Health and economic impact of PHiD-CV in Canada and the UK: a Markov modelling exercise
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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.

CRD summary
The study assessed the cost-effectiveness of 10-valent pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine (PHiD-CV) compared with 13-valent pneumococcal conjugate vaccine (PCV-13). The authors concluded that PHiD-CV provided greater potential to protect against NTHi infections than PCV-13. The quality of the study methodology was adequate. It was unclear how effectiveness data were identified and combined but the methods and results were reported adequately. The authors’ conclusions appear appropriate.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective of the study was to assess the cost-effectiveness of 10-valent pneumococcal non-typeable *Haemophilus influenza* protein D conjugate vaccine (PHiD-CV) compared with 13-valent pneumococcal conjugate vaccine (PCV-13) in newborns and young children.

Interventions
The study compared two vaccines. Pneumococcal non-typeable *Haemophilus influenzae* protein D conjugate vaccine (PHiD-CV), a 10-valent pneumococcal conjugate vaccine that included serotypes 1, 5, 7F, 4, 6B, 9V, 14, 18C, 19F and 23F, was compared with a recently licensed 13-valent pneumococcal conjugate vaccine, which contained serotypes 3, 6A and 19A in addition to the 10 serotypes in PHiD-CV.

Location/setting
UK and Canada/Primary care.

Methods
Analytical approach:
A Markov cohort model combined published evidence to simulate the epidemiological burden of pneumococcal and non-typeable *H. influenzae* (NTHi)-related diseases within hypothetical birth cohorts of newborns. The time horizon was the lifetime of the patient. The authors did not explicitly report the perspective adopted in the economic analysis.

Effectiveness data:
Effectiveness data were derived from sources such as national statistics, cohort studies, clinical trials, other published studies and the authors’ own assumptions. The main measures of effectiveness were the efficacy of each vaccine type against invasive disease, NTHi invasive disease, *Streptococcus pneumoniae* acute otitis media, acute otitis media caused by non-vaccine serotypes and acute otitis media caused by *H. influenzae* including NTHi. These measures of effectiveness were derived from previously published studies supplemented in some cases by the authors’ assumptions (for example, it was assumed that the efficacy of PCV-13 vaccination against acute otitis media was the same as that of PCV-7 vaccination).

Monetary benefit and utility valuations:
Utility estimates were derived from published studies. Disutilities for meningitis bacteraemia and pneumonia were taken from a published study that used computer-based utility assessments interviews to calculate utilities under several
pneumococcal disease states; these utilities were estimated from parents’ responses using standard gamble methods. Disutilities for acute otitis media were taken from a published study that estimated disutility from a survey of paediatricians.

Measure of benefit:
The measures of benefit were life years and Quality Adjusted Life Years (QALYs) discounted using an annual rate of 3.5% (UK) and 3% (Canada).

Cost data:
Direct costs were: vaccination and vaccine administration, disease-related treatment and treatment of long-term sequelae incurred over survivors’ lifetime. The estimates of healthcare resource utilisation were derived from the literature and validated expert opinion. Cost information was derived from published studies, health-related group unit costs for the UK, and micro-costing approaches. All costs were updated to 2007 prices using price indices from the respective countries. Future costs were discounted using an annual rate of 3.5% (UK) and 3% (Canada). Costs were reported in UK pounds sterling (£) and Canadian dollars ($).

Analysis of uncertainty:
A series of one-way sensitivity analyses were performed for each of the base case parameters (ranges deemed from published literature as realistic). This analysis was presented using a cost-effectiveness plane. A probabilistic sensitivity analysis included probability distributions around each model parameter and 1,000 Monte Carlo simulations.

Results
In Canada, QALYs gained in a cohort of 348,000 newborns were 8,560,707 for PHiD-CV vaccination and 8,560,219 for PCV-13 vaccination. In the UK, QALYs gained in a cohort of 772,500 newborns were 18,414,599 for PHiD-CV vaccination and 18,414,225 for PCV-13 vaccination.

In Canada, life-years gained were 9,312,026 for PHiD-CV vaccination and 9,312,014 for PCV-13 vaccination. In the UK, QALYs gained were 18,414,599 for PHiD-CV vaccination and 18,414,225 for PCV-13 vaccination.

In Canada, costs incurred were $320,273,189 for PHiD-CV vaccination and $329,276,094 for PCV-13 vaccination. In the UK, costs incurred were £180,376,006 for PHiD-CV vaccination and £185,275,445 for PCV-13 vaccination.

Costs and benefits were not combined as PHiD-CV vaccination was found to be dominant (more effective and less costly) over PCV-13 vaccination in both Canada and the UK.

The one-way sensitivity analysis found that the results were robust to the various changes in all the input parameters, apart from the acute otitis media-related outcome parameters. Results of the probabilistic sensitivity analysis showed that the probability that PHiD-CV was dominant over PCV-13 was 95% (UK) and 90% (Canada).

Authors’ conclusions
The authors concluded that PHiD-CV potential to protect against NTHi infections could provide a greater impact on disease burden than PCV-13.

CRD commentary
Interventions:
The interventions under study were reported adequately and appeared to be appropriate comparators.

Effectiveness/benefits:
Effectiveness data were derived several different sources. The methods used to identify the published evidence were not reported and it was unclear whether a systematic review was undertaken and all the best available evidence was included in the study. The authors noted a lack of head-to-head data as a limitation of their study. It was unclear how the effectiveness data were combined (given the lack of head-to-head data) and whether the appropriate statistical methods were undertaken.

The benefit measures appeared appropriate, particularly the QALY as it incorporated both morbidity and mortality. The
studies from which the utility estimates were derived were described briefly and readers should refer to the published studies to fully assess their quality. It appeared that a significant proportion of the utility estimates were derived from individuals (caregivers and paediatricians) and not the children being vaccinated; the authors provided a justification for their inclusion and suitability.

Costs:
The perspective adopted in the economic analysis was not explicitly reported by the authors but it appeared that a healthcare system perspective was adopted. All major relevant costs for this perspective appeared to be included in the analysis. The sources from which unit costs and resource use were derived were adequately reported, but the reader would need to refer to the relevant appendix for their full description. The time horizon, currency details, price year and discount rate were all reported and appear appropriate.

Analysis and results:
The analytical approach appeared appropriate. Adequate details of the model structure were reported and included a graphical depiction. The model uncertainty was fully represented with a series of one-way and probabilistic sensitivity analyses. The results were reported clearly. The authors reported the limited clinical trial data for the two vaccinations under study and a lack of head-to-head studies as the main limitations to their study.

Concluding remarks:
The study methodology was of adequate quality. It was unclear how published evidence on effectiveness was identified and combined but methods and results were reported adequately. The authors’ conclusions appear appropriate.

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