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
Four strategies were compared for the prevention of hepatitis A virus (HAV):
active immunisation with HAV vaccine (Havrix Monodose (1440E.U);
screening for anti-HAV and then vaccinating;
passive immunisation;
and screening for anti-HAV and then passive immunisation. The four strategies were also compared with a "do nothing" policy.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised 100,000 doctors or staff nurses (mean age 29 years) and 100,000 members of the general population (mean age 20 years - minimum 10, maximum 29). Each group had a mean prevalence of immunity of 43%.

Setting
The study setting was community. The economic study was carried out in the Republic of Ireland.

Dates to which data relate
The effectiveness data were taken from studies published between 1981 and 1997. The cost data were taken from studies published between 1991 and 1992. Prices were given in Irish punts (I£), although no price year was given.

Source of effectiveness data
Effectiveness data were derived from a review/synthesis of the literature and authors' assumptions.

Modelling
A decision model was developed in order to determine the most cost-effective method of preventing hepatitis A. The two cohorts of 100,000 doctors or staff nurses and 100,000 general population were faced with five options: active immunisation with HAV vaccine; screening for anti-HAV and then vaccinating; passive immunisation; screening for anti-HAV and then passive immunisation; and do nothing. Probabilities were used in the model to allow for the
prevalence of immunity and incidence and course of HAV infection.

Outcomes assessed in the review
The parameters used in the model were the incidence of HAV in both cohorts, the prevalence of immunity, the sensitivity and specificity of the HAV screening tests, and the protection rates of passive immunisation. The clinical course of HAV infection was estimated, including the probability of severity of infection, likelihood of symptoms, relapse rates, and probability of prolonged cholestatic jaundice.

Study designs and other criteria for inclusion in the review
Clinical and observational studies were used in order to provide the parameters of the model.

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
14 studies were used a sources of effectiveness data.

Methods of combining primary studies
Primary studies were combined using the narrative method.

Investigation of differences between primary studies
Not stated.

Results of the review
The values of the parameters used in the model were:

the incidence of HAV in both cohorts (0.01% for the general population, and a "guesstimate" of 0.015% for healthcare workers),

the prevalence of immunity (43% in both groups),

the sensitivity and specificity of the HAV screening tests (both 99%), and

the protection rates of passive immunisation (85%).

The probability of symptoms is related to age (20% of infections are asymptomatic for 20 to 29 years of age).

For symptomatic infections, 50% were mild, 30% moderate, 19.9% severe and 0.1% fulminant cases.

Relapse rates were 9% for mild cases, 7% for moderate and 2% for severe cases, and the chance of prolonged cholestatic jaundice was 0.5% for mild cases, 1% for moderate and 2% for severe cases.
Methods used to derive estimates of effectiveness
Compliance rates were assumed and were included in the model. The rates were assumed to be 100% for the first 5 years, and 50% for the remaining 5 years.

Measure of benefits used in the economic analysis
The benefit measure used in the study was HAV cases avoided.

Direct costs
Medical costs were estimated for the treatment of mild, moderate and severe hepatitis and the fulminant hepatitis A (these were 100, 380, 3,850 and 38,500 respectively). The cost of treating relapsed hepatitis was considered (380), as was the cost of treating prolonged cholestatic jaundice (380). The costs of screening (55), vaccinating (60.96 per dose) and passive immunisation (31 per year) were also included. No price year was given. Costs were discounted to the present year at a rate of 5%. The cost data were taken from 2 published studies.

Indirect Costs
Indirect costs of work-days lost were included in an alternative scenario. One published study was used to derive the estimates. It was not stated whether discounting was used, and no price year was given.

Currency
Irish punts (€). 1 Irish punt = 1.3 US dollars.

Sensitivity analysis
A one-way sensitivity analysis was performed to allow for variability in the data, although no ranges were specified in the study. Threshold analysis was also performed on the prevalence of immunity.

Estimated benefits used in the economic analysis
For 100,000 healthcare workers (and 100,000 general population), the benefits arising from the strategies over 10 years were:

- active immunisation with HAV vaccine = 147.2 (97.87) cases prevented;
- screening for anti-HAV and then vaccinating = 147.34 (98.19) cases prevented;
- passive immunisation = 119.1 (79.2) cases prevented; and
- screening for anti-HAV and then passive immunisation = 131.45 (87.6) cases prevented.

Doing nothing prevented no cases.

Cost results
For 100,000 healthcare workers (and 100,000 general population), the costs resulting from the strategies over 10 years were:

- active immunisation with HAV vaccine = 11,949,991 (11,949,563);
- screening for anti-HAV and then vaccinating = 12,312,024 (12,311,791);
- passive immunisation = 19,702,742 (19,696,602); and
screening for anti-HAV and then passive immunisation = 16,732,126 (16,727,578).

Doing nothing resulted in costs of 94,253 for 100,000 healthcare workers and 64,885 for 100,000 general population.

**Synthesis of costs and benefits**
A simple cost-effectiveness ratio (average) was presented for each strategy. No incremental analysis was performed.
For 100,000 healthcare workers (and 100,000 general population), the cost per HAV case prevented resulting from the strategies over 10 years was:

- active immunisation with HAV vaccine = 80,542 (121,433);
- screening for anti-HAV and then vaccinating = 82,922 (124,727);
- passive immunisation = 164,639 (247,875); and
- screening for anti-HAV and then passive immunisation = 126,572 (190,213).

Doing nothing resulted in infinite cost per HAV case prevented for both groups.

If incremental analysis is performed, then the passive immunisation, screening for anti-HAV then passive immunisation and "do nothing" strategies are all dominated. Screening and then vaccination resulted in the most cases prevented, but whilst this prevented 0.14 (0.32) more cases than the vaccination strategy, it cost an additional 362,033 (362,228) for the healthcare workers (general population) groups. The incremental cost-effectiveness ratios were 2,585,950 and 1,131,963 per HAV case prevented respectively.

The vaccination programme was sensitive to changes in the price of the vaccine, the incidence of HAV and the prevalence of immunity. When the prevalence of immunity increases to more than 45%, screening and then vaccination becomes the most cost-effective strategy. The model was relatively insensitive to changes in the costs of HAV treatments and compliance rates. The inclusion of indirect costs made little difference to the results. The model was extended to allow for the passing on of the infection, and this reduced the cost-effectiveness ratio by more than 50%.

**Authors’ conclusions**
The authors concluded that the vaccination programme was the most cost-effective method of preventing hepatitis A, given the parameters used in the model.

**CRD COMMENTARY - Selection of comparators**
The rational for the selection of comparators was clear. Four reasonable methods of preventing hepatitis A were compared, as well as a "do nothing” option.

**Validity of estimate of measure of effectiveness**
The effectiveness estimates used in the model were appropriately derived from the literature. However, it is not clear if the literature review was systematic and inclusive regarding existing evidence. More details regarding this aspect of the study could have been reported. It was not clear, however, as to what ranges were tested in the sensitivity analysis. An alternative scenario where the passing on of hepatitis A is considered was also included in the study.

**Validity of estimate of measure of benefit**
The benefit measure used in the study was HAV cases prevented, and this was derived through the use of a model. A limitation of the study was that the only benefit measure used was HAV infection; although mild, moderate and severe infections were used in calculating the costs, these were not considered separately as benefits. Since fulminant disease is likely to yield a greater loss of utility than mild infection, this could have significant impact upon the results. In addition, as the authors acknowledge, no attempts were made to include death (a significant factor in hepatitis A
course) within the study.

Validity of estimate of costs
The costs included in the study were appropriately derived from other published studies, and discounting was applied. Indirect costs such as work-days lost were included in alternative scenarios. The paper did not, however, report a price year for cost data.

Other issues
With the exception of not including incremental analysis, the authors reporting was very clear. Any assumptions and limitations in the study were well addressed. The authors noted that the prevalence of anti-HAV varied substantially between countries, and as a result, this study will not automatically apply to other settings.

Implications of the study
Vaccination is recommended as the most cost-effective method of preventing hepatitis A for members of the public between the ages of 10 and 29 and healthcare workers in Ireland. If the prevalence of immunity is higher than 45%, it is recommended that screening is performed first, followed by vaccination if necessary.

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