Prophylaxis against respiratory syncytial virus (RSV), varicella, and pneumococcal infections: economic-based decision-making

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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 study compared three preventive interventions for infants. The interventions compared were varicella vaccination, pneumococcal conjugate vaccination, and respiratory syncytial virus (RSV) prophylaxis with palivizumab (Synagis).

Type of intervention
Primary and secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population for varicella vaccination and pneumococcal conjugate vaccination comprised all healthy infants. The study population for RSV prophylaxis comprised infants at high-risk for severe RSV infection. No further inclusion or exclusion criteria were reported.

Setting
The setting was not explicitly stated. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness data were derived from studies published between 1974 and 2000. The cost data were derived from literature published between 1985 and 2000. All the costs were reported for the year 2002.

Source of effectiveness data
The effectiveness data were derived from a review and synthesis of completed studies.

Outcomes assessed in the review
The following outcomes were assessed in the review:

- the incidence of disease (varicella, invasive pneumococcal infections, bronchiolitis or pneumonia due to RSV);
- the hospitalisation rates;
- the death rates;
- the incidence of complications caused by disease (e.g. bacterial superinfection of the skin, lungs and bones, Reye syndrome, pneumonitis, encephalitis, glomerulonephritis, arthritis due to varicella, pneumococcal meningitis,
pneumococcal bacteraemia, pneumococcal pneumonia, otitis media episodes due to pneumococcal infection);
long-term disability due to disease;
efficacy of the vaccines; and
the efficacy of RSV prophylaxis with palivizumab.

**Study designs and other criteria for inclusion in the review**
The review included cost-effectiveness studies on varicella vaccination, pneumococcal conjugate vaccination and RSV prophylaxis with palivizumab, which were written in English. No further inclusion or exclusion criteria were reported.

**Sources searched to identify primary studies**
The authors searched MEDLINE for primary studies.

**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 authors cited 23 studies in total as sources of the effectiveness evidence.

**Methods of combining primary studies**
It was unclear whether the authors combined the results of the primary studies.

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

**Results of the review**
In the USA, almost 4 million cases of varicella occur each year. The annual hospitalisation rate is 0.0025 and the annual death rate is 0.0000107 among children younger than 15 years of age. Complications due to varicella included bacterial superinfection of skin, lungs and bones, Reye syndrome, pneumonitis, encephalitis, glomerulonephritis, arthritis and death. The mortality rate was found to be higher in infants (6.23 per 100,000) than in children and adolescents aged 1 to 14 years (0.75 per 100,000). The varicella vaccine was found to be 70 to 90% effective against infection, and more than 95% protective against severe for 7 to 10 years.

The incidence of pneumococcal infection was estimated to be 228 per 100,000 in children aged 6 to 11 months, and 87.6 per 100,000 in children under 5 years of age. Complications due to pneumococcal infections in children under 5 years of age included pneumococcal meningitis, pneumococcal bacteraemia and pneumococcal pneumonia. The incidence rates were not reported. The authors reported the results on the efficacy of pneumococcal conjugate vaccination, as derived from two published studies. The results were not combined.

It was found that almost 50% of children were infected with RSV during their first year of life, and almost all children have been infected by the age of 2 years. The highest incidence was found in infants born prematurely, with chronic lung disease, congenital heart disease, multiple congenital anomalies and certain immunodeficiencies.
Measure of benefits used in the economic analysis
The measures of benefits used were:

- the life-years saved because of each preventive intervention;
- deaths and cases prevented due to varicella vaccination and due to pneumococcal conjugate vaccination;
- major sequelae and long-term disability prevented by varicella vaccination;
- avoided cases of otitis media, pneumonia, bacteraemia and meningitis because of pneumococcal vaccination; and
- hospitalisations avoided due to RSV prophylaxis with palivizumab.

In general, all of the benefits were discounted at a rate of 5%. The exception was otitis media, pneumonia, bacteraemia and meningitis cases avoided, which were discounted at a rate of 3%.

Direct costs
The health service costs were included. The actual direct medical costs included in the analysis were not described in detail and cost components varied among the three prophylactic strategies. The direct costs were for illness, hospitalisation, emergency department visits, outpatient urgent care visits, advice calls, over-the-counter medications, vaccination (dose and administration), and long-term medical care (follow-up care) arising from disability. It was unclear whether the hospitalisation costs included overheads and capital costs. The unit costs and the resource quantities were not reported separately; indeed, the unit costs were not reported. The costs and the quantities of resources used were derived from the literature. All the costs were adjusted to 2002 levels using the medical care component of the Consumer Price Index and were discounted at a rate of 5%.

Statistical analysis of costs
The costs were treated deterministically.

Indirect Costs
The indirect costs included were non-medical costs associated with illness (travel costs, additional childcare), parents’ time spent caring for a sick child (parents’ work losses), special education costs for neurologically disabled survivors, and future productivity losses due to disability. The cost components varied between the three prophylactic strategies. For varicella and pneumococcal conjugate vaccination, future productivity losses due to a child's premature death were derived from the literature. However, these costs were not available for RSV prophylaxis (palivizumab). The costs and the quantities were not reported separately, indeed, the unit costs were not reported. All the costs were derived from the literature. They were adjusted to 2002 levels using the medical care component of the Consumer Price Index and were discounted at a rate of 5%.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
Incremental benefits were not reported.
Cost results
The total intervention costs were not reported.

Synthesis of costs and benefits
An incremental analysis was performed.

From the payers perspective (work-related costs were not included), the cost per life-year saved was $28,100 for varicella vaccination, $338,400 for pneumococcal conjugate vaccination, and $66,400 for palivizumab prophylaxis.

From the societal perspective, where the cost of lifetime lost productivity due to premature infant deaths was also included for RSV prophylaxis, the estimates of cost per life-years saved resulted in money savings for varicella, $175,300 for pneumococcal conjugate vaccination, and $66,200 for palivizumab prophylaxis.

Authors' conclusions
"All three of the prophylactic measures offer significant health benefits for infants, children and their families." In addition, when the societal perspective was adopted, varicella and pneumococcal conjugate vaccinations were characterised as "financially attractive".

CRD COMMENTARY - Selection of comparators
The characteristics of the vaccines (e.g. dosage or duration) and RSV prophylaxis (i.e. palivizumab dosage) were not described in detail. The comparators were justified on the grounds that the American Academy of Pediatrics recommended all three preventive interventions. You should decide if they are widely used technologies 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. The inclusion criteria and data extraction methods were not reported. It is therefore not possible to say whether or not the data from the available studies were used selectively. The authors did not note any differences between the studies, or report the methods used to combine the estimates, if in fact a synthesis was undertaken. Given the level of reporting it was difficult to judge the quality of the effectiveness estimates.

Validity of estimate of measure of benefit
Life-years saved were used as the primary measure of benefit. Although not explicitly stated, these were most probably derived from the literature. Further measures of benefits that were combined with costs were not all discounted at the same discount rate. No justification was provided for the use of different discount rates.

Validity of estimate of costs
The study adopted both a societal and health care payers' perspective. It was difficult to assess whether all the relevant costs were included, especially as the cost components varied between the strategies under study. For comparison purposes, the authors omitted work-related costs from the analysis from the payers' perspective. The cost-effectiveness of the strategies may therefore have been overestimated given that, according to the authors, much of the economic burden of childhood illness was indirect (e.g. lost productivity of parents of sick children). Respectively they included costs of lost productivity due to premature infant death for the RSV prophylaxis with palivizumab in the societal perspective, although such costs did not exist in the literature. The basis for the estimation of this cost was not reported. All the costs were taken from published sources and were appropriately adjusted to the year 2002. The authors used a 5% discount rate, reporting that a discount rate of 3% was not feasible, but did not justify this statement.

Other issues
The authors did not make appropriate comparisons of their findings with those from other studies. Nor did they address the issue of generalisability of the results to other settings. The authors pointed out a number of limitations of their study. For example, the three preventive strategies were not completely comparable, as the vaccination strategies prevented infection while the palivizumab prophylaxis reduced the risk of severe infection in a specific target population at risk. The authors referred to the limitations of using available cost-effectiveness studies as the basis for comparisons, as the studies reviewed did not use comparable methods of analysis (perspective adopted, denominator metric applied, type of data used, and resource use and cost components included). In addition, they mentioned that when using cost per life-years saved as a measure of benefit, the psychological costs of pain and suffering for the child were not considered, and neither were the stress and anxiety of the child and parents.

Implications of the study
The authors did not make any explicit recommendations for changes in policy or practice. However, they called for further research to quantify the impact of illness. In addition, their discussion highlighted some issues where greater information is needed.

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