New vaccines against otitis media: projected benefits and cost-effectiveness

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
This study assessed three vaccines, compared with no vaccination, for preventing acute otitis media in infants and young children. The authors found that these vaccines could prevent millions of acute otitis media episodes and pneumococcal non-typeable Haemophilus influenzae vaccine could be cost-effective, compared with heptavalent pneumococcal conjugate vaccine, if reasonably priced. There was considerable uncertainty in the effectiveness and cost estimates, but the authors appear to have adequately accounted for this in the sensitivity analyses and in their conclusions.

Type of economic evaluation
Cost-utility analysis

Study objective
The objective was to assess the cost-effectiveness of three vaccines, compared with no vaccination, in the prevention of acute otitis media in infants and young children. The population was assumed to have similar demographic characteristics to the general US population.

Interventions
A heptavalent pneumococcal conjugate vaccine (PCV7), a candidate pneumococcal non-typeable Haemophilus influenzae (NTH) vaccine, and a hypothetical pneumococcal NTH Moraxella vaccine were compared with no vaccination.

Location/setting
USA/primary care.

Methods
Analytical approach:
A micro-simulation model was used to synthesise the data and model the natural history of otitis media. The model had three health states, well, acute otitis media, and otitis media with effusion, along with a temporary state of tympanostomy-tube insertion. It had monthly cycles and a US birth cohort of 4.2 million children was simulated from birth to four years old. The authors stated that the perspective was societal.

Effectiveness data:
The average monthly probability of acute otitis media in children, along with the probability of otitis media with effusion, at different ages, was estimated using data from Northern California Kaiser Permanente medical charts. The data for the effectiveness of the tympanostomy tube and the monthly effectiveness of the three vaccines were from published studies. The effectiveness of the PCV7 vaccine was from one study and the monthly probabilities of acute otitis media were derived by calibrating the model until it produced the effectiveness results from this study. This procedure was used to derive the effectiveness of the pneumococcal NTH vaccine for single episodes of otitis media, with data from another study. The relative effectiveness of the hypothetical vaccine against single or multiple episodes, and that for the pneumococcal NTH vaccine, were assumed to be the same as that for PCV7. The main clinical estimates for the study were the probabilities of a child having acute otitis media in the current month, with the different vaccinations.

Monetary benefit and utility valuations:
The utility estimates were based on a published study, which used the time trade-off method. They were based on the perceived utility or disutility with pneumococcal disease, as well as the child's and parents’ pain and suffering and the family's inconvenience.

Measure of benefit:
The measure of benefit was quality-adjusted life-years (QALYs) and these were discounted at a rate of 3% per annum.

Cost data:
The cost data were estimated by analysing the health care records of US infants with acute otitis media, and using data from other published and unpublished sources. The cost categories were otitis media costs and vaccination costs. The otitis media costs included direct medical costs and parental time. The medical costs were calculated by applying estimated unit costs to the resource use reported in the computerised medical charts of Harvard Vanguard Medical Associates (HVMA), a large provider group in the greater Boston area. The cost of a tympanostomy-tube insertion was also included and was estimated using the Medicare Fee Schedule. Parental time was assumed to be two hours for each office visit and was valued using the average wage from the Bureau of Labor Statistics. The vaccination costs were based on expert opinion. All costs were in 2006 US dollars ($) and they were discounted at a rate of 3% per annum.

Analysis of uncertainty:
One-way sensitivity analyses were performed on all of the key model parameters and the ranges used were presented in a table. An additional analysis was performed to evaluate the impact on the results of altering the assumptions on the waning of vaccine effectiveness. Two-way sensitivity analyses and threshold analyses were also performed for several key variables, which included vaccine effectiveness, vaccine dose costs, and QALY assumptions. The results of the two-way sensitivity analyses were presented in a diagram. Scenarios were analysed with otitis media probability data from the Pittsburgh Child Development/Otitis Media Study and from HMVA medical charts.

Results
Without vaccination there were 13.7 million episodes of acute otitis media in the study population. The PCV7 vaccine prevented 878,000 episodes, the pneumococcal NTH vaccine prevented 3.7 million episodes, and the hypothetical pneumococcal NTH Moraxella vaccine prevented 4.2 million episodes. The total savings from otitis media episodes averted were $286 million with PCV7, $1.2 billion with pneumococcal NTH vaccine, and $1.3 billion with the hypothetical vaccine.

Compared with the next most effective strategy, the incremental cost-effectiveness for the hypothetical vaccine was $48,000 per QALY and for the pneumococcal NTH vaccine it was $13,000 per QALY. Both these vaccines dominated the PCV7 vaccine, as they had lower costs and greater benefits.

The one-way sensitivity analyses showed that the results of comparing pneumococcal NTH and PCV7 vaccines were most sensitive to the effectiveness and dose cost of the pneumococcal NTH vaccine. The two-way sensitivity analysis, varying the vaccine effectiveness and the dose costs, found that the pneumococcal NTH vaccine was cost saving compared with the PCV7 vaccine over a range of assumptions. For the cost-effectiveness ratio to be over $50,000 per QALY, at a vaccine price of $100 per dose, the monthly effectiveness would have to be close to 10%, down from 28% in the base case. Some additional waning patterns were also examined and were found to have little effect on the results.

Authors’ conclusions
The authors found that candidate vaccines could prevent millions of acute otitis media episodes in the USA and the pneumococcal NTH vaccine could be cost-effective, compared with the PCV7 vaccine, if it was priced comparably with other new vaccines.

CRD commentary
Interventions:
The interventions were adequately described and they appear to have been appropriate comparators.

Effectiveness/benefits:
The studies that were used for the effectiveness data were not described, which means that it is unclear if they were of
high quality. There was no evidence that a systematic review was conducted and it is uncertain whether all the best available evidence was used. There were important assumptions on the effectiveness of the two pneumococcal NTH vaccines, which introduced great uncertainty, but this was appropriately assessed, using wide ranges of values in the sensitivity analyses. The method used to derive the utility estimates was stated and appears to have been appropriate. Discounting was appropriately applied.

**Costs:**
The cost categories were consistent with the stated perspective. The methods used to estimate the costs appear to have been valid. No prices were available for the vaccines and these were estimated by clinical experts. The uncertainty in these estimates was assessed, using a wide range of dose costs, in the sensitivity analysis. The costs were appropriately discounted and adjusted for time differences.

**Analysis and results:**
The model was described well, but the actual costs and benefits of the base case were not explicitly reported. The synthesis of information appears to have been valid and there was a comprehensive analysis of uncertainty. The authors stated that a limitation of their study was that the assumptions on the effectiveness of the pneumococcal NTH vaccine were based on a recent trial, in which the definition of acute otitis media differed slightly from that used in this study. They also stated that no active surveillance for otitis media was conducted, in the trial, leading to a lack of precision in its frequency of diagnosis, and there was a limited follow-up within the trial.

**Concluding remarks:**
There was considerable uncertainty in the effectiveness and cost estimates, but the authors appear to have adequately accounted for this in the sensitivity analyses and in their conclusions.

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