Estimating the potential health gain and cost consequences of introducing a pre-school DTPa pertussis booster into the UK child vaccination schedule

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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 introduction of a pre-school booster vaccination, administered at age 4 to 5 years, for preventing Bordetella pertussis (whooping cough). This was in addition to the existing UK primary vaccination schedule.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised 4 to 5 year-old children.

Setting
The setting was not stated, although it appears to have been primary care. The economic study was carried out in the UK.

Dates to which data relate
The effectiveness data were mainly obtained from studies published between 1985 and 2001. Resource use and cost data seem to have been mainly related to the time between 1994 and 2000 (although some data were collected from private communications, for which the dates were not reported). The price year was 2000.

Source of effectiveness data
The effectiveness data were derived from published studies, augmented by the authors' assumptions.

Modelling
A Markov model was used to estimate the effectiveness and costs associated with the vaccination strategies under study. The cycle length was one month and the duration of the model was 5 years. Moreover, linear programming techniques were used to model household contacts between a susceptible person and an infected person, followed by pertussis infection. In addition, the model incorporated dynamic infection rates, which allowed herd-immunity effects to be taken into consideration.

Outcomes assessed in the review
The outcomes assessed in the review were:
the incidence of pertussis, both the official and the estimated figures, and the level of under-reporting by age groups;
the transmission rate because of household contact with an infected person (for under 4-year olds and 4 years or older);
the percentage of people that had had pertussis;
the vaccine efficacy under the current policy and with the introduction of the pre-school booster vaccination;
the mortality rates due to pertussis; and
the adverse reactions associated with the current policy and with the introduction of the pre-school booster vaccination.
These outcomes were included as parameters in the Markov model.

Study designs and other criteria for inclusion in the review
Not reported. Some epidemiological and statistical studies were considered in the revision.

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
At least 13 studies were included in the review.

Methods of combining primary studies
Different estimates were obtained from different studies, although several values from different studies were given for some of the outcomes. The main sources of effectiveness were not combined and, consequently, two separate scenarios were modelled.

Investigation of differences between primary studies
For some outcomes the authors reported alternative values obtained from two different studies. It was unclear whether the differences in studies, other than the two main sources, were examined.

Results of the review
Scenario one used efficacy rates calculated from Ramsey et al. (see Other Publications of Related Interest). The values of the main parameters included in the model were as follows:

the vaccine efficacy for children up to 4 years of age was 94% under the current policy, and 94% with the pre-school booster vaccination;
the vaccine efficacy for children between 5 and 14 years of age was 83% under the current policy, and 88% with the pre-school booster vaccination;
the vaccine efficacy for people between 15 and 29 years of age was 64% under the current policy, and 69% with the pre-school booster;  
the vaccine efficacy for people between 30 and 59 years of age was 30% under the current policy, and 35% with the pre-school booster; and 
the vaccine efficacy for those people aged 60 or older was 2% under current policy and 5% with the pre-school booster.

Scenario two used efficacy rates calculated from Jenkinson (see Other Publications of Related Interest). The values of the main parameters included in the model were as follows: 
the vaccine efficacy for children up to 4 years of age was 88% under the current policy, and 88% with the pre-school booster vaccination;  
the vaccine efficacy for children between 5 and 14 years of age was 24% under the current policy, and 49% with the pre-school booster vaccination; for people older than 14 years the vaccine efficacy was 0, independent of the vaccine policy considered. 
The mortality rate due to pertussis infection among children less than 5 years of age was 1 in 1,700 cases for both scenarios. 
The adverse reactions associated with the vaccine were similar between the current policy and the introduction of the pre-school booster vaccination for both scenarios.

Methods used to derive estimates of effectiveness  
The authors made assumptions to derive some estimates of effectiveness.

Estimates of effectiveness and key assumptions  
The authors formulated the following assumptions: 
the probability of infection varied in proportion to the number of individuals infected within the community;  
people experiencing a naturally acquired pertussis infection would have a protection factor of 99% against further potential transmission;  
the overall national coverage rate for primary vaccination of pertussis was 94%;  
the coverage rate for the pre-school booster vaccination was around 84 - 85%;  
the efficacy of the pre-school booster vaccination was the same as that achieved with the primary schedule;  
there was no under-reporting of hospitalisations associated with pertussis infection;  
adults were not hospitalised;  
only children under 5 years of age could die from pertussis;  
the population would remain constant during the 5-year period considered in the model; and  
there would be 233 household contacts per month between a susceptible person and an infected person, followed by pertussis infection.

Measure of benefits used in the economic analysis
The summary measure of benefit used in the economic analysis was the number of deaths occurring during a 5-year period. The authors also reported the number of pertussis cases and the number of hospitalisations during this period. These measures of benefits were obtained from the model, considering a 5-year period. In order to estimate the quality-adjusted life-years (QALYs), the authors assumed that there was a loss of utility equal to 0.2 due to hospitalisations. The utility loss associated with the pertussis cases was 0.02.

**Direct costs**

The resource quantities were reported separately from the unit costs. The direct costs considered in the study appear to have been those of the health service. These were general practitioner consultations, hospitalisations (e.g. paediatric ITU care and general ward stay) and specialist care. The authors stated that the costs associated with vaccine administration and the treatment of vaccine-related adverse effects were not included, as they were similar between the alternatives compared at analysis. The costs were derived from published studies, some authors' assumptions and clinician estimations. Therefore, the costs were based both on actual data and on assumptions. The price year was 2000. Since the costs were estimated over a 5-year period, discounting was performed at a rate of 6%. The study reported the total costs.

**Statistical analysis of costs**

No statistical analyses of the costs were reported.

**Indirect Costs**

No indirect costs were reported.

**Currency**

UK pounds sterling (€).

**Sensitivity analysis**

One-way sensitivity analyses were conducted. The parameters varied were:

- the costs of under-reported cases;
- the discount rate (i.e. 0%);
- the duration of a pertussis infection (from 7 to 21 days);
- the percentage of patients that had had pertussis (which was halved, or considered to be 0%);
- the percentage of natural acquired protected individuals (from 50% to 20 and 5%); and
- the booster uptake rate (i.e. 60%).

The loss of utility was also varied, considering it to be 0.1 for hospitalisations and 0.01 for pertussis cases. The area of uncertainty investigated was, therefore, variability in the data.

**Estimated benefits used in the economic analysis**

Under scenario one, there were 14,332 pertussis cases with the current schedule versus 10,219 with the pre-school booster. The pre-school booster resulted in 4,113 fewer cases.

There were 4.2 deaths with the current schedule versus 3.1 with the pre-school booster. The pre-school booster resulted in 1.1 fewer deaths.
There were 4,953 hospitalisations with the current schedule versus 3,583 with the pre-school booster. The pre-school booster resulted in 1,371 fewer hospitalisations.

Under scenario two, there were 91,177 pertussis cases with the current schedule versus 62,765 with the pre-school booster. The pre-school booster resulted in 28,412 fewer cases.

There were 4.1 deaths with the current schedule versus 3.0 with the pre-school booster. The pre-school booster resulted in 1.1 fewer deaths.

There were 4,798 hospitalisations with the current schedule versus 3,321 with the pre-school booster. The pre-school booster resulted in 1,478 fewer hospitalisations.

The numbers of QALYs obtained under each of the alternatives were not reported, but only the cost per QALY gained with the booster vaccination in comparison with current policy.

Cost results
For scenario one, the total costs were 10.71 million for the current policy versus 23.28 million with the introduction of the pre-school booster. The incremental cost of the booster was 12.57 million.

For scenario two, the total costs were 13.73 million for the current policy and 25.09 million with the introduction of the pre-school booster. The incremental cost of the booster was 11.36 million.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio (ICER) was reported for the base-case analysis as the cost per death avoided with the pre-school booster when compared to the current schedule. This ICER was 3,055 per death avoided for scenario one and 400 per case avoided for scenario two.

The cost per QALY gained with the pre-school booster, compared with the current schedule, was 35,000 per death avoided for scenario one and 14,500 per case avoided for scenario two. When the utilities were varied, the cost per QALY gained with the pre-school booster (compared to the current schedule) was 70,000 for scenario one and 29,000 for scenario two. The authors reported that the parameters that most affected the robustness of the results were the percentage of natural acquired protected individuals and the level of prior protection within the community.

Authors’ conclusions
A pre-school booster for pertussis is likely to significantly reduce the number of infections and also the associated costs during a 5-year period.

CRD COMMENTARY - Selection of comparators
The comparator chosen was the current UK vaccination policy, as this was the current practice in the authors' setting. You should decide whether the vaccination schedule in your setting is similar to the current UK vaccination policy (details available on http://www.netdoctor.co.uk/health_advice/facts/childhoodvaccinations.htm)

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken. Data from different studies appear to have been used selectively to obtain the effectiveness parameters included in the model. Two alternative scenarios were developed to consider differences in the vaccine efficacy that were found in what were deemed to be the two main studies. As stated by the authors, the consideration of a proportional variation of the probability of infection according to the number of infected individuals within the community helped to achieve a better estimate of the impact and effectiveness of the vaccine strategy. Some of the authors' assumptions were justified with reference to the medical literature, but not all. Most of the parameters were investigated in a sensitivity analysis. The ranges used appear to have been appropriate.
Validity of estimate of measure of benefit
The estimation of benefits was modelled. A Markov model was used to derive the number of deaths avoided with the pre-school booster, which seems to have been appropriate. Although the QALYs were also estimated, they were based on assumed utilities, which were not justified with reference to the medical literature. This introduced uncertainty into the QALY results. The authors were aware of this and recommended that further research be undertaken.

Validity of estimate of costs
All the costs relevant to the perspective adopted (i.e. that of the health service) may have been included. The exceptions were the costs associated with vaccine administration and adverse effects, which the authors reported to be similar for both vaccination schedules. The resource quantities were reported separately from the unit costs, although sensitivity analyses of the costs were limited. The price year was reported. Discounting was performed since the costs were calculated for a 5-year period, although the discount rate used (6%) did not correspond to the discount rate commonly used in the UK (3%). The sensitivity analyses also did not consider this commonly used discount rate. Clinician opinions were used to derive estimates of the costs, although the authors did not report how these estimates of costs were obtained. Appropriate sensitivity analyses of the costs do not appear to have been performed, which may limit the interpretation of the study findings.

Other issues
The authors did not make appropriate comparisons of the findings with those from other studies. The issue of the generalisability of the results to other settings was not addressed. The authors' conclusions reflected the scope of the analysis.

Implications of the study
The authors recommended further research on the potential re-boosting of immunity with sub-clinical infections, the impact of pertussis on quality of life, and the length and strength of protection following naturally acquired pertussis.

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Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Child, Preschool; Cost-Benefit Analysis; Diphtheria-Tetanus-acellular Pertussis Vaccines /administration & dosage