Projected cost-effectiveness of pneumococcal conjugate vaccination of healthy infants and young children


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 health intervention examined in the study was pneumococcal conjugate vaccination against meningitis, bacteremia, pneumonia, and otitis media (OM) in healthy infants.

Type of intervention
Other: vaccination.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised healthy US infants and young children.

Setting
The setting was community. The economic study was carried out in the USA.

Dates to which data relate
Data on effectiveness and resource use were derived from studies published between 1991 and 2000. The price year was 1997.

Source of effectiveness data
The effectiveness evidence was based on published studies and experts' opinions. Unpublished data were also used.

Modelling
A decision tree model was constructed to compare costs and benefits of the vaccination programme and the no-vaccination option. The two main branches of the tree (vaccination against no-vaccination) were identical, but disease incidence was reduced in the vaccination branch due to vaccine efficacy. The model was applied to the hypothetical birth cohort of 3.8 million infants in the USA. A semi-Markov approach was used in which incidence of disease was calculated on a monthly basis.

Outcomes assessed in the review
The outcome measures used as model inputs were the number of clinically diagnosed pneumonia cases per 100 population, the number of clinically diagnosed OM episodes per person, the number of tympanostomy tube placements per 100 population, the proportion of invasive disease cases that were meningitis, the proportion of clinically diagnosed OM episodes that were complex, the rates of deafness and disability after meningitis, and the following
probabilities: invasive disease (meningitis or bacteremia) due to pneumococcal vaccine serotypes, pneumonia due to pneumococcal vaccine serotypes, clinically diagnosed pneumonia, clinically diagnosed OM (simple, complex, or with tympanostomy tube placement), and OM due to vaccine serotypes (simple or complex).

Study designs and other criteria for inclusion in the review
The authors stated that one of the primary studies was a randomised controlled trial.

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
Eleven studies were used as the main source of effectiveness evidence.

Methods of combining primary studies
The results of the primary studies were combined using narrative methods.

Investigation of differences between primary studies
Not carried out.

Results of the review
The results of the review were as follows:

The number of clinically diagnosed pneumonia cases per 100 population was 2.8;
the number of clinically diagnosed OM episodes per person was 1.18;
the number of tympanostomy tube placement per 100 population was 16.8;
the proportion of invasive disease cases that were meningitis was 0.03;
the proportion of clinically diagnosed OM episodes that were complex was 0.07;
the rates of deafness and disability after meningitis were 0.13 (deafness) and 0.07 (disability); and

the probability values were 1 for invasive disease (meningitis or bacteremia) due to pneumococcal vaccine serotypes, 0.90 for pneumonia due to pneumococcal vaccine serotypes, 0.11 for clinically diagnosed pneumonia, 0.07 for clinically diagnosed simple OM, 0.19 for clinically diagnosed complex OM, 0.20 for clinically diagnosed OM with tympanostomy tube placement, and 0.64 for OM due to vaccine serotypes (simple or complex).

Methods used to derive estimates of effectiveness
A modified Delphi process was conducted to derive data not available from the literature. A panel of nine experts was
convened for one day and when agreement on estimates or assumptions was not easily reached, conservative assumptions favouring the no-intervention option were selected. The authors also utilised unpublished data from the Centers for Disease Control and Prevention’s Active Bacterial Core Surveillance/Emerging Infections Program Network.

**Estimates of effectiveness and key assumptions**
The authors assumed that routine vaccination would require four doses (at 2, 4, 6, and 12-15 months), while catch-up vaccination of children aged 2 to 4.9 years required only one dose.

The assumptions made in the analysis were as follows:

the number of invasive pneumococcal disease cases per 100,000 population was 185.6;

the proportion of simple OM episodes due to pneumococci was 0.19;

the proportion of complex OM/tympanostomy tube placement episodes due to pneumococci was 0.50;

the rate of death after meningitis was 0.05, and the rate of death after bacteremia was 0.007;

the proportion of invasive disease was 0.80, and the proportion of pneumonia was 0.80; and

the proportion of OM (simple, complex, or with tympanostomy tube placement) was 0.60.

**Measure of benefits used in the economic analysis**
The main benefit measure used in the economic analysis was the number of life-years lost with the two strategies. The number of episodes of OM (simple, complex, and with tympanoscopy tube replacement), pneumococcal pneumonia cases, pneumococcal bacteremia cases, pneumococcal meningitis cases, and deaths were also reported. A 3% discount rate was applied to future benefits.

**Direct costs**
A 3% discount rate was used as costs were incurred over a period longer than two years. Unit costs and quantities of resources were not reported separately. The health services included in the economic evaluation were costs related to pneumococcal disease (such as hospital, emergency department, outpatient costs, and medications) and vaccination programme costs. The cost/resource boundary adopted in the analysis of direct costs was that of the health care payer. The estimation of both quantities of resources and costs of disease were based on actual data derived from the Northern Carolina Kaiser Permanente Cost Management Information System. Other costs were estimated from published sources. The price year was 1997.

**Statistical analysis of costs**
Costs were treated deterministically in the base case.

**Indirect Costs**
A 3% discount rate was applied to costs due to the long time horizon of the analysis. Unit costs were not reported separately from quantities of resources. The indirect costs included in the analysis referred to lost time from work, estimated during a survey period from interviews with parents. The cost/resource boundary adopted in the analysis was that of society when indirect costs were included. Some assumptions were made to estimate quantities of resources. The price year was 1997.

**Currency**
US dollars ($).
Sensitivity analysis
Several one-way sensitivity analyses were conducted to assess the robustness of the decision model to variations in several assumptions, such as incidence of invasive disease, proportion of meningitis, rates of OM-related use, vaccine efficacy, cost of vaccine administration, costs of clinical visits and hospitalisation, discount rate, coverage rate, and costs of medical use and work loss due to vaccine adverse reactions. Best- and worst-case scenarios were also modelled.

Estimated benefits used in the economic analysis
The number of discounted life-years lost was 4,300 with no vaccination and 970 with vaccination (difference: 3,300).

The number of episodes of simple OM was 12,360,000 with no vaccination and 11,755,000 with vaccination (difference: 875,000).

The number of episodes of complex OM was 1,045,000 with no vaccination and 893,000 with vaccination (difference: 152,000).

The episodes of OM with tympanostomy tube placement were 149,000 with no vaccination and 119,000 with vaccination (difference: 30,000).

The episodes of pneumococcal pneumonia were 77,000 with no vaccination and 24,000 with vaccination (difference: 53,000).

The number of episodes of pneumococcal bacteremia was 15,000 with no vaccination and 3,300 with vaccination (difference: 11,700).

The episodes of pneumococcal meningitis were 790 with no vaccination and 180 with vaccination (difference: 610).

The number of deaths was 150 with no vaccination and 34 with vaccination (difference: 116).

Cost results
Total disease costs were $5,521 million with no vaccination and $4,764 million with vaccination (difference: $757 million in favour of vaccination).

Three vaccine costs were considered in the analysis: $20, $40, and $58, thus resulting in three vaccination programme costs: $295 million, $589 million, and $855 million.

Vaccine administration costs were $74 million.

Synthesis of costs and benefits
An incremental cost-effectiveness analysis was performed to combine costs and benefits of the two strategies. Cost-effectiveness ratios were calculated as costs invested in the vaccination programme minus costs saved due to disease episodes averted divided by health benefits, such as life-years saved or averted episodes of meningitis, bacteremia, pneumonia, or OM.

The vaccination programme for infants would be cost-saving at a vaccine cost of $46 or less from the societal perspective and at a vaccine cost of $18 or less from the healthcare payer's perspective.

At a vaccine cost of $25, the cost per life-year saved would be $25,000 from the healthcare payer's perspective.

At a vaccine cost of $58 (the most likely vaccine price), from the societal perspective the cost would be $80,000 per life-year saved, $160 per episode of OM averted, $3,200 per case of pneumonia averted, $15,000 per case of bacteremia averted, and $280,000 per meningitis episode averted (and $176,000 per life-year saved, $550 per episode...
of OM averted, $11,000 per case of pneumonia averted, $50,000 per case of bacteremia averted, and $970,000 per meningitis episode averted, from the perspective of the healthcare payer).

These cost-effectiveness ratios were particularly sensitive to the incidence of invasive disease.

The break-even cost of vaccine was $112 in the best-case scenario and $10 in the worst-case scenario.

In the secondary analysis, catch-up vaccination for all 2 to 4.9-year-old children would be cost-saving at a vaccine cost of $60 or less.

This analysis was sensitive to the relative risk of pneumococcal disease and vaccine cost.

**Authors' conclusions**
The authors concluded that routine pneumococcal conjugate vaccination of healthy US infants had the potential to be a cost-effective intervention in comparison with other preventive programmes. The analysis showed that vaccine cost represented a key factor.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparator was clear. No vaccination was selected as the aim of the study was to assess the active value of vaccination. You, as a user of this database, should decide whether it represents a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**
The analysis of effectiveness was based on data derived from published studies and experts' assumptions. As regards the published studies, a formal review of the literature was not undertaken and primary studies were combined using narrative methods, thus the impact of differences in factors such as sample size and vaccine coverage was not considered. Regarding the assumptions, a modified Delphi panel of nine experts was assembled to derive estimates of effectiveness, but the authors did not report the method by which the physicians were selected. In both cases, the estimates were investigated by extensive sensitivity analyses and the ranges used appear to have been appropriate.

**Validity of estimate of measure of benefit**
The main benefit measure used in the economic analysis was life-years saved, which represent a widely used benefit measure in vaccine programmes, thus facilitating comparison with the benefits of other programmes. The decision model used to derive life-years was reported in detail and the appropriate discounting was performed.

**Validity of estimate of costs**
The analysis of costs was conducted from the perspective of both society and the healthcare payer. A cost-breakdown was provided, but unit costs and quantities of resources were not reported separately. Costs and quantities of resources were treated deterministically in the base case, but several sensitivity analyses were conducted. The source of cost data was reported.

**Other issues**
The authors compared their findings with those from other vaccination programmes. The issue of the generalisability of the results to other settings was not addressed, but extensive sensitivity analyses were conducted. The study referred to the general population of infants and children and this was reflected in the conclusions of the study. The authors discussed some limitations of their analysis.

**Implications of the study**
The authors highlighted the importance of considering reductions in morbidity episodes that were not captured in the present analysis, mainly due to reduction in mortality. The authors also noted that their analysis might have underestimated other indirect benefits of the vaccinations, such as reduced transmission of pneumococcal disease in the unvaccinated population due to the higher number of vaccinated children. These indirect benefits may be even greater in developing countries where pneumococcal disease has a higher incidence and, as a result, a greater impact. Finally, the authors stated that "postimplementation research should evaluate the effects of vaccination on disease incidence, in unvaccinated persons, use of antimicrobial drugs, and carriage and disease due to nonvaccine serotypes".

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