The potential cost-effectiveness of acellular pertussis booster vaccination in England and Wales

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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 the acellular pertussis vaccine in children and adults.

Type of intervention
Primary prevention (vaccination).

Economic study type
Cost-effectiveness analysis.

Study population
The study referred to the general population. The analysis focused on a hypothetical cohort of children aged 4 or 15 years, because these represented the ages at which diphtheria and tetanus boosters doses were routinely given in the UK.

Setting
The setting was not explicitly stated, but it appears to have been primary care. The economic study was conducted in England and Wales.

Dates to which data relate
The effectiveness evidence came from studies published in 1999 and 2000. Some epidemiological data covered the period 1995 to 1998. No explicit dates for resource use data were reported, but some data were gathered from 1989 to 1998. Prices were reported in 1999/2000 values (financial year).

Source of effectiveness data
The effectiveness evidence came from completed studies, supplemented by authors' assumptions.

Modelling
A model was used to calculate the expected impact of pertussis vaccination in the cohort of vaccinees and in those younger than them over their lifetime. A transmission dynamic model was used, which tracks the numbers of diseased, immune, carriers, and so on, over time, given various assumptions on, for example, prevalence, transmission rates and vaccine efficacy. The model took into account herd immunity.

Outcomes assessed in the review
The outcomes estimated from the literature were:

the consultation rate,
the number of consultations per episode,
the admission rate,
the length of stay (LOS) per admission,
the percentage of time in intensive care,
the death rate,
booster coverage,
booster vaccine efficacy,
the duration of protection with booster,
the years of delay to herd immunity, and
the rate of under-reporting.

**Study designs and other criteria for inclusion in the review**
A systematic review of the literature was not performed and the designs of the primary studies were not described. However, some data came from the Royal College of General Practitioners Weekly Returns Service, and the Hospital Episode Statistics database.

**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**
The effectiveness evidence used in the model came from approximately 4 studies.

**Methods of combining primary studies**
The estimates were derived from the primary studies using narrative methods.

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

**Results of the review**
In the aged-based sub-groups of patients, the consultation rates per 100,000 population per year were:

38.58 (age less than 3 months);
107.88 (0.25 - 4 years);
49.27 (5 - 14 years);
5.33 (14 - 44 years); and
2.21 (older than 45 years).

The numbers of consultations per episode were 1.70 in all sub-groups.

The admission rates per 100,000 population per year were:
89.58 (age less than 3 months);
15.17 (0.25 - 4 years);
2.11 (5 - 14 years);
0.02 (14 - 44 years); and
0.02 (older than 45 years).

The LOS per admission was:
7.27 (age less than 3 months);
2.33 (0.25 - 4 years);
2.36 (5 - 14 years);
8.33 (14 - 44 years); and
9.31 (older than 45 years).

The percentage time in intensive care was 1.1% in the less than 3 months sub-group, and 0% in the remaining sub-groups.

The death rate per 100,000 population per year was 1.29 in the less than 3 months sub-group, 0.04 in the 0.25 - 4 years sub-group, and 0 in the remaining sub-groups.

The booster coverage was 84% and the booster vaccine efficacy was 95%.

The booster provided 5 years’ protection.

The delay to herd immunity was 5 years.

The rate of under-reporting was 2.5.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions that were used in the decision model.

**Estimates of effectiveness and key assumptions**
It was estimated that disease incidence remained unchanged at the initial level in absence of changes to the immunisation programme. It was also assumed that vaccine efficacy declined with time since administration of the booster dose at a constant rate. Also, early deaths from pertussis occurred during the first 3 months of life.
Measure of benefits used in the economic analysis
The summary benefit measure was life-years gained (LYG) with the vaccination strategy in comparison with no vaccination. The LYG were discounted at an annual rate of 3%. However, the numbers of hospitalisations and consultations avoided were also assumed to reflect the morbidity impact of the disease. Thus, they were also considered as benefit measures.

Direct costs
A 3% annual rate was used to discount the future costs due to the long time horizon of the analysis. The unit costs were reported separately from the quantities of resources used. The health services included in the economic evaluation were vaccine booster, general practitioner (GP) consultations, inpatient day, intensive care day, and disease treatment. The delivery costs were not considered because the pertussis vaccine was administered in a combined preparation with diphtheria and tetanus. The cost/resource boundary adopted in the analysis was that of the health care provider. The costs were estimated using actual data. These came from the Personal Social Services Research Unit (GP costs and inpatient day), the British Medical Formulary (drugs used to treat pertussis) and the Department of Health (on-line data; intensive care day). The cost of the vaccine was based on authors' assumptions, as were most of the data concerning resource use. The total costs were estimated by modelling. All the costs were inflated to 1999/2000 values using the Hospital and Community Health Services Pay and Price Index, and the average increase in wages where necessary.

Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were included in the economic analysis because a societal perspective was adopted. Discounting was relevant and appears to have been conducted. Data on lost work-days, because of children with pertussis, were obtained from studies referring to US settings because UK data were not available. The average daily wage for women aged 25 to 34 years was used for pertussis cases in children, while the average adult wage was selected for other cases. The price year was not reported, but it was likely to have been the same as that used for the analysis of the direct costs (1999/2000).

Currency
UK pounds sterling (£). The exchange rate from into US dollars ($) was reported to have been approximately 1 = $1.5.

Sensitivity analysis
Sensitivity analyses were conducted to investigate variability in the values of the model inputs. One-way sensitivity analyses were conducted on all estimates (both probabilities and costs). In addition, a probabilistic multivariate sensitivity analysis was also carried out. It was assumed that, with the exception of hospitalisation and GP visits and the incidence between age groups, the parameter values were independent of each other. The model was run 1,000 times to generate a distribution for the outcome variables. The relationship between different input parameter values and the results of the model was investigated by a regression analysis. The ranges used in the sensitivity analyses came from the literature. Variations of between +/- 25% were used for most cost categories.

Estimated benefits used in the economic analysis
The model showed that there were 35,000 annual GP consultations and 1,165 hospitalisations, with a loss of 688 undiscounted life-years in each birth cohort. The actual number of LYG with the vaccination strategy was not reported.

Cost results
Under the base-case scenario, the annual cost due to burden of pertussis was £2.6 million to the health service and the annual indirect costs were £7.14 million. The total costs associated with the strategy of pertussis vaccination were not
reported.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio (ICER, cost per LYG) was calculated to combine the costs and benefits of the vaccination strategy.

In the base-case, from the perspective of the health care provider, the ICER ranged from 49,511 (20% level of indirect protection) to 8,463 (80% level of indirect protection) for the booster at 4 years, and from 55,884 to 7,661 for the booster at 15 years. From the perspective of society, the ICER ranged from 36,941 to 2,489 for the booster at 4 years, and from 46,869 to -633 for the booster at 15 years.

Clearly, the higher the degree of indirect protection, the lower the ICER, and the more cost-effective the vaccination programme was.

The results were extremely sensitive to variations in the degree of herd-immunity protection, mortality rate, degree of under-reporting, vaccine cost, and the discount rate for both the costs and benefits. The impact of such variables on the estimated ICER was also confirmed in the regression analysis.

The multivariate sensitivity analyses showed that, from the perspective of the health care provider, approximately 50% of the simulations resulted in an ICER of less than 10,000 for the vaccination programme at 4 years. About 35% of the simulations resulted in an ICER of less than 10,000 for the vaccination programme at 15 years.

Authors’ conclusions
The results of the analysis did not permit any strong conclusion to be drawn about the cost-effectiveness of the vaccination programme. However, under specific scenarios, the incremental cost-effectiveness ratio (ICER) was well below the threshold of 20,000 per life-year saved, which is widely used in the UK to evaluate the cost-effectiveness of health interventions. The pertussis vaccination programme had the potential to be cost-effective in the UK, particularly at 4 years.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear, although the authors did not provide an explicit justification for its selection. No vaccination was selected as the basic comparator because it was likely to represent the standard care across most developed countries. You should decide whether it represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used data that were selectively identified from the literature. A formal review of the literature was not conducted. Details of the primary studies were not reported, although the most common source of data was represented by official statistics on UK patterns of disease and treatment. Some estimates used in the model were derived from authors' assumptions. The authors dealt with the issue of uncertainty in the input parameters by conducting sensitivity analyses and considering several scenarios.

Validity of estimate of measure of benefit
The LYG were used as the summary benefit measure in the economic analysis. These were calculated using the decision model. Appropriate discounting was conducted. The authors discussed the choice of the dynamic model. The use of LYG permits the benefits of the intervention to be compared with those associated with other vaccination programmes. However, the authors also considered other benefit measures (hospitalisations and consultations avoided) to reflect the morbidity impact of the disease, which was not taken into account when LYG alone were considered. Issues related to quality of life were not discussed.
Validity of estimate of costs
The analysis of the costs was conducted from two distinct perspectives. It appears that all the relevant categories of costs have been included in the economic evaluation. The unit costs and the quantities of resources used were analysed separately and the prices used to express the costs were reported. These factors facilitate the replication of the study in other contexts. The source of the cost data was reported for each cost component. Resource use was estimated from published data and authors’ assumptions. The authors noted that the days of absenteeism were estimated using information coming from countries other than the UK. The cost estimates were treated deterministically in the base-case, but sensitivity analyses were conducted on all items. The authors stated that results from the societal perspective might have been less reliable than those estimated from the health care provider perspective, because there was more uncertainty surrounding the absenteeism data.

Other issues
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. However, the external validity of the study was enhanced because extensive sensitivity analyses were conducted and results were presented in detail for each input parameter. The authors noted some limitations of their analysis. First, the accuracy of the results depended on the distribution of the input parameters. Second, the dynamic model was used only indirectly because the main analysis focused on very different scenarios of disease development.

Implications of the study
The authors noted that future research, to allow more definitive conclusions about the cost-effectiveness of the pertussis vaccination programme in the UK, should be conducted. The present study indicates the input parameters that have the greatest impact on the ICER.

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