authors performed a systematic literature review, and quality assessment of the primary studies included in the review. Details of the protocol for the literature review would have been helpful.

Validity of estimate of costs
Adequate details of methods of cost estimation were given. However, the cost results may not be generalisable outside the authors' settings.

Other issues
Sensitivity analyses were carried out to test the robustness of the findings. The issue of generalisability to other settings or countries was partially addressed; the study results were deemed to be of interest to other low-prevalence Western countries. Adequate comparisons were made with other studies.

Implications of the study
Troops on short notice (less than 14 days) for overseas deployments should be vaccinated routinely, and troops on longer notice should be vaccinated only before departure to a risk area.

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None stated.

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