Cost-benefit analysis of Haemophilus influenzae type b vaccination in children in Spain
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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
Universal vaccine against Haemophilus influenzae type b (Hib) in children.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
Spanish children under 1 year of age.

Setting
Primary care. The economic study was carried out in Spain.

Dates to which data relate
Effectiveness data were collected from studies previously published between 1985 and 1997. Cost data were collected from 1996 sources. The price year was 1996.

Source of effectiveness data
Effectiveness data were derived from a review of previously published studies and authors' assumptions.

Modelling
Details of the model used were not explicitly stated. However, it can be inferred that costs and effectiveness measures were combined over a 5-year period, using a simple decision tree model.

Outcomes assessed in the review
The review assessed the following outcomes: annual incidence of Hib invasive disease, age distribution of Hib invasive disease, nature of Hib invasive disease, mortality rate and the effectiveness of vaccine. The rate of adverse events following Hib vaccination and the probability of Hib invasive disease sequelae were also estimated.

Study designs and other criteria for inclusion in the review
Not stated.
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
Estimates of effectiveness were derived from approximately 11 primary studies.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
For the base case analysis, the average annual incidence of Hib invasive disease was estimated to be 15 cases per 100,000 children under 5 years of age. 17% of these cases were estimated to occur during the first 6 months of age, 27% during the second half of the first year, 39% during the second year, and 17% between the second and fifth year of age. It was also estimated that 67% of cases of invasive disease would correspond to meningitis, 11% to pneumonia, 7% to epiglottitis, 5% to cellulitis, 3% to arthritis and 7% to sepsis and other manifestations. The mortality rate was estimated to be 3.5%. The effectiveness of the vaccine was assumed to be 26% after the first dose and 99% after the second dose. The rate of adverse events following Hib vaccination was estimated to be 1 per 60,000 administered doses. When invasive disease occurred, 10% of meningitis cases were estimated to be associated with serious sequelae and an additional 11% with moderate sequelae. It was estimated that 11% of patients with Hib arthritis would have moderate sequelae.

Methods used to derive estimates of effectiveness
Estimates of effectiveness were also based on the authors’ assumption about the coverage rate for the diphtheria-tetanus-polio (DTP) immunisation programme.

Estimates of effectiveness and key assumptions
The coverage of the universal vaccine programme was assumed to be 90%.

Measure of benefits used in the economic analysis
Benefit was measured as the expected number of cases of Hib invasive disease prevented over 5 years for a cohort of children undergoing the universal vaccination programme. The number of deaths prevented was also estimated.

Direct costs
Quantities and costs were reported separately. The quantity/cost boundary adopted was that of society. Direct medical costs included the cost of vaccine doses, vaccine warehousing and storage, nurse time used to administer the vaccine, training time for the nurses and the cost of treating adverse reactions produced by the vaccine. The direct non-medical
costs of transport and domestic help were incorporated into indirect costs. Dosage and price estimates of the vaccine were provided by the manufacturer. Remaining resource use estimates were taken from the medical literature or based on assumptions. Direct costs of inpatient hospital stays, inpatient CT scans and outpatient consultations were obtained from the 1996 update of the Price Agreements for Health Services to External Providers of Spain's National Health Service. The price year was 1996. The authors also estimated the direct medical cost of treating invasive disease (and associated sequelae) that would be expected to occur over a five-year period, in the absence of a universal vaccination programme. This included the cost of emergency and inpatient care, CT scans and outpatient consultations. An annual discount rate of 5% was applied to these costs.

**Statistical analysis of costs**

Not applicable.

**Indirect Costs**

Quantities and costs were reported separately, from a societal perspective. Indirect costs reflected the loss of income due to lost work days of one of the parents, due to invasive disease. The estimation of quantities was based on assumptions, with the average Spanish hourly wage rate (in 1994) used as the basis for prices. This rate was multiplied by 1.5 to include the cost of transport and domestic help. Indirect costs were discounted at 5% p.a.

**Currency**

Spanish pesetas (Pta), with Pta 126.5 = US$1 in April 1996.

**Sensitivity analysis**

Univariate sensitivity analyses were conducted on the following parameters: annual incidence rate, cost of vaccine, vaccine efficacy, cost of sequelae, and the assignment of an economic value to lost lives.

**Estimated benefits used in the economic analysis**

It was estimated that the universal vaccination programme would prevent 219 cases of invasive disease and 8 deaths.

**Cost results**

The total per-patient cost of the universal vaccination programme was estimated to be Pta 7,058, which includes the cost saving resulting from a cessation of selective vaccination. The cost of the latter was not explicitly reported, but can be inferred to be Pta 7,620,690. The five-year discounted cost of treating invasive disease, in the absence of a universal vaccination programme, was estimated to be Pta 2,182,868,907.

**Synthesis of costs and benefits**

The universal vaccination programme would result in an incremental cost per case of invasive disease prevented of Pta 1,196,288. If the incidence of invasive disease were 10 per 100,000 under-fives, the incremental cost per case of invasive disease prevented would rise to Pta 6,767,721. If this incidence rate were 30, then an incremental cost saving of Pta 4,389,051 per case averted would be achieved. Sensitivity analysis indicated that cost savings would also arise if the efficacy of the vaccine were 100% or if the cost of the vaccine were Pta 1165. Assigning a value of Pta 200,000,000 to the cost of life also resulted in cost savings.

**Authors' conclusions**

A programme of universal vaccination against Hib in Spain would be cost saving for annual incidence rates above 20 cases of invasive disease per 100,000 children under 5 years of age, while for lower rates, a net economic benefit would depend on the price of the vaccine dose.
CRD COMMENTARY - Selection of comparators

Rationale for the choice of the comparator is clear. You, as a user of this database, should consider whether a selective vaccination programme is relevant to your own setting.

Validity of estimate of measure of benefit

Authors define benefit as costs averted due to the universal immunisation programme. However, this is not the definition conventionally used in economic analysis. For this reason, the abstract describes the analysis as one of cost-effectiveness rather than of cost-benefit. Benefit was also measured in terms of cases of invasive disease averted and was based on a literature review. Insufficient details were provided concerning the type of review, the inclusion criteria used and the methods used to extract data: the validity of the estimate of effectiveness is therefore uncertain. The authors did acknowledge certain limitations regarding their estimate of the incidence rate and used sensitivity analysis to investigate these areas of uncertainty, reporting the results comprehensively.

Validity of estimate of costs

Relevant costs were considered and appear to have been discounted appropriately, although the cost of care prior to hospitalisation for those with invasive disease was not included in the analysis. Costs and quantities were reported separately, which allows the analysis to be reworked for other settings. However, many of the resource use estimates were either based on assumption or taken from the literature review. The limitations outlined above in the section 'Validity of estimate of measure of benefits' may also apply to estimates of cost. The authors acknowledged some of these limitations and sensitivity analysis was performed to investigate these areas of uncertainty.

Other issues

Authors did not explicitly address the issue of generalisability of the results to other settings or countries, but comparisons of findings with those from other studies were made.

Implications of the study

An economic analysis that was based on a systematic review of both clinical and economic evidence, would give a more accurate estimate of the cost-effectiveness of a universal Hib vaccination policy.

Source of funding

Grant from Wyeth-Lederle, Madrid, Spain.

Bibliographic details


PubMedID

10345159

Other publications of related interest


**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Child; Cost-Benefit Analysis; Haemophilus Infections /economics /prevention & control; Haemophilus Vaccines /economics /therapeutic use; Haemophilus influenzae type b /immunology; Humans; Spain; Vaccination /economics

**AccessionNumber**
21999008092

**Date bibliographic record published**
31/01/2000

**Date abstract record published**
31/01/2000