An economic assessment of pre-vaccination screening for hepatitis A and B

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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
Three prevention protocols against hepatitis A and B were examined:

"screen and defer" vaccination until the serology results are known;
"screen and begin" vaccination immediately to avoid a missed vaccination opportunity; and
"vaccinate without screening".

For pre-vaccination screening, sera would be obtained at baseline to determine the presence of hepatitis A antibody (Anti-HAV) and hepatitis B core antibody (Anti-HBc). The bivalent vaccine for hepatitis A and B was 720 El U inactivated hepatitis A antigen and 20 microg recombinant HbsAg protein. The dose of the hepatitis A vaccine was 1,440 El U and that of the hepatitis B was 20 microg.

Type of intervention
Primary prevention (vaccination).

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised 10 hypothetical cohorts of 1,000 adult vaccination candidates. These cohorts corresponded to first-year college students aged 18 years, military recruits aged 18 years, travellers to hepatitis A-endemic areas aged 25, 45 and 65 years; patients aged 25 and 35 years seen in public STD clinics, and prison inmates aged 25 and 35 years.

Setting
The setting was primary, secondary and community care. The economic analysis was conducted in the USA.

Dates to which data relate
The effectiveness data were gathered from studies published between 1993 and 2002. The resource data were gathered from unpublished and published sources between 1998 and 2002. The price year was 2002.

Source of effectiveness data
The effectiveness data were gathered from a review of the literature and authors’ assumptions.

Modelling
A decision analytic model was constructed to estimate the cost-effectiveness of the three prevention protocols, using a
spreadsheet. The time horizon was 6 months.

**Outcomes assessed in the review**
The epidemiological and effectiveness model parameters assessed in the review were seroprevalence rates of immunity against hepatitis A and B, vaccination success rates, and compliance rates for college students only.

**Study designs and other criteria for inclusion in the review**
No criteria were reported. There was no evidence that a systematic review had been undertaken.

**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**
Two clinical trials were included in the analysis of vaccination success rates. Three studies were included in the analysis of compliance.

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

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
For the bivalent vaccine, 93.6% of vaccinees gained hepatitis A protection after one dose, 99.0% after two doses, and 99.9% after three doses.

For the bivalent vaccine, 29.7% of vaccinees gained hepatitis B vaccination after one dose, 77.4% after two doses, and 98.2% after three doses.

For college students, the compliance with the first vaccine dose (if deferred) was 85%. The compliance with subsequent vaccine doses was 83% at month 1 and 80% at month 6.

For patients in STD clinics, the hepatitis B seroprevalence was assumed to be 10% among those aged 25 years and 15% among those aged 35 years.

For prisoners, the hepatitis B seroprevalence was assumed to be 25% among those aged 25 years and 35% among those aged 35 years.

**Methods used to derive estimates of effectiveness**
The authors made several assumptions on the pre-vaccination immunity, on vaccine series compliance, and on vaccine protection.

**Estimates of effectiveness and key assumptions**
The authors assumed that college students, military recruits and travellers were at normal age-specific risk of prior hepatitis A or B infection, and that their risks of prior hepatitis A and B infection were independent. The authors assumed that anti-HBc-negative prisoners and STD clinic patients were at normal age-specific risk of hepatitis A immunity, and that those who were anti-HBc positive were at twice the normal risk.

The authors assumed 100% compliance with the first vaccine doses. For military recruits, they assumed 100% compliance with subsequent vaccine doses, while for prisoners, they assumed 95% compliance with subsequent doses. The authors assumed that for patients in STD clinics, the completion rates were 67% as great as those for adults in general. They also assumed that compliance rates for travellers fell midway between those for college students and STD clinic patients.

For the 1,440 El U hepatitis A vaccine dose, the authors assumed that 98.1% of recipients were protected after one dose and 99.3% after two doses.

Considering the hepatitis A protection with a 720 El U dose at month 1 and a 1,440 El U dose at month 6, the authors assumed that the second dose increased the proportion protected from 93.6 to 99.0%.

**Measure of benefits used in the economic analysis**
The measure of benefits used was the number of vaccine protections conferred.

**Direct costs**
The direct costs of the health system were included. These were for serology, vaccine acquisition and administration. Administration costs were based on private sector and public sector prices. The base year of the cost analysis was 2002. All the costs were adjusted to 2002 levels using the Consumer Price Index for Medical Care. It would appear that the resource quantities have been derived using actual data. Several assumptions about the costs were made. Military recruits, prisoners and STD clinic patients were assumed to receive publicly purchased vaccines. Travellers were assumed to receive vaccines purchased in the private sector. The administration costs of the vaccine for college, STD and travel medicine settings were assumed to be $11.13 per dose. The authors assumed that the costs would be 50% less in military and prison settings.

**Statistical analysis of costs**
No statistical analysis of the costs was performed.

**Indirect Costs**
The indirect costs were not included.

**Currency**
US dollars ($).

**Sensitivity analysis**
One-way sensitivity analyses were conducted. The serology and administration costs were individually increased and decreased (+/- 33% and +/- 67%).
**Estimated benefits used in the economic analysis**
The "vaccinate without screening" and "screen and begin" protocols were equally (or near equally) effective in each population.

Both "screen and begin" or "vaccinate without screening" protocols were more effective than "screen and defer", except for military recruits. For example:

- the number of vaccine protections conferred by the "screen and defer" protocol in college students aged 18 years was 1,439, versus 1,693 with the "screen and begin" or "vaccinate without screening" protocols;
- the number of vaccine protections conferred by the "screen and defer" protocol in travellers aged 25 years was 1,059, versus 1,491 with the "screen and begin" or "vaccinate without screening" protocols;
- the number of vaccine protections conferred by the "screen and defer" protocol in STD clinic patients aged 35 years was 698, versus 1,224 with the "screen and begin" or "vaccinate without screening" protocols.

The number of vaccine protections conferred by the three prevention protocols in military recruits aged 18 years was 1,853.

**Cost results**
In each population considered, "vaccinate without screening" was less costly than "screen and begin" vaccination.

- "Vaccinate without screening" was less costly than "screen and defer" vaccination in only 3 populations (college students with access to publicly purchased vaccines, military recruits and prisoners aged 25 years),

The total costs of the "vaccinate without screening" protocol ranged from $88,073 to $221,467.

The total costs of the "screen and begin" vaccination protocol ranged from $114,728 to $249,820.

The total costs of the "screen and defer" vaccination protocol ranged from $75,672 to $214,632.

**Synthesis of costs and benefits**
Average and incremental cost-effectiveness ratios (CERs) were calculated. An average CER divides the cost of a strategy by its benefits. An incremental CER divides the difference in cost between one strategy and the next most effective by the difference in benefits between the same strategies.

The average CER was lowest for the "vaccinate without screening" protocol in 9 of the 10 populations examined and in 69 of the 80 sensitivity analyses conducted. The exception was for prisoners aged 35 years, for whom "screen and defer" provided the most favourable average CER.

In each population, "vaccinate without screening" dominated the "screen and begin" protocol.

In 3 populations (college students with access to publicly purchased vaccine, military recruits, and prisoners aged 25 years), "vaccinate without screening" also dominated the "screen and defer" protocol.

In the remaining 7 populations, the incremental CERs of "vaccinate without screening" compared with "screen and defer" ranged from $17 to $162 per vaccine protection conferred.

The added cost of "vaccinate without screening" was warranted for all groups except 65-year-old travellers and 35-year-old prisoners.

In the sensitivity analyses, the "vaccinate without screening" protocol remained the most cost-effective through the range of screening and vaccine administration costs considered for college students, military recruits, travellers aged 25 years, and STD clinic patients. For travellers aged 65 years and prisoners aged 25 years, "screen and defer" became the
most cost-effective strategy when the serology costs were reduced by 33%. For prisoners aged 35 years, "vaccinate without screening" was the most cost-effective strategy when the serology costs were increased by 33%. No change in vaccine administration costs resulted in a different ranking of prevention protocols.

Authors' conclusions
Unless directed at vaccination candidates with the highest probability of immunity, pre-vaccination screening for hepatitis A and B immunity was not cost-effective. Balancing a cost-reduction with reduced effectiveness, "screen and defer" may be preferred for older travellers and prison inmates.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparators was clear. All pre-vaccination protocols were selected because they represented valid approaches for the prevention of hepatitis A and B. You should decide whether they represent currently used tools in your own setting.

Validity of estimate of measure of effectiveness
The authors did not state whether a systematic review of the literature had been undertaken. They also did not report the method used to judge the validity of the studies included in the review. Several assumptions were made on the main outcomes (seroprevalence, compliance) and these may have introduced biases. A strong assumption was made but not reported in the text, namely, the authors assumed that the screening programme had a sensitivity and specificity of 100%. In fact, false-positive and false-negative results may occur. In addition, the estimates were not investigated in the sensitivity analyses. These factors may limit the validity of the results.

Validity of estimate of measure of benefit
The number of vaccine protections conferred by pre-vaccination protocols was used as the measure of benefits. The authors acknowledged that the assumption that hepatitis A and B risks were independent might have favoured the "vaccinate without screening" protocol. The authors also acknowledged that targeted sub-groups in each population would have been more appropriate for evaluating the cost-effectiveness of pre-vaccination protocols.

Validity of estimate of costs
Some cost items were not included in the analysis and no justification was provided for their exclusion. The authors acknowledged that this exclusion would change the results obtained. With the inclusion of these costs, the results would have been more favourable to the "screen and begin" protocol and less favourable to the "screen and defer" protocol. Details of the unit costs and quantities of resources used were not reported separately, which limits the possibility of replicating the study in other settings. The price year was reported. Statistical tests were not carried out and the costs were treated deterministically. Sensitivity analyses were performed on the costs. The authors justified the ranges of variation they investigated. No discounting was performed, which was appropriate since the follow-up period was less than one year.

Other issues
The authors did not make appropriate comparisons of their findings with those from other studies, but they did address the generalisability of the results to other settings. The authors highlighted some limitations of their study (see prior sections of the commentary). A strong limitation of this study concerns the analysis of effectiveness. The authors do not appear to have reported their results selectively.

Implications of the study
When considering 10 populations that may present for hepatitis A and B vaccination, the study found that routine screening would seldom prevent enough unneeded vaccine doses to justify the serology costs. In most settings, the cost-effective use of pre-vaccination screening will require the selection of vaccine candidates with the highest probabilities
of hepatitis A and B.

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