The cost-burden of paediatric pneumococcal disease in the UK and the potential cost-effectiveness of prevention using 7-valent pneumococcal conjugate vaccine

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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
The use of a 7-valent pneumococcal conjugate vaccine (PCV) (Prevanar/Prevenar, Wyeth Pharmaceuticals) in the prevention of pneumococcal disease.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of a cohort of children from birth to 10 years of age. The cohort was divided into 6-month age bands, and infants aged younger than 6 months were further divided into those aged 0 - 2 and 2 - 6 months.

Setting
The setting was unclear. The economic analysis was conducted in the UK.

Dates to which data relate
The effectiveness data were gathered from studies published between 1999 and 2001. Data on the incidence of pneumococcal bacteraemia related to 1996 to 1998. The cost data were derived from studies published between 2000 and 2002. The price year was 2001.

Source of effectiveness data
The effectiveness data were gathered from a review of completed studies.

Modelling
A model was developed in MS-Excel to estimate the epidemiology and cost of pneumococcal disease in children in the UK. The time horizon was 10 years.

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

the age-specific incidence of pneumococcal meningitis, pneumococcal septicaemia, all-cause pneumonia and all-cause otitis media (OM);
the disease-specific vaccine efficacy; and
the mortality rates from invasive pneumococcal disease (IPD).

**Study designs and other criteria for inclusion in the review**
Not reported.

**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**
About 7 studies were included in the review of the literature.

**Methods of combining primary studies**
The method used to report the outcome estimates was unclear. Sometimes the authors extrapolated estimates using either only one study, calculations, or assumptions derived from published data.

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

**Results of the review**
The age-specific incidences were not reported.

The efficacy of the vaccine in year one was 97.4% against IPD, 6.0% against pneumonia, 7.0% against OM and 5.4% against pneumococcal meningitis.

**Methods used to derive estimates of effectiveness**
The authors made several assumptions to estimate the outcomes.

**Estimates of effectiveness and key assumptions**
The authors assumed:

95% coverage in the primary cohort and 75% coverage for the alternative vaccination schedules (see 'Sensitivity Analysis' section);

the efficacy of the vaccine decreased by 1% per year up to age 5 years, followed by 3% per year between ages 6 and 10;

the disease-specific efficacy against all-cause pneumonia and OM would decline over time in the same manner as for
IPD;

the mortality rate from OM was 0.0%;

the life expectancy was 78 years and the mean age at death was 3 years.

**Measure of benefits used in the economic analysis**
The benefit measures used were the number of episodes of illness due to pneumococcal infection prevented and the number of life-years saved (LYS). The benefits were not discounted.

**Direct costs**
The perspective of the UK NHS was adopted. Only the direct costs were included in the base-case analysis. The direct costs were for treating infections (using experts' opinions), long-term sequelae, death and vaccination (dose and administration). In terms of long-term sequelae, the frequencies of brain damage and deafness were estimated from published literature, while the costs were taken from the Medical Protection Society. The resource quantities and the costs were not reported separately. All the costs were adjusted to 2001 UK pounds sterling. The costs were discounted at an annual rate of 6% (based on recommendations made by NICE).

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

**Indirect Costs**
The indirect costs were included in the sensitivity analysis. Lost wage costs were estimated using the human capital method and the average UK gross hourly wage was reported. The resource use data were derived from the frequency of visits and admissions.

**Currency**
UK pounds sterling (£).

**Sensitivity analysis**
A series of one-way sensitivity analyses was performed. These considered three alternative vaccination schedules:

- infant catch-up (three doses for infants aged 7 - 12 months at time of first dose);
- toddler catch-up 1 (two doses at least 2 months apart for toddlers aged 12 - 18 months at time of first dose);
- toddler catch-up 2 (two doses at least 2 months apart for toddlers aged 18 - 24 months at time of first dose).

The variables investigated were serotype coverage (+/- 5%), the discount rate, disease incidence (half and twice the base-case incidence), case fatality, the cost of brain damage due to meningitis (range of payouts reported) and the efficacy of vaccination (range of 95% confidence limits).

**Estimated benefits used in the economic analysis**
The model estimated that, in the UK in each annual birth cohort, there were a total of 881,146 episodes of illness due to pneumococcal infection and 149 deaths associated with IPD and all-cause pneumonia.

The 7-valent PCV would prevent a total of 54,384 episodes of these infections and 29 deaths.

The number of LYS with vaccination was 2,187.
The side effects of vaccination were not considered in the economic analysis.

**Cost results**
The total direct cost was 135.5 million for no vaccination and 204.5 million for vaccination. Thus, the net cost of vaccination versus no vaccination was 68.9 million.

**Synthesis of costs and benefits**
An incremental cost-effectiveness ratio was calculated to combine the costs and benefits of the vaccination programme relative to the no-vaccination strategy. The incremental direct cost per LYS with vaccination was 31,512 compared with no vaccination.

When considering the parents' time off work in addition to NHS costs, the estimated cost per LYS was 28,156.

Higher costs per LYS were obtained for vaccine schedules that started at or above 12 months of age.

The findings were sensitive to the ability of vaccination to reduce the incidence and cost of pneumococcal meningitis and its long-term sequelae, and the cost of giving vaccination.

**Authors' conclusions**
A universal and early childhood immunisation programme with the 7-valent pneumococcal conjugate vaccine (PCV) in the UK would reduce the incidence of pneumococcal infection at a cost of 31,512 per life-year saved (LYS). The authors stated that this figure is close to the limit at which PCV would be considered cost-effective in the UK.

**CRD COMMENTARY - Selection of comparators**
The reason for the choice of the comparator (no vaccination) was clear, as the main objective of the study was to evaluate the active value of the vaccination programme. You should decide whether the no-vaccination option represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The principal input parameters for the model were derived from published studies, although it was unclear whether the review was conducted systematically to identify relevant research and minimise biases. The authors did not report age-specific incidences in the text, perhaps due to the large number of estimates. The authors made several assumptions to estimate the outcomes, but the assumptions were not clearly justified. However, the estimates and assumptions were investigated by sensitivity analyses, using ranges that appear to have been appropriate. The authors also stated that conservative assumptions were made whenever possible. It was noted though that some estimates, such as brain damage data, which represented critical variables in the model, were derived from a small number of cases.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled. The decision analysis model used to derive the measure of health benefit was not described clearly. However, the benefits were not discounted whereas the costs were discounted at an annual rate of 6%. The application of a discount rate to the benefits was not tested in the sensitivity analysis. The reader should decide whether the time horizon (10 years) for evaluating the effects was sufficient. The use of the LYS means that comparisons with the benefits of other health care interventions can be made. The use of quality-adjusted life-years would have been more appropriate. The authors stated that the inclusion of quality of life aspects would have provided a better estimate of the burden of disease and the benefits of the vaccination programme.

**Validity of estimate of costs**
The authors limited the estimation of the costs to the NHS perspective, although a societal perspective would have
been more appropriate. Indeed, indirect costs were included in the sensitivity analysis. The costs and the quantities were not reported separately. The costs of treating infections were based on experts' opinions; this was not an appropriate method of cost estimation. There were few details of the cost items included in direct costs. Consequently, it is uncertain whether all the relevant costs were included in the analysis. Sensitivity analyses were conducted on the cost of brain damage only. These facts hinder the reproducibility of the results in other settings. Since the time horizon of the model was 10 years, discounting was undertaken and a sensitivity analysis on the discount rate was performed. The price year was reported, thus facilitating reflation exercises in other settings.

Other issues
The generalisability of the results was not addressed explicitly, although several sensitivity analyses were carried out and their results were reported extensively. The authors made only few comparisons of their findings with those from other studies. The authors reported a number of limitations to their study, which have been highlighted already, and do not appear to have reported their results selectively.

Implications of the study
The authors made no recommendations for changes in policy or practice.

Source of funding
None stated.

Bibliographic details

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Other publications of related interest


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Subject indexing assigned by NLM

MeSH
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