Economic evaluation of the 7-vaccine routine childhood immunization schedule in the United States, 2001


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 study investigated the routine US childhood vaccination schedule, which includes immunisation with:

diphtheria and tetanus toxoids and acellular pertussis (DTaP);
tetanus and diphtheria toxoids (Td);
Haemophilus influenzae type b (Hib) conjugate;
inactivated poliovirus (IPV);
measles, mumps and rubella (MMR);
hepatitis B (HB); and
varicella vaccines.

The authors excluded the potentially relevant alternatives of including pneumococcal conjugate and influenza vaccines, as they are not yet fully implemented in the study setting.

Type of intervention
Primary prevention.

Economic study type
Cost-benefit analysis.

Study population
The hypothetical study population was formed by the 2001 US birth cohort.

Setting
The setting for the vaccinations was primary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness data related to 1929 to 2004. The resource use and cost data related to 1985 to 2004. The price year was 2001.

Source of effectiveness data
The effectiveness data were derived from a review of published studies, expert opinion and national databases.
Modelling
A decision tree was used to calculate the lifetime costs and benefits associated with no vaccination or the full vaccination schedule. For no vaccination, the decision tree estimated the number of infections. For vaccination, the decision tree recorded the number of adverse events with vaccination, the number who remained susceptible and, among those still susceptible, the number infected. A lifetime horizon was used.

Outcomes assessed in the review
The review assessed:

- the annual incidence rates,
- the probability of adverse events from vaccination,
- the proportion of patients immunised following vaccination, and
- the proportion of patients who remained susceptible who became infected.

The review also assessed the burden of disease without vaccination.

Study designs and other criteria for inclusion in the review
The authors reported that surveillance data, study data and meta-analyses were used.

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
The effectiveness data were derived from 45 studies.

Methods of combining primary studies
Where multiple publications were available for any model parameter, the authors used results from existing meta-analyses where possible. Where meta-analyses were not available, they stated that they made a conservative assumption, aimed at underestimating the benefits of vaccination.

Investigation of differences between primary studies
The authors did not investigate differences between the primary studies.

Results of the review
The annual incidence of disease per 100,000 population without vaccination was estimated to be 600 for diphtheria, 0.3 for tetanus, 4,720 for pertussis, 104 for Hib meningitis, 9.4 for Hib epiglottis, 12 for Hib septicaemia, 13.4 for Hib
pneumonia, 14.7 for Hib cellulitis, 2.7 for Hib arthritis, 1.3 for Hib other invasive disease, 31 for paralytic
poliomyelitis, 10,641 for measles, 6,205 for mumps, 3,300 for rubella and 9,839 for varicella.

The annual incidence of disease per 100,000 population with vaccination was estimated to be 0.001 for diphtheria,
0.015 for tetanus, 33 for pertussis, 0.1 for Hib meningitis, 0.004 for Hib epiglottis, 0.05 for Hib septicaemia, 0.05 for
Hib pneumonia, 0.009 for Hib cellulitis, 0.004 for Hib arthritis, 0.05 for Hib other invasive disease, 0 for paralytic
poliomyelitis, 1 for measles, 7 for mumps, 0.2 for rubella and 1,091 for varicella.

The probabilities of adverse events per 100,000 doses of vaccine were as follows.

With the DTaP vaccine: 8 for hypotonic hyporesponsive episodes, 10 for uncomplicated seizures, 63 for protracted
crying or screaming, and 2 for anaphylaxis.

With the Hib vaccine: 2000 for fever.

With the MMR vaccine: 50 for additional outpatients visits for minor reactions, 1,600 for parotitis, 1,000 for arthralgia
or arthritis, 33 for febrile seizures, 3 for thrombocytopenic purpura, and 0.1 for anaphylaxis, aseptic meningitis and
encephalitis.

With the Varicella vaccine: 2,000 for rash, 1,000 for additional outpatient visits, 0.2 for pneumonia, and 1.4 for Herpes
zoster.

Methods used to derive estimates of effectiveness
The authors used several assumptions to supplement their review.

Estimates of effectiveness and key assumptions
The assumptions were too numerous to report here. The reader is referred to the original paper for further details.

Measure of benefits used in the economic analysis
The measures of health benefit were the number of infected cases prevented and deaths saved by the vaccination
programme. These were estimated from the decision tree model. The benefits were discounted at a rate of 3% per
annum.

Direct costs
The authors reported the resource use quantities and the costs separately. The study included direct public and private
health care costs, and direct patient and relative costs. These comprised the costs of vaccination (e.g. distribution,
administration, care-giver time and travel), treatment (e.g. inpatient and outpatient costs) for infections and any
sequelae of diseases, and complications. Vaccine prices were obtained from a published pricing list. The source of
many of the other unit costs was unclear, as the cost data were derived from published studies. In addition, assumptions
were made to assess some cost components. Some of the unit costs were based on charge data. The costs were
discounted at a rate of 3% per annum. The study reported the total costs. The method used to inflate costs to the price
year 2001 was not reported.

Statistical analysis of costs
Patient level data were not available, thus a statistical analysis of the costs was not relevant.

Indirect Costs
The indirect costs were included in the analysis, which was appropriate given the societal perspective. The indirect costs
included productivity losses due to premature morbidity, indirect costs arising from permanent disability, and the
opportunity cost of work missed by caregivers. The quantity and cost data were derived from published studies, the
Bureau of Labour Statistics and the Bureau of the Census. In addition, assumptions were made to assess some cost components (such as the indirect costs for caregivers). The authors assumed that days of morbidity were distributed randomly throughout the week.

**Currency**

US dollars ($).

**Sensitivity analysis**

One-way sensitivity analyses were undertaken to explore uncertainty in the data and variations in the discount rate. The authors stated that a full probabilistic analysis was not possible since data on the probability distributions of variables were unavailable.

**Estimated benefits used in the economic analysis**

The authors reported the number of infected cases and deaths averted for each preventable disease. In total, the full vaccination schedule would prevent 13,622,004 cases and save 33,101 deaths.

**Cost results**

The direct disease costs in the absence of vaccination programmes were estimated to be $12,307 million and the societal costs (both direct and indirect costs) $46,557 million over the lifetime of the hypothetical birth cohort, using a discount rate of 3% per annum.

The direct disease costs averted with the vaccination schedule were estimated to be $12,175 million and the societal costs $46,075 million.

The direct immunisation programme costs (including vaccine, administration, parent travel, and direct costs for treatment of adverse events) were estimated to be $2,293 million and the societal costs (including direct programme costs and parent time lost for vaccination and treatment of adverse events) $2,789 million over the lifetime of the hypothetical birth cohort, using a discount rate of 3% per annum.

**Synthesis of costs and benefits**

The costs and benefits were combined to calculate the net present value and benefit-cost ratios.

The net present value of the vaccination schedule was estimated to be savings of $9.9 billion from a direct cost perspective and savings of $43.3 billion from a societal perspective over the lifetime of the hypothetical birth cohort, using a discount rate of 3% per annum.

The benefit-cost ratio for the vaccination schedule was estimated to be 5.3 from a direct cost perspective and 16.5 from a societal perspective, that is, for every dollar spent, the vaccination programme saved more than $5 in direct costs and approximately $11 in additional costs to society.

The results were not sensitive to the variables explored in the sensitivity analyses.

**Authors' conclusions**

The current routine schedule of vaccinations in the USA is cost-saving.

**CRD COMMENTARY - Selection of comparators**

The authors chose to compare the current vaccination schedule in their setting with historical data on the rates of disease without vaccination. They did not seek to compare alternative vaccination schedules. You must decide whether
this analysis is useful in your own setting.

**Validity of estimate of measure of effectiveness**
The authors did not state that a systematic review of the literature had been undertaken. They reported little detail on the conduct and methodology of the review, although it might have been due to space restrictions. It does, however, limit the interpretation of the study results. The authors used estimates from published meta-analyses where possible; where these were unavailable, they selected a single value aimed at being conservative towards estimating the benefits of vaccination. They stated that data were unavailable to adequately represent the uncertainty in the available data by means of a fully probabilistic analysis, thus the overall uncertainty was likely to be underestimated. The authors acknowledged that some of the data sources were not ideal, which also increases uncertainty in the study results.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled using a decision tree to calculate excess morbidity and mortality. The authors acknowledged that their estimate of health benefits did not incorporate pain or quality of life, which would underestimate the benefits of a vaccination programme.

**Validity of estimate of costs**
The authors estimated the costs from a societal perspective and included all cost categories appropriate to this perspective. In particular, an estimate of economic productivity lost, not just due to the initial illness but also for caring for sick children, was made. To assess the indirect costs, such as caregiver time lost to illness, the authors used the human capital approach which is appropriate for this purpose. The costs were reported separately from the quantities, which improves the generalisability of the study results. The cost data were subject to univariate sensitivity analyses. The authors acknowledged that some of the cost data might not be representative as they were derived from commercial databases. In addition, some of the unit costs were based on charge data, which may not represent the opportunity cost of resource use and may limit the generalisability of the study results. The authors did not report the method used to inflate the cost data to the stated price year (2001). Discounting was conducted, which was appropriate given the long time horizon.

**Other issues**
The authors did not compare their results with the findings from other studies. They addressed the issue of generalisability to other settings, and stressed the need for caution when interpreting the study results because of the assumptions made in the model. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors acknowledged several limitations to their study. For example, incomplete costing, particularly for the indirect costs, and the underestimation of benefits arising from vaccination programmes.

**Implications of the study**
The authors suggested that efforts should continue to increase vaccination coverage.

**Source of funding**
None stated.

**Bibliographic details**

**PubMedID**