Cost-effectiveness of the pneumococcal vaccine in healthy younger adults
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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
Routine vaccination for Streptococcus pneumoniae was studied.

Type of intervention
Primary prevention.

Economic study type
Cost-utility analysis.

Study population
The study population comprised a hypothetical cohort of 22- and 35-year-old healthy young adults.

Setting
The setting was primary care. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness and resource use data were derived from studies published between 1972 and 2002. The price year was 2001.

Source of effectiveness data
The effectiveness evidence was derived from a review of completed studies.

Modelling
A decision model based on a Markov chain was constructed to assess the long-term benefits and costs of vaccination versus no vaccination over the patients’ lifetime. A daily cycle length was considered. Individuals left the model when they died from pneumonia or from other causes (based on age-specific mortality). The structure of the model was depicted.

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

the rate of contracting pneumococcal pneumonia;

the length of vaccine protection;

the probabilities of hospitalisation given pneumonia, death given admission for pneumonia, and death given outpatient pneumonia treatment;
the number of days hospitalised for pneumonia, out of work due to pneumonia with or without hospital admission, out of work due to life-threatening reaction, and out of work due to moderate systemic reaction; and

the probabilities of life-threatening side effects, death from life-threatening side effects, moderate systemic reaction, and vaccine efficacy in preventing pneumonia; and

the utilities associated with current health, death, hospitalised with pneumonia, hospitalised with anaphylaxis, outpatient pneumonia, convalescence from pneumonia, and severe side effects.

**Study designs and other criteria for inclusion in the review**
A formal review of the literature was not conducted. The studies appear to have been identified selectively. Only the designs of those primary studies that assessed vaccine efficacy were described in detail.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
The primary studies used for vaccine efficacy were mainly randomised controlled trials.

**Methods used to judge relevance and validity, and for extracting data**
Not stated.

**Number of primary studies included**
The model inputs were derived from approximately 40 studies.

**Methods of combining primary studies**
Not stated.

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

**Results of the review**
The rate of contracting pneumococcal pneumonia was 0.0003 to 0.0004 (0.03 - 0.04 per 1,000 people/year) in 22-year-olds and 0.00085 to 0.00095 (0.85 - 0.95 per 1,000 people/year) in 35-year-olds.

The length of vaccine protection was 10 years (range: 5 - 20).

The probabilities values were 0.10 (range: 0.05 - 0.35) for hospitalisation given pneumonia, 0.01 (range: 0.005 - 0.025) for death given admission for pneumonia, and 0.001 for death given outpatient pneumonia treatment.

The number of days hospitalised for pneumonia was 4 (range: 2 - 8).

The number of days out of work due to pneumonia were 5 (range: 2 - 7) without hospital admission and 9 (range: 3 - 11) with hospital admission.

The number of days out of work due to a life-threatening reaction was 4 (range: 2 - 6).

The number of days out of work due to a moderate systemic reaction was 2 (range: 1 - 3).
The probability values were 0.000005 for life-threatening side effects, 0.000001 for death from life-threatening side effects, 0.0001 (range: 0.001 - 0.00001) for moderate systemic reaction, and 0.50 (range: 0.25 - 0.75) for vaccine efficacy in preventing pneumonia.

The utility values were 1 for current health, 0 for death, 0.85 for hospitalised with pneumonia and hospitalised with anaphylaxis, and 0.90 for outpatient pneumonia, convalescence from pneumonia, and severe side effects.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the quality-adjusted life-years (QALYs). These were derived using a modelling approach. The utility values and mortality rates were obtained from published studies. An annual discount rate of 3% was applied. It was not stated whether the utility values were elicited from the general public or other groups of people.

**Direct costs**
An annual discount rate of 3% was applied since the costs were incurred over lifetime. The unit costs and the quantities of resources used were not reported for all items. The health services used in the economic evaluation were vaccine, chest X-ray examination, outpatient physician services and antibiotics, treatment of a moderate systemic reaction, and hospitalisation for pneumonia or a life-threatening reaction. The patients were assumed to receive vaccination when accessing the health care system for routine medical care. Accordingly, the costs of a formal vaccination programme were not considered. The cost/resource boundary of the study appears to have been that of the third-party payer. Resource use was estimated on the basis of probabilities of events that were mainly derived from the literature. The costs were estimated from the DRG Handbook, published studies, average prices for drugs, and Current Procedural Terminology. All the costs were presented in 2001 values.

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

**Indirect Costs**
Although the authors did not explicitly report the inclusion of the indirect costs, the estimation of days out of work for hospitalisation or life-threatening reaction suggests that costs associated with productivity loss were considered. However, the unit costs were not reported, and little information about the methods used to estimate productivity costs was provided.

**Currency**
US dollars ($).

**Sensitivity analysis**
Univariate and multivariate sensitivity analyses were conducted to assess the robustness of the estimated cost-effectiveness ratios to variations in the data. The variables investigated were disease incidence, cost of vaccination, cost of hospitalisation, cost of treating side effects, incidence of side effects, length of convalescence, discount rate, number of days of hospitalisation per pneumonia or anaphylaxis, in-hospital mortality rate, and the duration of vaccine protection. The ranges of values used were derived from the literature.

**Estimated benefits used in the economic analysis**
In the cohort of 22-year-olds, the estimated QALYs were 24.0276 with no vaccination and 24.0280 with vaccination.

In the cohort of 35-year-olds, the estimated QALYs were 20.1738 with no vaccination and 20.1744 with vaccination.
Cost results
In the cohort of 22-year-olds, the estimated costs were $47.95 with no vaccination and $68.41 with vaccination.

In the cohort of 35-year-olds, the estimated costs were $49.39 with no vaccination and $64.78 with vaccination.

Synthesis of costs and benefits
An incremental cost-effectiveness ratio was calculated to combine the costs and benefits of the study interventions.

Under base-case assumptions, the cost per QALY gained with vaccination relative to no vaccination was $54,764 in the cohort of 22-year-olds and $23,726 in the cohort of 35-year-olds.

The sensitivity analysis revealed that the estimated cost-effectiveness ratios were sensitive to variations in incidence of disease, length of vaccine protection, vaccine efficacy, and the cost of the vaccine.

The multivariate analysis showed that the cost-effective threshold for efficacy was 71% in 22-year-olds and 30% in 35-year-olds.

When the vaccine cost was higher than $25 at an incidence of 0.4/1,000 or less, vaccination was very expensive per QALY gained.

If vaccine protection lasted for more than 10 years, the cost-effectiveness ratio was well below the threshold of $50,000 per QALY in both study populations.

Authors’ conclusions
Routine pneumococcal vaccination in healthy young adults was a cost-effective strategy, although this conclusion depended on some factors, such as disease incidence, vaccine efficacy and cost.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator (no vaccination) was appropriate as it reflected the standard approach for healthy young adults. You should decide whether it is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used data derived from the literature. However, a review of the literature was not conducted. It appears that the primary studies have been identified selectively. Further, the methods used to combine the primary estimates were not reported. Most of the primary studies were not described in detail, with the exception of those studies that assessed vaccine efficacy. The authors acknowledged that uncertainty and variability was observed in the literature. Extensive sensitivity analyses were therefore conducted. These increased the validity of the analysis as key model inputs were identified.

Validity of estimate of measure of benefit
The summary benefit measure appears to have been appropriate for assessing the impact of vaccination on all dimensions of patient health, such as mortality, morbidity and quality of life. Appropriate discounting was applied, and variations in the base-case discount rate were investigated in the sensitivity analysis. The utility values were derived from the literature, but it was unclear whether they applied to the general public. The total QALYs were calculated using a modelling approach, which was useful in assessing the long-term benefits. The use of QALYs allows comparisons to be made with the benefits of other health care interventions.

Validity of estimate of costs
The authors stated that a societal perspective was adopted, but little information on the methods used to obtain the
indirect costs was given. The unit costs were reported only for some items. The price year was given, which facilitates reflation exercises in other settings. The sources of the cost data were reported for all items and they appear to have been appropriate. The costs were treated deterministically in the base-case, but extensive sensitivity analyses were conducted for key items.

**Other issues**
The authors compared their findings with those from other studies. They did not specifically address the issue of the generalisability of the study results to other settings. However, the use of extensive sensitivity analyses enables the impact of vaccination in alternative scenarios to be considered. The authors stressed that their analysis did not consider the impact of vaccination on the incidence of meningitis, otitis media and bacteraemia. The inclusion of such issues would further improve the cost-effectiveness of routine vaccination.

**Implications of the study**
The authors suggested that the vaccination of closed populations of young adults, such as college students, military members and young people incarcerated in prisons, could be a reasonable option, although the cost-effectiveness of such a targeted vaccination programme would depend on disease incidence, costs and vaccine efficacy. The development of a more efficacious vaccine would make routine vaccination for healthy young adults a very cost-effective strategy. The use of a randomised trial, which would provide more robust conclusions, does not appear to be feasible.

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**Other publications of related interest**

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