Cost-effectiveness of a pneumococcal conjugate immunisation program for infants in Switzerland
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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 pneumococcal conjugate heptavalent vaccine (PCV7) (Prevenar) for the routine vaccination of newborns. The other strategies investigated included additional vaccination of all infants less than 24 months and less than 60 months. No vaccination was the base comparator. There were four strategies in all.

Type of intervention
Primary prevention: vaccination.

Economic study type
Cost-utility analysis.

Study population
The study population consisted of newborns and healthy children aged up to 24 and 60 months.

Setting
The setting was unclear. The economic analysis was carried out in Switzerland.

Dates to which data relate
The effectiveness evidence data were derived from studies published between 1984 and 2000. The resource use quantities were obtained from a subgroup of 114 paediatric patients treated at the University Hospital in Geneva between 1991 and 2000. The price year was not stated.

Source of effectiveness data
The effectiveness evidence was derived from a non-systematic review of published studies or reports, and from the authors' assumptions.

Modelling
A decision analytic model was used to model the experiences of five birth cohorts of 80,000 children from birth to age 5 (between 2002 and 2006).

Outcomes assessed in the review
The health outcomes related to the health technology assessed in the review were the vaccine efficacy for invasive disease, clinically diagnosed pneumonia and otitis media (OM), and vaccine coverage. Other epidemiological data were also assessed in the review. These estimates were used as model inputs.
Study designs and other criteria for inclusion in the review
A non-systematic review was conducted. For information on the incidence of meningitis and invasive pneumococcal disease, the authors referred to two nationwide studies, one retrospective and the other prospective. For information on the incidence of both pneumonia and OM, the authors referred to the paediatricians and general practitioners' reports to the Federal Swiss Health Office in the Sentinel System. Vaccine efficacy data were based on the findings of the Northern California Kaiser Permanente randomised trial.

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
Estimates of the clinical and epidemiological parameters in the study were derived from 11 primary and secondary sources.

Methods of combining primary studies
The primary studies were not combined since one study was used to inform one outcome.

Investigation of differences between primary studies
Not stated.

Results of the review
The vaccine efficacy was 97% for invasive disease, 11% for clinically diagnosed pneumonia and 7% of all OM episodes. See the 'Estimates of Effectiveness and Key Assumptions' section for the derivation of the number of cases averted by vaccination.

Methods used to derive estimates of effectiveness
Some assumptions were used to derive the life expectancy in Switzerland and in children with sequelae from meningitis. The authors also combined the serotype coverage with the vaccine efficacy to derive the percentage of averted cases with PCV7.

Estimates of effectiveness and key assumptions
Considering that invasive pneumococcal disease in children occurs mostly under the age of 2, for each death, 78 years of life lost have been considered (instead of 79 years). Considering that children with sequelae from meningitis have a shortened life expectancy, the authors assumed a life expectancy of 65 years.

Considering that PCV7 covers 73% of the serotypes producing invasive disease in Switzerland among children less than 5 years old, PCV7 was considered to avert 71.5% (0.97 multiplied by 0.73) cases of invasive disease, 8% of clinically diagnosed pneumonia and 5% of clinically diagnosed OM.
**Measure of benefits used in the economic analysis**

The measure of benefit used in the economic analysis was the number of quality-adjusted life-years (QALYs) gained. This was calculated from the number of cases of invasive pneumococcal disease, pneumonia and OM averted. Only a quality of life utility value, which was taken from the literature, was reported for severe neurological sequelae of meningitis. The utility values for other health states were needed. There was no indication that the QALYs were discounted.

**Direct costs**

Societal and sickness funds' perspectives were adopted in the analysis. From the societal perspective, hospital charges for the sickness funds were considered to represent half of the real costs, with a cost-to-charge ratio of about 2:1. The direct medical costs were those associated with the disease (tests, drugs, supplies and days in hospital) and with vaccination (price of vaccine, application and visit to the paediatrician, and adverse event associated with administration of PCV7). The disability costs in children with serious OM were excluded, as they had not been studied in Switzerland. The costs of the patients' time were excluded due to biased results for women.

For children with sequelae from meningitis, additional future medical costs were assumed and were discounted at 3% per year. The costs related to disabilities in children with serious OM were not included. The non-medical direct costs associated with sequelae of meningitis were valued at SFr 30,000 per year and were discounted at 3%. The costs and the quantities were not reported separately. The resource use quantities were obtained from a subgroup of 114 paediatric patients treated at the University Hospital in Geneva between 1991 and 2000. The price of the vaccine has been negotiated with the authorities (SFr 99 per dose). The price year was not stated.

**Statistical analysis of costs**

No statistical analysis of the costs was carried out.

**Indirect Costs**

The indirect costs were not included as they were deemed to be controversial.

**Currency**

Swiss francs (SFr). The conversion rate was US dollars (US$)1.00 = SFr 1.36.

**Sensitivity analysis**

Univariate sensitivity analyses were performed on the most uncertain parameters. The first was the incidence of invasive disease among Swiss children, which was varied from 3.2 to 12.4 cases per 100,000 for infants under 2 years old, and from 1.5 to 8.2 cases per 100,000 for infants under 5 years old. The second was the case fatality rate of bacteraemia. The cost estimates of disease were also varied from 50 to 200%. A two-way sensitivity analysis was performed on the incidence and case fatality rate of bacteraemia. A multivariate sensitivity analysis, in the form of a best-case and worse-case scenario, was also performed.

**Estimated benefits used in the economic analysis**

The vaccination of all newborns would result in an increase of 2,382 QALYs over no vaccination from the morbidity and mortality avoided.

Compared with vaccination restricted to newborns, the additional vaccination of all infants aged less than 24 months (catch-up 1 strategy) would result in 4 additional lives saved and 624 additional QALYs gained.

Compared with the catch-up 1 strategy, a catch-up vaccination of all children aged less than 60 months (280,000 supplementary children) would result in one additional life saved and 215 additional QALYs.
Cost results
The total cost associated with vaccination (doses of vaccine and additional costs), and the savings associated with
disease prevention in the 5 years studied were reported.

Assuming 70% coverage of newborns, the net cost of the vaccination programme for the first year was SFr 19 million
per year for the sickness funds and SFr 22 million per year for society.

The total savings from the vaccination of all newborns were SFr 11.5 million for the sickness funds and SFr 31.7
million for society.

It was not clear exactly what the incremental costs were for the additional catch-up strategies. However, the authors said
that there would be cost reductions from the additional vaccination of all infants aged less than 24 months, and that
there would be a significant increase in the costs for vaccination of all children aged less than 60 months. The
incremental cost-effectiveness ratios (ICERs) are reported in the 'Synthesis of Costs and Benefits' section.

Synthesis of costs and benefits
During the 5-year follow-up, the ICER of the vaccination of all newborns was SFr 39,300 (US$28,900) per QALY
gained from the sickness fund perspective and SFr 35,700 (US$26,300) per QALY gained from the societal
perspective.

The additional catch-up vaccination of all children aged less than 24 months in the years after vaccine introduction
resulted in an ICER of SFr 33,600 per additional QALY gained from the sickness funds’ perspective. The ICER was
SFr 30,890 per QALY gained from the societal perspective.

The ICER of catch-up vaccination of all children aged less than 60 months was SFr 162,000 per QALY gained from
both the societal and third-party payer perspectives.

The results were most sensitive to variations in the incidence of invasive disease. The ICER moved between more than
SFr 60,000 and SFr 20,000 per QALY gained for both the sickness funds and societal perspectives. The results were
also sensitive to the case fatality rate of bacteraemia. A higher incidence with lower fatality rate changed little in the
results.

Authors’ conclusions
The routine vaccination of healthy infants aged less than 2 years old in Switzerland can reduce mortality and long-term
neurologic impairment resulting from invasive pneumococcal disease, at a reasonable cost-utility ratio.

CRD COMMENTARY - Selection of comparators
The authors justified the strategies compared. However, they also noted that the recommendation of the Swiss
Committee on Immunisation Practices was to vaccinate children at risk, but they did not have the data necessary for this
analysis at the time of the study.

Validity of estimate of measure of effectiveness
The principal input parameters for the model were derived from published studies. There was no evidence that the
review was conducted in a systematic way to identify relevant research and minimise biases. The authors acknowledged
that the epidemiological data used in the model were insufficient due to the lack of available data in Switzerland. For
example, data on the incidence of OM in Switzerland were only an estimation. The reader should decide whether the
time horizon for evaluating the effects was sufficient.

Validity of estimate of measure of benefit
The QALYs gained was the measure of benefit used in the economic analysis. Only one QALY value was reported in
the study when there were many health states, and this was derived from the literature. There was no indication that the QALYs gained were discounted. The effect of discounting costs, but not benefits, is to derive a more favourable ICER.

Validity of estimate of costs
The authors reported that the costs were estimated from a societal perspective, but they limited their analysis to the direct costs on the basis that the indirect costs were controversial. Most costs seem to have been included, with the exception of disability-related costs since no data were available for them. The costs and the quantities were not reported separately and no price year was reported. The cost estimates of invasive pneumococcal disease were specific to the University hospital in Geneva. The authors acknowledged that those estimates may not represent the practice and the resource quantities used in other cantons. However, sensitivity analyses were conducted on the medical costs and no relevant changes in ICER were obtained. The authors performed an appropriate currency conversion. Discounting was undertaken since the costs were incurred over more than 2 years. A cost-to-charge ratio was used to assess the real costs for the societal perspective.

Other issues
The results do not appear to have been presented selectively. However, the absolute and incremental benefits and costs of the strategies could have been more clearly presented. The generalisability of the results to other settings or countries was discussed, and the authors made appropriate comparisons of their results with those from other studies. The authors reported a number of limitations to their study, which have been highlighted already. More details on the catch-up strategies (number of additional immune children, total and incremental costs) would have been useful. Although the authors adopted two specific perspectives, they did not discuss their findings according to the perspective adopted.

Implications of the study
For the authors, routine vaccination with pneumococcal conjugate has the potential to alter the disease epidemiology of invasive pneumococcal disease and its sequelae. It can also have a significant impact on medical utilisation due to OM.

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Bibliographic details

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Other publications of related interest


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