Impact of universal Haemophilus influenzae Type b vaccination starting at 2 months of age in the United States: an economic analysis

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 use of universal Haemophilus influenzae Type b (Hib) vaccination, starting at the age of 2 months.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of a hypothetical US birth cohort of 3,815,469 infants (the estimated number of births in 2000).

Setting
The (hypothetical) setting was primary care. The economic analysis was conducted in the USA.

Dates to which data relate
The effectiveness data were collected from the literature. The data related to two periods, the pre-vaccine era (1976 - 1984) and the vaccine era (1995 - 1999). The cost data were estimated from the Marketscan database for 1993 to 1997, and from unpublished and published studies between 1998 and 2001. All the costs were adjusted to year 2000.

Source of effectiveness data
The effectiveness data were derived from a non-systematic review of the literature.

Modelling
A decision analysis model was used to determine whether the current Hib vaccination programme was cost-effective and cost-beneficial in comparison with no vaccination. The duration of follow-up was from birth to 5 years of age.

Outcomes assessed in the review
The outcomes assessed in the review and used as model inputs were:

- the age-specific incidence of Hib invasive diseases (meningitis, epiglottitis, bacteraemia, pneumonia, cellulitis, arthritis, and other invasive diseases with isolation of Hib), and

- case-fatality ratio and possible sequelae among children with meningitis (mental retardation, severe hearing loss,
epilepsy, and spasticity or hemiplegia).

**Study designs and other criteria for inclusion in the review**
The surveillance data used to determine the age-specific number of Hib cases occurring in the presence of Hib vaccination were obtained from the National Notifiable Disease Surveillance System, the National Bacterial Meningitis and Bacteremia Reporting System, and the Active Bacterial Core Surveillance (ABCs). Details of these have been described elsewhere.

**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**
The ABCs system reported Hib cases to the Centers for Disease Control and Prevention (CDC), and Haemophilus influenzae isolates were re-serotyped at the CDC.

**Number of primary studies included**
The burden of Hib invasive disease without vaccination was estimated from 10 studies, while the burden with vaccination was estimated from 3 sources of surveillance data.

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

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

**Results of the review**
The case fatality ratio was 3.78% for Hib invasive disease.

The probability of mental retardation was 6.1%, of severe hearing loss 6.7%, of epilepsy 6.1%, and of spasticity or hemiplegia 5.1%.

The incidence of meningitis was:

- at 0 to 5 months, 101.0 per 100,000 in the pre-vaccine era and 0.6133 in the vaccine era;
- at 6 to 11 months, 179.0 in the pre-vaccine era and 0.3417 in the vaccine era;
- at 1 year, 104.0 in the pre-vaccine era and 0.1100 in the vaccine era;
- at 2 years, 31.0 in the pre-vaccine era and 0.0131 in the vaccine era;
- at 3 years, 17.0 in the pre-vaccine era and 0.0129 in the vaccine era; and
- at 4 years, 4.0 in the pre-vaccine era and 0.0378 in the vaccine era.
Full details of the other Hib invasive diseases (for all relevant age groups) were presented in the paper.

**Methods used to derive estimates of effectiveness**
The authors made an assumption to evaluate the incidence rate of Hib disease among the current birth cohorts in the absence of vaccination.

**Estimates of effectiveness and key assumptions**
The authors assumed that the incidence rate of Hib disease among the current birth cohorts in the absence of vaccination would be the same as was observed in pre-vaccination birth cohorts.

**Measure of benefits used in the economic analysis**
The benefit measures used were the gains in years of life and the quality-adjusted life-years (QALYs). The authors assumed that the health utility indices were 0.840 for hemiplegia, epilepsy and mental retardation, and 0.977 for severe hearing loss. The authors assumed that acute Hib infections without sequelae have only a transitory effect on the patients’ quality of life. The benefits were discounted at an annual rate of 3%.

**Direct costs**
The health care system and the societal perspectives were used in the economic analysis. The health care system perspective included the direct health care costs and other direct costs. The direct health care costs were those associated with vaccination (e.g. vaccines, administration and adverse effects), prophylactic intervention using rifampin, treatment (including rifampin prophylaxis), complications, sequelae of Hib invasive disease and hospitalisation. Both outpatient and inpatient costs were included in the analysis. These were obtained from the Marketscan database and published studies.

The price of Hib in combination vaccines was calculated as a proportion of the individual vaccine prices. The authors used a commonly accepted guideline to determine the duration and frequency of the typical treatment regimens and the average costs of medication using the price derived from the survey. The other direct costs included institutional care for mental retardation, special schooling for deafness and mental retardation, and long-term care for epilepsy and hemiplegia. The resource quantities and the costs were not reported separately. The price year was 2000. The costs were discounted at the same annual rate as that used for the benefits (3%).

**Statistical analysis of costs**
The costs were treated deterministically.

**Indirect Costs**
The authors estimated the economic value of life lost prematurely (using the human capital approach), indirect costs from permanent disability, and indirect costs associated with parents who missed work and stayed at home to care for sick children. The cost data were taken from published reports, the Bureau of Labor statistics, and the Bureau of the Census. The indirect costs were discounted at an annual rate of 3%.

**Currency**
US dollars ($).

**Sensitivity analysis**
Univariate sensitivity analyses were performed. These assessed:

the effect of varying the proportion of vaccines purchased and administered in the public versus the private sector (90%
purchased by public sector and administered by private sector versus 80% purchased by private sector),

the administration cost (200% of base-case),

the wastage rate (15 and 25%),

the discount rate (0, 5 and 8%),

the Hib incidence rate (50 to 200% of base-case), and

the proportion of combination versus monovalent vaccines administered (0 versus 100%).

**Estimated benefits used in the economic analysis**

In the presence of a national Hib vaccination programme, the number of Hib cases was reduced by 99.7% and the number of deaths by 99.6%.

The Hib vaccination programme resulted in 97,878 life-years saved (LYS) (27,301 discounted LYS) and 113,644 QALYs gained.

**Cost results**

The direct cost of Hib disease was $1,345,704,895 without the vaccination programme and $3,241,119 with the vaccination programme.

The indirect cost of Hib disease was $1,229,459,922 without the vaccination programme and $3,520,312 with the vaccination programme.

The total cost of Hib disease was $2,575,164,817 without the vaccination programme and $6,761,431 with the vaccination programme.

The total costs averted by the Hib vaccination programme were $2,568,403,386.

The total costs of the Hib vaccination programme were $0.39 billion from the direct cost perspective and $0.48 billion from the societal perspective.

The total net saving (NPV) with the vaccination programme was $0.95 billion from the direct cost perspective and $2.09 billion from the societal perspective.

**Synthesis of costs and benefits**

From the health service perspective, the Hib vaccination programme would save $9,710 per additional discounted LYS and $8,363 per additional QALY gained.

From the societal perspective, the Hib vaccination programme would save $54,620 per additional discounted LYS and $13,121 per additional QALY gained. However, those calculations did not reflect the difference between the NPV ($2.09 billion) and the discounted LYS (27,301) or the QALY gained (113,644).

The direct and societal benefit-cost ratios for the Hib vaccination programme were 3.4 and 5.4, respectively.

The results were not strongly affected by most factors. However, the results were very sensitive to variation in the incidence of Hib disease without a national vaccination programme.

**Authors' conclusions**

The current Haemophilus influenzae Type b (Hib) vaccination programme is highly cost-beneficial and results in
substantial cost-savings.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator (no vaccination) was clear and explicitly justified. The aim was to assess the cost-effectiveness of the current vaccination programme.

**Validity of estimate of measure of effectiveness**
The Hib incidence rates were estimated from surveillance data and population-based studies, which the authors acknowledged might be subject to reporting biases. The other input parameters were derived from published studies, but it was unclear whether the review was conducted systematically to identify relevant research and minimise biases. In addition, assumptions were made to estimate the incidence of Hib invasive disease in the absence of vaccination. However, the estimates were investigated in sensitivity analyses, although the variations in parameter estimates seem to have been arbitrary and all the analyses were one-way. It was difficult to assess the validity of the estimates due to a lack of transparency in the reporting.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled. The decision tree used to derive a measure of health benefit is likely to have been appropriate. However, it was unclear how the time horizon was introduced in the model. The authors derived the utility weights for calculating QALYs from assumptions only. The relevance of the effectiveness results may be questionable on account that the authors did not provide justifications, and the utility weights should be derived directly from patient preferences. The reader should decide whether the time horizon (5 years from birth) was sufficient for evaluating the effects. The use of QALYs will allow the results to be compared with those of other studies evaluating different technologies.

**Validity of estimate of costs**
The analysis of the costs was conducted from two distinct perspectives. It appears that all the relevant categories of costs have been included in the study. However, the authors did not compare and discuss the results according to the perspective chosen. The unit costs were reported for almost all of the cost items, but a detailed breakdown of the cost components (e.g. staff and materials) was not given. The cost estimates were treated deterministically. The source of the cost data was reported. In the text, the authors reported the formulae used to calculate the cost-effectiveness ratio. However, the authors did not refer to the comparator when calculating the incremental cost-effectiveness ratio. In the last column of table 4 the authors provided figures that are unclear in that they do not apparently correspond to the difference between NPV and outcomes, and it is not obvious what they do correspond to.

The costs and the quantities were not reported separately and the resource use estimates were taken from the literature review. Hence, the analysis could not be reworked for other settings. The price year was reported, thus assisting any reflation exercises. Since the time horizon of the model was 5 years, appropriate discounting was undertaken and sensitivity analyses on the costs were performed.

**Other issues**
The issue of the generalisability of the results to other settings or countries was not addressed. The authors did, however, make non-explicit comparisons of their findings with those from other studies. The authors reported a number of limitations to their study, which have been highlighted already. The authors do not appear to have reported their results selectively.

**Implications of the study**
According to the authors, universal Hib vaccination of infants, starting at 2 months of age, has been and remains an excellent societal investment. The authors noted that their study should help guide policy formulation and the adoption of strategies that have potential for reducing disease burden and saving costs.
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Not stated.

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Other publications of related interest


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MeSH
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