Cost effectiveness of child pneumococcal conjugate vaccination in middle-income countries
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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.

CRD summary
The study examined cost-effectiveness of pneumococcal conjugate vaccine (PCV) in 77 middle-income countries taking into account both direct protection of vaccinated children and indirect effects of vaccination on unvaccinated children and adults. The authors concluded that pneumococcal was highly cost-effective in middle-income countries, especially when using 10- and 13-valent PCV. The study used valid and robust cost-effectiveness methodology. Data sources and results were extensively reported in the supplementary appendix. The authors’ conclusions appear valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The study examined the cost-effectiveness of pneumococcal conjugate vaccine (PCV) in 77 middle-income countries taking into account both direct protection of vaccinated children and indirect effects of vaccination on unvaccinated children and adults.

Interventions
Seven-valent, 10-valent and 13-valent PCV (PCV-7, PCV-10, and PCV-13) were considered. A three-dose schedule administered at six, 10 and 14 weeks of age (with no catch-up vaccination for older children) was considered for each vaccination strategy. The background comparator was no vaccination.

Location/setting
Seventy-seven middle-income countries: 42 classified by the World Bank as upper-middle-income countries and 35 lower-middle-income countries that were ineligible for Global Alliance for Vaccines and Immunization (GAVI) assistance. Primary care.

Methods
Analytical approach:
The analysis was based on a decision tree model, which considered the direct effect of vaccination on vaccinated children under the age of five years as well as the two indirect effects of vaccination (herd immunity and serotype replacement). The costs and benefits of the first 10 years of the vaccination programme were modelled over a lifetime horizon. The perspective was that of society.

Effectiveness data:
Clinical inputs were taken from selectively identified sources. Data were based on middle-income studies where possible and included national databases and published sources. Otherwise inputs were extrapolated from other countries. For example, USA surveillance databases were used for the indirect effects of vaccination. In general, data were pooled when obtained from several sources. Vaccine efficacy was a key input of the model and was taken from a recently published meta-analysis for PCV-7. Due to a lack of published evidence on the efficacy of PCV-10 and PCV-13, all vaccines were assumed to have the same efficacy against invasive pneumococcal disease but PCV10 and PCV-13 were projected to prevent more disease owing to their greater serotype coverage.

Monetary benefit and utility valuations:
Standard disability weights for specific health conditions related to pneumococcal disease were taken from the World Health Organisation (WHO) Burden of Disease Study.
Measure of benefit:
Disability-adjusted life-years (DALYs) were used as the summary benefit measure and were discounted at an annual rate of 3%.

Cost data:
The economic analysis included direct medical costs associated with pneumococcal disease (medical facility personnel, diagnostic tests, procedures and medications), non-medical direct and indirect costs (patient or caregiver time lost from work and transportation) and vaccination costs (acquisition and administration). The same cost was assumed for all vaccines. Most costs were taken from the WHO Choosing Interventions that are Cost-Effective (CHOICE) initiative and from published and unpublished country- and regional-level studies. Vaccine costs were taken from expert opinions and for a price negotiated by Brazil. Costs were in USA dollars ($). The price year was 2005. A 3% annual discount rate was applied.

Analysis of uncertainty:
Conventional one-way sensitivity analyses were carried out using plausible ranges of values for the inputs: disease incidence, case fatality ratios, serotype coverage, vaccine efficacy and level of herd protection. Additional analyses were carried out for regional subgroups of countries and by excluding China from the pooled analysis because of the consistent economic and health burden of this country.

Results
When all countries were pooled, compared to no vaccination the additional costs of vaccination and DALYs averted were $18.1 billion and 11.1 million with PCV-7, $17.1 billion and 16.4 million with PCV-10 and $16.6 billion and 18.5 million with PCV-13. The incremental cost per DALY averted with vaccination over no vaccination was $1,600 with PCV-7, $1,000 with PCV-10 and $900 with PCV-13. These ratios were $1,500, $920, and $800 in 35 lower-middle-income countries and $1,900, $1,300, and $1,100 in 42 upper-middle-income countries.

Using the recommended WHO threshold of three times the gross domestic product (GDP) per capita, PCV-7 would be cost-effective for all countries except five and PCV-10 and PCV-13 would be cost-effective for all countries.

The most influential inputs were vaccine dose cost, vaccine serotype coverage and pneumococcal disease incidence. Base case results were generally stable.

When China was excluded from the pooled analysis, the incremental cost per DALY averted for PCV-7 decreased to $1,100 in the lower-middle-income countries and to $1,500 in the middle-income countries.

Regional analysis showed that the greatest health benefits were observed in Africa, Asia and Latin America.

Authors’ conclusions
The authors concluded that pneumococcal conjugate vaccination was highly cost-effective in middle-income countries, especially when PCV-10 and PCV-13. Further analyses should considered specific issues related to budget impact and affordability of vaccination policies.

CRD commentary
Interventions:
The selection of the comparators was appropriate as no vaccination represented the pattern of care in several of these countries. The three available PCV vaccines were considered.

Effectiveness/benefits:
Clinical inputs were taken from several different sources including local databases, international agencies and published studies. Given the lack of valid national estimates for some middle-income countries, data from other countries were used in some circumstances and adapted to the local context. This was particularly relevant for the indirect effect which was taken from USA data which were likely to differ from those of the countries analysed. A detailed description of sources selected and methods used to extrapolate data to all countries was provided in an online appendix. Several clinical parameters were varied in the sensitivity analysis. DALYs were an appropriate benefit measure to capture the burden of disease in middle-income countries. Limited information was given on the derivation of utility valuations.
Costs:
The economic analysis was performed appropriately, considered a wide range of costs and was consistent with the perspective of society. Country-specific sources of costs were used. These were supplemented with data from international agencies that were relevant for middle-income countries. A clear description of all model sources was provided in an online appendix. Unit costs and resource quantities could not be presented separately due to the high number of countries and items involved. The methods used to extrapolate cost data to countries that lacked valid data (regression analyses) appeared appropriate. The price year was stated explicitly and enables future reflation exercises. Cost estimates were treated deterministically and were not subjected to analysis of uncertainty.

Analysis and results:
The study results were presented extensively. An incremental approach was used to synthesise costs and benefits of the alternative strategies. The issue of uncertainty was investigated using a deterministic approach, which considered only variations in individual inputs and alternative scenarios. The authors acknowledged some limitations of their analysis, mostly the lack of valid data for several clinical and costs items for the countries analysed and the need for using estimates from different settings (such as USA). The analysis clearly covered all middle-income countries and was specific to these settings.

Concluding remarks:
The study used valid and robust cost-effectiveness methodology. Data sources and results were extensively reported in the supplementary appendix. The authors’ conclusions appear valid.

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