Cost-effectiveness of 13-valent pneumococcal conjugate vaccine: Germany, Greece, and The Netherlands

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 compared the cost-effectiveness of two newer pneumococcal conjugate vaccines (10-valent and 13-valent serotypes) with the widely available 7-valent vaccine in national immunisation programmes for children in three European countries. The authors concluded that the 13-valent vaccine was likely to be cost-saving and cost-effective compared with the other pneumococcal conjugate vaccines. The analysis was based on valid methods. Assumptions on vaccine efficacy were extensively tested. The authors’ conclusions appear robust.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The cost-effectiveness of two newer pneumococcal conjugate vaccine serotypes (10-valent vaccine and 13-valent vaccine) were compared with the more widely available 7-valent vaccine serotype in paediatric national immunisation programmes against Streptococcus pneumoniae-related diseases in three European countries (Germany, Greece and The Netherlands).

Interventions
Pneumococcal conjugate 13-valent vaccine was compared with either 7-valent or 10-valent vaccine. Children under one year old were vaccinated with one of the three pneumococcal conjugate vaccines and received a booster dose in their second year of life.

Location/setting
Germany, Greece, The Netherlands/primary care.

Methods
Analytical approach:
The analysis was based on a decision-tree model with a lifetime horizon. The authors stated that the perspective of the third-party payer was used.

Effectiveness data:
A selective approach was used to identify relevant sources of evidence. Data were retrieved from national surveillance databases for each country (especially for epidemiological estimates) or based on the published literature. Some assumptions were required. For example, the effectiveness of 13-valent and 10-valent pneumococcal conjugate vaccines (key inputs of the model) was derived from 7-valent pneumococcal conjugate vaccine effectiveness, assuming an effect proportional to additional serotype coverage. Assumptions about the indirect effect of vaccination were another crucial input. In particular, no indirect effect was attributed to 10-valent pneumococcal conjugate vaccine (based on some published evidence); the indirect effects of 13-valent vaccine came from the portion of disease covered by each vaccine relative to the 7-valent vaccine. Treatment effect for 7-valent pneumococcal conjugate vaccine was taken from published studies; key results were reported. It was also assumed that indirect effects of the vaccines were identical in all countries. Additional details on input value categories were available in a separate online appendix.

Monetary benefit and utility valuations:
Utility valuations associated with specific health conditions were taken from country-specific sources.
Measure of benefit:
Life-years, quality-adjusted life-years (QALYs), and cases of illness avoided were the three summary benefit measures. Life years and QALYs were discounted at an annual rate of 5% in Germany, 3% in Greece, and 1.5% in The Netherlands.

Cost data:
Direct medical costs considered were associated with vaccination (acquisition and administration), illness, and sequelae. Disease costs included diagnostics, physician time, hospitalisations, prescriptions, and over-the-counter medications. Most economic data came from country-specific sources. Costs were in Euros (EUR). The price year was 2008.

Analysis of uncertainty:
Five scenarios were analysis where 13-valent pneumococcal conjugate vaccine was compared with the 10-valent vaccine. Firstly, the direct effects of 10-valent pneumococcal conjugate vaccine were adjusted for immunogenic response and no indirect effects occurred. Secondly, 10-valent vaccine direct effects were adjusted for immunogenic response and indirect effects were assumed to be equal to 50% of the serotype extrapolated values. Thirdly, 10-valent vaccine direct effects were adjusted for immunogenic response and neither the 13-valent nor the 10-valent vaccine incurred indirect effects. Fourth, 10-valent vaccine direct effects were adjusted for immunogenic response and full extrapolated indirect effects were assumed. Fifth, 10-valent vaccine direct effects were assumed as in the base case and indirect effects were assumed to be equal to the full serotype extrapolated values.

Results
When 13-valent pneumococcal conjugate vaccine was compared with the 7-valent vaccine, the 13-valent vaccine reduced costs by EUR 235,981,618 in Germany, and EUR 2,653,781 in Greece, with additional costs of EUR 131,992 in The Netherlands. The life years with the 13-valent vaccine were 31,960 in Germany, 1,255 in Greece, and 3,752 in The Netherlands. The QALYs gained with the 13-valent vaccine were 28,828 in Germany, 1,51 (taken from Table 3) in Greece, and 3,468 in The Netherlands. Cases of disease were avoided in all three countries with 13-valent pneumococcal conjugate vaccine. Regardless of the benefit measure used, the 13-valent vaccine was dominant (both cost-saving and more beneficial) over the 7-valent vaccine in Germany and Greece. In The Netherlands, the incremental cost per life year gained or QALYs gained was below EUR 20,000.

In the comparison between 13-valent and 10-valent pneumococcal conjugate vaccine, the 13-valent vaccine dominated the 10-valent vaccination strategy in all countries.

The scenario analysis showed that 13-valent pneumococcal conjugate vaccine remained the preferred strategy (dominant or cost-effective at a threshold of EUR 50,000 per QALY) over the 10-valent vaccine in all but one of the assumed scenarios. Where 10-valent vaccine direct effects were adjusted for immunogenic response and neither the 13-valent nor the 10-valent vaccine incurred indirect effects, the 13-valent vaccine was not cost-effective as incremental cost-utility ratios were above the threshold of EUR 50,000 per QALY in all countries.

Authors' conclusions
The authors concluded that paediatric national immunisation programmes with 13-valent pneumococcal conjugate vaccine serotype in Europe were likely to be cost-saving and highly cost-effective compared with other available pneumococcal conjugate vaccine serotypes.

CRD commentary
Interventions:
The rationale for the selection of the comparators was clear as the available pneumococcal conjugate vaccine serotypes were considered. These strategies also appear to be valid for other countries.

Effectiveness/benefits:
Little information was provided on sources of clinical inputs. It appeared that local data were mostly used for epidemiological estimates, while treatment effect was estimated from published studies that were not described. Some assumptions were needed because of the lack of available data on 10-valent and 13-valent pneumococcal conjugate vaccines. Indirect effects were obtained from US studies as no valid European data were found. Overall it was difficult to objectively assess the quality of the clinical evidence. Various benefit measures were used and were appropriate for
capturing the impact of the disease on children's health. In particular, life years and QALYs allowed cross-disease comparisons. Details of the derivation of utility valuations (the values and instruments used) were not reported.

Costs:
The costs were consistent with the perspective of the public payer in all three countries, so only direct medical costs were taken into account. However, the costs were presented as totals and were not broken down into individual items. This approach (although quite common in vaccination studies) reduced the transparency of the economic evaluation. In addition, no clear information on data sources was provided, but country-specific sources were used for each cost category. The authors stated that costs were not discounted as they were incurred within a one-year time frame; they also stated that the final acquisition prices of 10-valent and 13-valent pneumococcal conjugate vaccines were not known for certain in some markets. The price year was appropriately reported, which would allow reflation exercises in other time periods. Cost estimates were treated deterministically and were not subjected to uncertainty analysis.

Analysis and results:
An incremental approach was used to identify the dominant strategy or to synthesise costs and benefits of the alternative vaccination serotypes when required. Given the uncertainty underlying the efficacy of vaccines, a strength of the study was the scenario analysis, which considered various assumptions on the inclusion/exclusion of indirect effects of vaccination. However, the sensitivity analyses were restricted to these assumptions and did not consider variations in other model inputs. In addition, the 13-valent pneumococcal conjugate vaccine was not compared with the 7-valent vaccine in the sensitivity analysis; it would have been interesting to estimate the impact of exclusion of indirect effect in this comparison. The study results were presented in detail for each of the three countries. The authors acknowledged some limitations of their analysis, mainly the need for assumptions in the case of lack of valid local data. Transferability of the results was not explicitly addressed, but the analysis was conducted in three European countries, so it was likely to be relevant for other similar settings.

Concluding remarks:
The analysis was based on valid methods. Key assumptions on vaccine efficacy were extensively tested. The authors’ conclusions appear robust.

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