Comparative cost effectiveness of varicella, hepatitis A and pneumococcal conjugate vaccines
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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 varicella, hepatitis A and pneumococcal conjugate vaccines was examined.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of children in an age group that could be affected by day care or school entry.

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

Dates to which data relate
The effectiveness data were gathered from studies published between 1986 and 2000. The resource use data were obtained from studies published between 1994 and 2001. The price year was 2000.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of completed studies and authors' assumptions.

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

the number of deaths averted with vaccination,

expected age distribution of cases,

age-specific case fatality rates, and

US life expectancies.

Study designs and other criteria for inclusion in the review
The authors stated that all relevant studies examining the three vaccines were reviewed. Of the 7 studies initially identified, three were excluded because the children were too old to be affected by day care or school entry (2 studies) or because the results were not provided for a single cohort (1 study). Thus, 4 studies were considered (2 studies on varicella vaccine, 1 study on hepatitis A vaccine and 1 study on pneumococcal conjugate vaccine). No details on the primary studies were given. Three further studies were identified selectively in order to provide data needed to standardise the primary evidence (including US life tables).

**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**
Seven primary studies provided evidence.

**Methods of combining primary studies**
The primary studies were not combined as each study provided a series of estimates.

**Investigation of differences between primary studies**
The authors investigated the differences in the methods and characteristics of the primary studies. When methodological discrepancies were observed, the studies were standardised using a common methodology.

**Results of the review**
The outcomes derived from the literature were not reported.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions when the primary estimates were standardised.

**Estimates of effectiveness and key assumptions**
A median decedent age of 3 years was assumed for pneumococcal infections.

**Measure of benefits used in the economic analysis**
The summary benefit measure used was the number of life-years saved (LYS) with each vaccination strategy. This was obtained from each primary study. The results were presented both discounted and undiscounted. Two discounting approaches (passive and aggressive) were used.

**Direct costs**
Discounting was relevant because of the long timeframe of the analysis. An annual discount rate of 3% was applied. The unit costs were not presented separately from the quantities of resources used, although some sparse data were provided (e.g. vaccine administration cost per dose). The primary health services included in the economic evaluation
were vaccine acquisition and vaccine administration. Savings in direct costs were also considered and these included reductions in medical treatment costs. A detailed breakdown of items was not given. The costs associated with vaccine adverse events were not included because only the 2 published studies on varicella vaccine included this category of costs. The cost/resource boundary of the health care system was adopted in the analysis of direct costs. Resource use was estimated using data derived mainly from the primary studies. The costs came from multiple sources, including published studies and data from the US Centers for Disease Control and Prevention. Some assumptions were also made. All of the costs were adjusted to 2000 prices using the Consumer Price Index for Medical Care.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs were included in the economic evaluation in order to reflect a societal perspective. Three main categories of indirect cost reductions were considered. More specifically, work time missed by parents caring for sick children, work time missed by vaccinees after they reach working age, and lost productivity capacity caused by fatal infections (the latter was estimated using the human capital approach). The unit cost of each work-loss day was derived from median wages for American workers. Resource use was estimated using data derived from the primary studies, whenever available. Other resource use data were obtained from other published studies or based on authors' opinions. Discounting was carried out at 3%, as in the analysis of the direct costs. The price year was 2000.

Currency
US dollars ($).

Sensitivity analysis
A sensitivity analyses was carried out by varying the discount rate. Other analyses were not performed.

Estimated benefits used in the economic analysis
In a cohort of 100,000 vaccinated children, the undiscounted (passive discounting; aggressive discounting) life-years were:

99.46 (79.93; 33.81) with the varicella vaccine (first study);

118.45 (95.20; 40.27) with the varicella vaccine (second study);

432.91 (231.01; 106.45) with the hepatitis A vaccine; and

223.36 (204.40; 86.84) with the pneumococcal conjugate vaccine.

Cost results
In a cohort of 100,000 vaccinated children, the total vaccination costs (vaccine acquisition plus administration) were $5,362,800 with the varicella vaccine, $5,735,600 with the hepatitis A vaccine, and $25,205,600 with the pneumococcal conjugate vaccine. The reductions in medical costs were $1,097,800 (varicella, first study), $2,847,500 (varicella, second study), $2,679,300 (hepatitis A), and $9,913,600 (pneumococcal conjugate), respectively. Thus, the net health system costs (vaccination costs minus reductions in future medical costs) were $4,265,000 with the varicella vaccine (first study), $2,515,300 with the varicella vaccine (second study), $3,056,300 with the hepatitis A vaccine, and $15,292,000 with the pneumococcal conjugate vaccine.

In a cohort of 100,000 vaccinated children, the reduction in parent work-loss costs was $22,208,200 with the varicella vaccine (first study), $24,704,800 with the varicella vaccine (second study), $344,400 with the hepatitis A vaccine, and
$3,874,800 with the pneumococcal conjugate vaccine. The reductions in vaccinee work-loss costs was $577,800 (varicella, first study), $642,700 (varicella, second study), $2,716,800 (hepatitis A), and $0 (pneumococcal conjugate), respectively. The reduction in mortality costs were $1,625,500 (varicella, first study), $1,895,400 (varicella, second study), $5,486,100 (hepatitis A), and $3,419,100 (pneumococcal conjugate), respectively. The total vaccination costs avoided (including reduced medical costs) were $25,509,300 with the varicella vaccine (first study), $30,090,500 with the varicella vaccine (second study), $11,226,600 with the hepatitis A vaccine, and $17,207,500 with the pneumococcal conjugate vaccine.

Therefore, the ratio of the vaccination costs saved (economic benefits) to the costs of vaccination was 4.76:1 with varicella vaccine (first study), 5.61:1 with varicella vaccine (second study), 1.96:1 with hepatitis A vaccine, and 0.68:1 with pneumococcal conjugate vaccine.

Synthesis of costs and benefits
The average and incremental cost-effectiveness ratios were calculated to combine the costs and benefits of the vaccination strategies.

From the health system perspective, the average cost per undiscounted (passive discounting; aggressive discounting) LYS was:

$42,900 ($53,400; $126,100) with the varicella vaccine (first study);

$21,200 ($26,400; $62,500) with the varicella vaccine (second study);

$7,100 ($13,200; $28,700) with the hepatitis A vaccine; and

$68,500 ($74,800; 176,100$) with the pneumococcal conjugate vaccine.

The incremental cost per undiscounted (passive discounting; aggressive discounting) LYS was:

$1,700 ($4,000; $8,200) with the hepatitis A vaccine over varicella vaccine and

$121,800 ($117,000; $274,400) with the pneumococcal conjugate vaccine over varicella vaccine.

The incremental analysis revealed also that the pneumococcal conjugate vaccine was dominated by the hepatitis A vaccine, which was more effective and less costly.

The sensitivity analysis showed that all cost-effectiveness ratios became less attractive when a 5% discount rate was applied to both the costs and benefits. However, the ranking of the alternative vaccination strategies did not change. Hepatitis A vaccination was the most affected by the use of a 5% discount rate because more infections were prevented in adolescence and adulthood.

Authors’ conclusions
After standardising the available studies using a common methodological framework, both the varicella and hepatitis A vaccinations were cost-effective strategies. However, the pneumococcal vaccine cost the health care system more than twice as much as the varicella and hepatitis A vaccines combined, and its cost-effectiveness ratio was well above the commonly used threshold for definition of cost-effectiveness.

CRD COMMENTARY - Selection of comparators
The authors justified their selection of the comparators, which represented three common vaccination options that could become conditions of day care or school entry in several US states. However, no information on the types and characteristics of the vaccines was provided. You should decide whether they are valid comparators in your own setting.
Validity of estimate of measure of effectiveness
The effectiveness data came from published studies. The authors stated that all known US studies were reviewed and exclusion criteria (all aimed to include comparable studies) were reported. However, the designs of the primary studies were not described, which limits the possibility of assessing the validity of the sources used. The authors stated that some relevant assumptions made in the primary studies, such as vaccine protective efficacy and duration of protection, could not be standardised.

Validity of estimate of measure of benefit
The use of life expectancy as the summary benefit measure was appropriate as it is a measure comparable with the benefits of other health care interventions. Further, the impact of vaccination on survival represented the most relevant dimension of health. However, an evaluation of the effect of vaccination on quality of life would have been interesting. Different approaches for discounting were applied, and the use of an alternative discount rate was investigated in the sensitivity analysis.

Validity of estimate of costs
The cost analysis was carried out from two different perspectives, both of which were relevant. Indeed, the societal perspective was the most appropriate, but the health care system perspective could have been of more interest to decision-makers. Few data on the unit costs and quantities of resources used were given, but in general the costs were presented as macro-categories and no information on single cost items was given. This reduces the possibility of replicating the cost analysis in other settings. The authors justified the exclusion of some categories of costs. The price year was reported, which aids reflation exercises. The costs were not varied in the sensitivity analysis. The source of the economic data was reported.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. They also did not explicitly address the issue of the generalisability of their results to other settings. In fact, sensitivity analyses were not carried out, except for discount rate, and this limits the external validity of the analysis. The study referred to children eligible for vaccination and this was reflected in the authors' conclusions.

Implications of the study
The study results supported the implementation of varicella vaccination (which provided the greatest financial gain to society) and hepatitis A vaccination (which provided greater longevity gains). However, implementation of pneumococcal conjugate vaccination would provide considerably less benefit for each dollar invested.

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None given.

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Other publications of related interest


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