Cost effectiveness of hepatitis B vaccination strategies in Ireland: an economic evaluation

Lesley Tilson, Lelia Thornton, Darina O’Flanagan, Howard Johnson, Michael Barry

Background: In accordance with World Health Organization recommendations, many European countries have introduced universal hepatitis B vaccination policies. The UK and Ireland are exceptions. In this study, we conducted an economic evaluation of a universal infant hepatitis B vaccination programme, using a six-component vaccine, compared with the current selective strategy of vaccinating high-risk infants with a monovalent hepatitis B vaccine. Methods: A cost effectiveness analysis was conducted using a Markov model. The perspective of the analysis was the Irish Health Service Executive. Unit cost and resource utilization data were derived from expert clinical opinion, published sources, diagnosis-related group costs for hospital admissions and local cost estimates for medical fees and laboratory investigations. A full probabilistic sensitivity analysis was undertaken. Both costs and outcomes were modelled over a period of 80 years and discounted at 3.5%. Results: Assuming an incidence of acute hepatitis B virus (HBV) infection in Ireland of 8.4 per 100 000 population, the incremental cost effectiveness ratio ranged from €10.992/life years gained (LYG) to €67.200/LYG, at the lowest and highest price estimates for the six-component vaccine, respectively. The cost effectiveness of universal versus selective hepatitis B vaccination was sensitive to the risk of acute HBV infection, the cost of the universal infant vaccination programme and the discount rate. Conclusion: At a cost of €29.00 per dose of the six-component vaccine, universal infant hepatitis B vaccination is cost effective at €37.018/LYG. This compares favourably with other preventive programmes in Ireland.

Keywords: cost-effectiveness, economic, hepatitis B, Ireland, vaccination

Introduction

Set against the background of an increasing annual incidence of hepatitis B virus (HBV) infection, the World Health Organization recommended that all member countries include hepatitis B vaccine in their national immunization programmes by 1997. Although many European countries have introduced universal hepatitis B vaccination policies, The United Kingdom, Ireland, the Scandinavian countries and the Netherlands have not.

Ireland is considered a low endemicity country for HBV infection and the current immunization policy is based on targeting identifiable risk groups for vaccination. However, notifications of HBV infection have increased almost 30-fold between 1997 (31 cases) and 2005 (890 cases) (figure 1).

The majority of cases relate to chronic infections, acquired outside Ireland in countries of high endemicity for HBV infection. Where information is available on acute cases, the majority were born in Western Europe and were related to sexual exposure. Acute cases occurred predominantly in young adults (table 1).

The increase in notifications may be attributed to the combined effects of changes in immigration patterns, increased overseas travel, raised levels of sexually transmitted infections and the introduction of active screening in high risk populations, including asylum seekers and injecting drug users.

There has been a steep rise in immigration to Ireland since the mid-1990s, with an estimated high of 86 900 immigrants in the 12 months to April 2006. Nearly half of immigrants were nationals of the 10 new accession states which joined the EU in May 2004, and 23% originated from outside the EU and USA. Thus, many of these immigrants have come from countries of high or intermediate endemicity. There has also been a significant rise of 64% in estimated overseas travel by Irish residents between February 2003 (302 000 trips) and February 2007 (494 600 trips).

National trends in notified sexually transmitted infections (STIs) have shown an increase of ~200% between 1995 and 2005. Given the above trends in immigration, travel abroad and in STIs, it is likely that the number of people infected with hepatitis B in Ireland will continue to rise. This raises the question of whether a universal vaccination programme should be introduced in Ireland. It is clear that a universal infant vaccination policy would not eliminate HBV infection, as immigration from intermediate to highly endemic countries is a major cause of chronic HBV infection in Ireland. However, the universal vaccination programme would confer protection from acute HBV infection on successfully vaccinated Irish born infants who may be at risk, particularly from perinatal transmission, from horizontal transmission in childhood or sexual transmission at a later age.

In the literature, there are a considerable number of economic evaluations of HBV vaccination programmes. Holliday and Faulds reviewed the early studies (1982–93) and Beutels reviewed subsequent published analyses (1994–2000). The authors highlight that the methods used to estimate the cost effectiveness of HBV vaccination programmes are not always uniform, making comparison of results difficult. Furthermore, the results of these evaluations are strongly

1 National Centre for Pharmacoeconomics, St James’s University Teaching Hospital, James’s St, Dublin 8, Ireland
2 Health Protection Surveillance Centre, Health Service Executive, 25 Middle Gardiner St, Dublin 1, Ireland
3 National Population Health Directorate, Health Service Executive, Dr Stevens Hospital, Dublin 8, Ireland
Correspondence: Lesley Tilson, National Centre for Pharmacoeconomics, St James’s University Teaching Hospital, James’s St, Dublin 8, Ireland, tel: +353 1 4103427, fax: +353 1 4730596, email: ltilson@stjames.ie
Evaluation of the cost effectiveness of HBV vaccination for low prevalence countries remains inconclusive. Two infant vaccination strategies were compared in this economic evaluation: selective and universal. The selective strategy is currently used in Ireland and involves vaccination of infants at high-risk of HBV infection using a monovalent vaccine. The first dose of vaccine is administered in the hospital setting and the subsequent two doses may either be administered in the hospital or in primary care. The current uptake of the three-dose HBV vaccine schedule in infants born to high-risk mothers was assumed to be 64%, based on data collected at the Rotunda Maternity Hospital, Dublin between 1998 and 2000.12

The alternative strategy is the universal administration of HBV vaccine to all infants. At present, there is a five-component universal infant vaccination programme in Ireland, which provides immunization against diphtheria, tetanus, pertussis, poliomyelitis and Haemophilus influenzae type b (Hib). In this study, we establish the cost effectiveness of adding hepatitis B to this universal infant vaccination programme. This would involve administration of a six-component vaccine (Infanrix hexa™). Based on currently available evidence, it was assumed that a booster dose would not be administered.13 The anticipated uptake of the six-component vaccine was estimated at 90%. The uptake was varied from 85% to 95% in a sensitivity analysis.

Structure of model
A decision analytic model, involving a Markov process to model the long-term sequelae of HBV infection, was constructed to estimate the expected costs and life expectancies for a cohort of newborn infants under the selective and universal infant vaccination strategies. The model was constructed using Treeage software.14

The Markov model of HBV infection is run over a total of 80 cycles of 1 year each. A period of 80 years was chosen as the lifetime period for the model based on the average life expectancy for the Irish population.9 Potential outcomes were defined as specific ‘health states’ in the model. Infants move through one of seven health states, as defined by transition probabilities based on Irish epidemiological data and published estimates (table 2).15,16 The seven different health states in the model are:

(i) Susceptible: infants who are not vaccinated and those in whom seroprotection is not conferred from vaccination start out in the susceptible health state. They have an annual age-dependent probability of becoming acutely infected with HBV. Following infection they can recover and develop natural immunity, they can become chronically infected or they can develop fulminant hepatitis, which is associated with a high risk of death. If patients are not acutely infected they remain in the

Methods
Vaccination strategies
Two infant vaccination strategies were compared in this economic evaluation: selective and universal. The selective
Table 2  Age-specific transition probabilities across health states

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Age specific annual probabilities</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of acute HBV infection:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Non-fulminant</td>
<td>0.999</td>
<td>Expert opinion SJH*</td>
</tr>
<tr>
<td>Fulminant</td>
<td>0.001</td>
<td>Harris et al. 2001*</td>
</tr>
<tr>
<td>Outcome of non-fulminant acute HBV infection:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recover/immunity</td>
<td>0.10–0.9</td>
<td>Harris et al. 2001*</td>
</tr>
<tr>
<td>Chronic infection</td>
<td>0.9–0.10</td>
<td>Harris et al. 2001*</td>
</tr>
<tr>
<td>Outcome of fulminant acute HBV infection:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recover/immunity</td>
<td>0.02</td>
<td>Harris et al. 2001*</td>
</tr>
<tr>
<td>Chronic infection</td>
<td>0.08</td>
<td></td>
</tr>
<tr>
<td>Death from hepatitis</td>
<td>0.9</td>
<td></td>
</tr>
<tr>
<td>Outcome of chronic HBV (chronic carrier state):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recover/immunity</td>
<td>0.02</td>
<td>Harris et al. 2001*</td>
</tr>
<tr>
<td>Chronic HBV (chronic carrier phase)</td>
<td>#</td>
<td></td>
</tr>
<tr>
<td>Chronic HBV (chronic active hepatitis phase)</td>
<td>0.0012</td>
<td></td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Death (unrelated to HBV)</td>
<td>Age dependent probability of death from all causes</td>
<td><a href="http://www.cso.ie">www.cso.ie</a>*</td>
</tr>
<tr>
<td>Outcome of chronic HBV (chronic active hepatitis state):</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Chronic HBV (chronic active hepatitis phase)</td>
<td>#</td>
<td>Harris et al. 2001*</td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Death (cause specific)</td>
<td>0.0028</td>
<td></td>
</tr>
<tr>
<td>Outcome of cirrhosis state:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cirrhosis</td>
<td>#</td>
<td>Harris et al. 2001*</td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>0.0465</td>
<td></td>
</tr>
<tr>
<td>Death (cause specific)</td>
<td>0.0071</td>
<td></td>
</tr>
<tr>
<td>Outcome of hepatocellular carcinoma state:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatocellular carcinoma</td>
<td>0.05</td>
<td>Harris et al. 2001*</td>
</tr>
<tr>
<td>Death (cause specific)</td>
<td>0.95</td>
<td></td>
</tr>
</tbody>
</table>

a: Expert clinical opinion from St James’s University Teaching Hospital  
b: Transition probabilities range from 0.9 for infants acquiring HBV infection at birth becoming chronically infected, to 0.5–0.7 for infants who are infected between age 1 and 5. The probability of becoming chronically infected then falls to 0.1 up to 19 years of age and then to approximately 0.05 for adults7,8  
c: All probabilities for a particular health state in the model must sum to 1.0. The hashmark (#) in Table 2 is used in place of a probability expression for one transition state (i.e. it equates to 1.0 minus the other probabilities in a given health state)

susceptible health state and have an annual age-dependent probability of dying from other causes.

(ii) Recovery/immunity: patients who recover from acute or chronic HBV infection remain in this healthy state and have an annual age-dependent risk of dying from other causes.

(iii) Chronic carrier phase: patients in this health state may either recover from HBV infection, continue in this health state, or progress to chronic active hepatitis, hepatocellular carcinoma or death from causes unrelated to HBV infection.

(iv) Chronic active hepatitis phase: in this phase, patients can progress to cirrhosis, hepatocellular carcinoma or death.

(v) Cirrhosis: patients who progress to cirrhosis have an increased risk of hepatocellular carcinoma and a high probability over time of death from liver failure.

(vi) Hepatocellular carcinoma: those who enter this health state have a very high annual probability of death.

(vii) Death: all patients eventually end up in this health state, which is called the absorbing health state.

Each cycle spent in one health state accrues a health cost and a year of life. Therefore, the Markov model projects the lifetime burden of illness caused by HBV infection and the total costs associated with vaccination and HBV disease.

The model was constructed to distinguish between those infants at high- and low-risk of infection. It was assumed that the relative risk of HBV infection for high-risk compared with low-risk infants was 24.9,16

Routine antenatal screening data from the Rotunda Maternity Hospital in Dublin in 2005 illustrated that 0.96% of mothers were hepatitis B surface antigen (HBsAg) positive. This was used as the upper estimate (as this population is considered at higher risk of HBV infection than the overall national level of risk) and an estimate 50% below the Rotunda data (0.48%) was used as the lower estimate for the proportion of high-risk infants. The average between the two values (0.72%) was used as the base case estimate.

The universal infant vaccination policy will protect infants born in Ireland from HBV infection. The policy of screening/vaccinating high-risk children and adults would need to continue unchanged when the universal infant vaccination programme is introduced. This is why no costs have been estimated for the current opportunistic screening and vaccination of high-risk children and adults, as this is common to both arms of the model.

Vaccine effectiveness

In 2003, Curran and Goa17 conducted a review of all open label, randomized studies in healthy infants that investigated the immunogenicity of the hexavalent combination vaccine (Infanrix hexaTM) administered in three-dose primary immunization schedules. One month after completion of a three-dose vaccination course, a high degree of seroprotection against HBV surface antigen (99–100%) was achieved. More recently, Tichmann et al.18 conducted a multi-centre randomized controlled trial in 45 centres in Germany. The immunogenicity of two hexavalent vaccines administered to 214 infants at age 2, 4 and 6 months as a primary vaccination schedule was investigated. Seroprotection of 98.6% was reported with three doses of Infanrix hexaTM. The universal infant vaccination programme investigated in this economic
evaluation would be administered according to a similar schedule as used in the German trial. Therefore, the more up to date and conservative estimate of immunogenicity reported by Tichmann et al. was included in the base case analysis. A range of 98–100% seroprotection from administration of three doses of HBV vaccine was incorporated into the model in a sensitivity analysis.19

Transition probabilities
The age-specific annual risk of acquiring acute HBV infection was estimated from the number of acute events of hepatitis B by age reported in Ireland in 2005.20 Reports of acute HBV infection underestimate the true incidence because of the occurrence of under-reporting and asymptomatic cases. The proportion of under-reporting was assumed to be 25%.21,22 The proportion of asymptomatic infections is age dependent and it was assumed that 90% of children (0–19 years) and 66% of adults were asymptomatic.22 Having corrected for under-reporting and asymptomatic cases, the overall age adjusted incidence of acute HBV infection in Ireland in 2005 was estimated at 8.4 per 100,000 population (table 2). The transition probabilities for chronic HBV infection, cirrhosis and hepatocellular carcinoma were derived from the literature and expert opinion (table 1). Age-dependent annual transition probabilities were used to estimate disease progression rates over a lifetime. Age-dependent probability of death from causes unrelated to HBV infection were derived from Irish life tables.5

Vaccination costs
Selective strategy
The price of Engerix B (€10.76 per dose excluding VAT) was used to estimate the cost of the selective vaccination programme, as this was the most widely used preparation for children in 2005. The first dose is given in hospital but the system for delivery of subsequent doses varies. It was assumed that 50% of second and third doses were given in the hospital setting and 50% in primary care. General practitioners (GPs) are paid a fee of €77.20 for administration of two doses.23 The hospital administration fee was estimated at €66 per course, based on time taken by nursing staff to administer the vaccine and clerical staff to follow-up patients.24 Salary estimates for nurses and clerical staff were based on the mid-point of Department of Health and Children salary scales 2005.25 Therefore, the total cost of selective vaccination was estimated at €104 (€32.38 for the vaccine and 50% x €77.20 plus 50% x €66 (€71.61) for administering the vaccine). As a result of the uncertainty in the estimates for administration of the selective vaccination programme, a wide range around the base case estimate of €104 (€72–€148) was incorporated in a sensitivity analysis.

Universal strategy
The cost of the universal vaccination programme is based on the incremental price of the six-component vaccine (Infanrix hexa26) over the currently used five-component vaccine. As there is no six-component vaccine available on the Irish market at present, a range of prices were included in the analysis, to evaluate the effect of vaccine price on the cost effectiveness of the universal vaccination strategy. The incremental cost per course of the six over the five-component vaccine was €36 (range €16.65–€58.44). In the base case analysis, it is assumed that no additional fee for administering the vaccine is incurred (i.e. the fee for administration of the vaccine will be the same as the current fee for the administration of the five in one vaccine). The lower price estimate includes a volume-based discount and the upper estimate includes a payment to GPs for administering the vaccine.

Direct medical costs of Hepatitis B infection
Unit cost and resource utilization data for each of the health states for HBV infection were estimated from a range of standard sources. Irish cost and resource utilization data were incorporated into the model and when data were not available were adapted from other settings. All prices were inflated to 2005 Euro, using the consumer price index for health.5 A detailed description of resource utilization and unit costs data is included in a supplementary data. A direct cost was not assigned to asymptomatic cases. The following direct costs were included in the model:

- Acute HBV infection without hospitalization (90% of cases): €796.
- Acute HBV infection with hospitalization (10% of cases): €3,833.
- Chronic HBV infection (chronic carrier phase): €586.
- Chronic HBV infection (chronic active phase)—without treatment (40% of cases): €802.
- Chronic HBV infection (chronic active phase)—with treatment (60% of cases): €4,091.
- Cirrhosis: €9,363.
- Hepatocellular carcinoma: €15,738.

Uncertainty in the estimation of the direct medical costs was investigated in a sensitivity analysis. Costs and outcomes were discounted at an annual rate of 3.5%.

Indirect costs were not included as the main focus of the evaluation is whether it would be cost effective for the State to fund a universal vaccination programme against HBV infection.

Sensitivity analysis
One-way sensitivity analyses were performed to establish any differences in the incremental cost effectiveness ratio (ICER) by varying the main parameters included in the model: cost of universal infant vaccination (€36; €16.65–€58.44); direct medical costs (±50%); proportion of infants at high risk of HBV infection (0.72%; 0.48–0.96%); cost of selective infant vaccination (€104; €72–€148); uptake of selective vaccination (64%; 50–90%); uptake of universal vaccination (90%; 85–95%); seroprotection from hepatitis B vaccination (98.6%; 98–100%), discount rate (3.5%; 0 and 5% for costs and outcomes) and finally the time horizon was changed from 80 to 100 years. Furthermore, a two-way sensitivity analysis on the cost of the universal infant vaccination programme and the age-specific risk of acquiring acute HBV infection was undertaken. A probabilistic sensitivity analysis, using second-order Monte Carlo simulation is presented in which input parameters were allowed to vary according to estimated probability distributions. The choice of distribution was based on consideration of the properties of the parameters and data informing the parameters. The probability parameters were specified as beta distributions because of the special relationship between the beta distribution and the binomial data used to populate probabilities.26 The direct medical cost parameters were specified as gamma distributions as they are constrained to be positive, and are fully continuous. Finally, the 95% confidence interval was included for the vaccine efficacy parameter and was assumed to be normally distributed. The results are presented as a cost effectiveness acceptability curve.
Table 3  Incremental cost effectiveness ratio (ICER) for the base case scenario and one-way sensitivity analysis

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Cost (£)</th>
<th>Incremental cost (£)</th>
<th>Effect (LYG)</th>
<th>Incremental effect</th>
<th>ICER (£/LYG)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ICER for base case scenario</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selective</td>
<td>860 000</td>
<td>2 593 413.00</td>
<td>2 593 479.99</td>
<td>66.99</td>
<td>37 018</td>
</tr>
<tr>
<td>Universal</td>
<td>3 340 000</td>
<td>2 480 000</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Model variable (base case)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ICERs for one-way sensitivity analysis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incremental cost of universal vaccination (£36)</td>
<td>€16.65</td>
<td>10 992</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Direct medical costs</td>
<td>€58.44</td>
<td>67 200</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of infants at high risk of HBV infection (0.72%)</td>
<td>+50%</td>
<td>31 652</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost of selective vaccination (£104)</td>
<td>0.48%</td>
<td>37 934</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uptake of selective vaccine (64%)</td>
<td>€72</td>
<td>37 238</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uptake of universal vaccine (90%)</td>
<td>€148</td>
<td>36 715</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uptake of universal vaccine (90%)</td>
<td>50%</td>
<td>35 952</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seroprotection from hepatitis B vaccine (98.6%)</td>
<td>95%</td>
<td>36 756</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Proportion of infants at high risk of HBV infection (0.72%)</td>
<td>0.96%</td>
<td>36 127</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost of selective vaccination (£104)</td>
<td>0.48%</td>
<td>37 934</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost of selective vaccination (£104)</td>
<td>0.48%</td>
<td>37 934</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uptake of selective vaccine (64%)</td>
<td>€72</td>
<td>37 238</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uptake of universal vaccine (90%)</td>
<td>€148</td>
<td>36 715</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uptake of universal vaccine (90%)</td>
<td>50%</td>
<td>35 952</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Seroprotection from hepatitis B vaccine (98.6%)</td>
<td>95%</td>
<td>36 756</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Discount rate for costs and outcomes (3.5%)</td>
<td>0%</td>
<td>2197</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time horizon (80 years)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Figure 2  Two-way sensitivity analysis: sensitivity to incidence of acute HBV infection and incremental cost per course of universal vaccination

Results

Over the 80-year time horizon for a birth cohort of 60 000 infants, the model predicts that 316 cases of acute HBV infection, 95 cases of chronic active HBV infection, 13 cases of cirrhosis and six cases of hepatocellular carcinoma would be averted by introducing a universal vaccination strategy compared to the current selective strategy.

Under the base case scenario, which assumes an incidence of acute HBV infection of 8.4 per 100 000 population, the incremental cost effectiveness of the universal compared with the selective vaccination programme is €37 018 life years gained (LYG) (table 3). The ICER ranges from €10 992/LYG to €67 200/LYG at the lowest price (£16.65 per course) and the highest price (£58.44 per course) estimates for the incremental cost of the six-component vaccine, respectively.

The ICER is sensitive to the incidence of acute HBV infection; as the incidence increases universal vaccination becomes more cost effective (figure 2). The ICER ranges from €32 573/LYG to €42 730/LYG when the incidence of acute HBV infection is increased and decreased by 1/100 000, respectively.

The choice of discount rate has a marked effect on the ICER, which ranges from €2197/LYG to €77 984/LYG when costs and outcomes are discounted at 0 and 5%, respectively.

Variation of the other parameters in a series of one-way sensitivity analyses demonstrates that there is a minor impact on the ICER, with a maximum variation of approximately €5500/LYG around the base case ICER of €37 018/LYG (table 3).

The cost effectiveness acceptability curve demonstrates the probability that universal infant HBV vaccination is a cost-effective therapy for a range of values (figure 3). The curve suggests that if the decision maker is willing to pay €45 000/LYG, one can be 83.9% certain that this is a cost-effective intervention.

Discussion

This cost effectiveness analysis demonstrates that universal infant vaccination would be a cost-effective intervention, compared with a selective vaccination policy, at the base price.
of the six-component vaccine. The economic model is sensitive to the risk of acquiring HBV infection, the cost of the universal vaccination programme and the discount rate. This is consistent with the findings of other economic evaluations of HBV vaccination strategies.8,16,27,28

Difficulties in estimating the true incidence of HBV infection are well documented in the literature.21,22 In the base case analysis of this evaluation, an incidence of 8.4 per 100 000 was assumed, based on the number of cases reported to the HPSC in 2005 and adjusted for asymptomatic cases and under-reporting. In comparison, the estimated incidence in England and Wales, based on surveillance data from 1995 to 2000 and the same assumptions to account for under-reporting and asymptomatic cases, was 7.4 per 100 000.21

Based on recent trends in Ireland, the incidence of HBV infection would be expected to rise in the future. Therefore, it was appropriate to explore the effect of an increasing risk of infection over time in this study.

The results of the cost effectiveness analysis are highly sensitive to the cost of the universal vaccination programme. The universal strategy involves administering a combined vaccine as opposed to a single vaccine. There are a number of advantages to adopting such an approach, including fewer healthcare visits and fewer injections per visit. Storage requirements are reduced and there is a better use of time and lower programme costs.29 The trade price of the vaccine is included in the base case analysis and this is considered a conservative assumption. If a universal immunization programme were introduced it could be anticipated that a volume based discount price would be negotiated, which would improve the cost effectiveness of the programme.

Previous economic evaluations of hepatitis B vaccination programmes illustrate that the results are also sensitive to the rate of discounting. Universal infant vaccination becomes less cost effective, when health benefits are discounted and this finding is consistent with the results of other studies.30–32 However, it is particularly important to discount benefits in economic evaluation of vaccination programmes, as costs occur immediately but benefits occur many years in the future. In Ireland, it is currently accepted that a rate of 3.5% for both healthcare visits and fewer injections per visit. Storage requirements are reduced and there is a better use of time and lower programme costs.29 The trade price of the vaccine is included in the base case analysis and this is considered a conservative assumption. If a universal immunization programme were introduced it could be anticipated that a volume based discount price would be negotiated, which would improve the cost effectiveness of the programme.

In this economic evaluation, health outcomes are measured in terms of survival (LYG), rather than quality adjusted life years (QALYs). Most of the published economic evaluations of HBV vaccination programmes have not adjusted for improvements in quality of life.15,16,27,30,32,34–37 One study conducted in 1995, which investigated the impact of including QALY weights found that there was minimal change from the cost per LYG result.31 The authors concluded that the main benefits of preventing hepatitis B infection lie in extending life and not quality of life, and as a result estimates of benefits are not reported.28 In 2003, Aggarwal et al.10 reported that universal HBV vaccination in a country with intermediate endemicity was highly cost effective with marginal cost effectiveness ratios of US$16.27/LYG and US$13.22/QALY. The utility values for this study were derived from clinician judgement. There has been little research into deriving reliable and accurate utility values for chronic HBV infection. Beutels (2001) stated that the effort required to determine utility values accurately is out of proportion to the additional information obtained by them, particularly if health gains are discounted.8 A conservative approach has been adopted in our study by using survival as the health outcome measure.
Economic evaluations in other countries of low endemicity have produced variable results. The studies differ in terms of the measure of health outcomes, time horizon, discount rate employed, estimates of vaccine administration costs, estimates of incidence of disease and proportion of cases treated, study perspective and inclusion of direct/indirect costs. As a result of different methodologies and different assumptions, it is not possible to compare these studies directly.

In addition to the cost effectiveness of universal infant vaccination strategies, research has also been conducted to investigate the costs and cost effectiveness of implementing universal adolescent HBV vaccination programmes. Although this strategy was found to be cost effective in the US and Canada, the investigators assumed that the costs would be similar to the costs of implementing a universal infant programme. In Ireland, it would be more costly to introduce a school-based adolescent programme compared to the universal infant programme, as additional administration fees, as well as higher vaccine costs for a single component vaccine, would be incurred. Wallace et al. highlight that the vaccine accounted for the 70–80% of the overall costs of such a programme in Scotland. As the vaccine cost is such a key cost driver, this would have a significant impact on the overall expenditure associated with an adolescent programme.

There has been extensive debate over the implementation of universal hepatitis B vaccination in low prevalence countries. In the UK, for example, there is still no consensus on which HBV immunization option should be adopted. Although there is no fixed threshold below which an ICER would be considered cost effective in Ireland, the ICER of €37 018/LYG is comparable to that of other interventions which have been reimbursed in the Irish setting. The ICERs for statin therapy for primary prevention of cardiovascular disease, for example, ranged from €17 900 for atorvastatin to €33 800/LYG for pravastatin. The cost effectiveness of a universal infant pneumococcal vaccination programme is €98 279/LYG in the base case model and €316 2/LYG when the effect of herd immunity on unvaccinated adults is included. Many of the technologies approved by NICE in the UK, fall below a threshold of £30 000/QALY (€45 000). In the US, thresholds in the area of US$50 000 (€37 000) have often been mentioned. The universal infant HBV vaccination programme could be considered a cost-effective intervention in Ireland, compared with a selective vaccination policy, at the base price of the six-component vaccine.

Conclusions

Conclusions on the cost effectiveness of hepatitis B vaccination are sensitive to assumptions regarding the incidence of HBV infection in Ireland, the cost of the six-component vaccine and the discount rate. At the base price estimate of the six-component vaccine, universal infant immunization would be a cost-effective intervention in Ireland. While our study may be relevant to other countries considering introducing a universal immunization programme the findings should be interpreted within the context of disease occurrence and costs in the specific country.

Supplementary data

Supplementary data are available at European Journal of Public Health online.

Acknowledgements

Niamh Murphy, HPSC; Dr S. Norris, St James’s Hospital; Dr K. Bennett, Trinity College Dublin; Dr M. Caffrekey, The Rotunda Maternity Hospital; Dr B Corcoran and C. Kiersey, National Immunisation Office; Dr J. Heslin, HSE South Eastern Region. This study was funded by The Health Service Executive.

Conflict of interest: None declared.

Key points

- Ireland has one of the lowest reported incidences of HBV infection worldwide, but the reported incidence increased 30-fold between 1997 and 2005.
- There is currently a selective immunization programme for HBV infection, targeting high-risk groups. However, selective vaccination programmes are more difficult to implement than universal programmes and are seldom as effective.
- The results of this study suggest that universal infant immunization against HBV infection, using the six-component vaccine, would be a cost-effective intervention in Ireland.
- Assuming an incidence of HBV infection of 8.4 per 100 000 population, the incremental cost effectiveness of the universal infant vaccination programme, compared to the current selective strategy, ranges from €10 992/LYG to €67 200/LYG, at the lowest and highest price estimates for the six-component vaccine, respectively.

References


Received 12 March 2007, accepted 14 November 2007