Health economics of a hexavalent meningococcal outer-membrane vesicle vaccine in children: potential impact of introduction in the Dutch vaccination program


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
A new hexavalent meningococcal B outer-membrane vesicle (OMV) vaccine was studied. This vaccine is administered to new-born infants in four doses at the age of 2, 3, 4 and 11 months.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness and cost-utility analyses.

Study population
The patient population comprised all new-borns in The Netherlands.

Setting
The setting for the study and the administration of the vaccine was not specifically stated. The study postulated that the new vaccine would be administered in conjunction with an existing programme containing vaccinations for diphtheria, tetanus, pertussis, polio, mumps, measles, rubella and Haemophilus influenzae type B. Data on the costs were collected for primary care (GP visits), secondary care (hospitalisation) and institutions (capturing long-term care and special educational requirements).

Dates to which data relate
The effectiveness data were obtained from studies published between 1993 and 2000. Resource use was estimated using data from 1993 to 1997. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from published studies and the authors' assumptions.

Modelling
A decision model was used to simulate the costs and effects if vaccination of new-born babies against meningococcal B did or did not take place. The time frame was 76 years.

Outcomes assessed in the review
The following outcomes were used to populate the model:

vaccine coverage and efficacy;
the vaccination rate;
the incidence of meningococcal infection leading to septic shock or complicated meningitis, or non-complicated meningitis;
the mortality rate from both meningitis and septic shock;
the duration of the efficacy of the vaccine after four doses;
the percentage of patients with neurological sequelae, and amputations or scars;
the quality of life for patients with neurological sequelae, and amputations or scars.

**Study designs and other criteria for inclusion in the review**
Parameters relating to the efficacy, coverage and rate of vaccination were obtained from published clinical trials.

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

**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**
Eleven studies were included in the review.

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

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

**Results of the review**
The vaccine coverage was 75%.

The efficacy of the vaccine after the complete four doses was 90%.

The rate of meningococcal infection leading to septic shock or complicated meningitis was 15%.

The rate of meningococcal infection leading to non-complicated meningitis was 85%.

The mortality rate was 5% from meningitis and 35% from septic shock.

The quality of life was 0.75 quality-adjusted life years (QALYs) for patients with neurological sequelae and 0.83 QALYs for those with amputations or scars.
**Methods used to derive estimates of effectiveness**
The authors made assumptions about the vaccine efficacy and the vaccination rate.

**Estimates of effectiveness and key assumptions**
It was assumed that a minimum of three doses was required to ensure that the vaccine was effective. The efficacy of the vaccine after three doses (70%) was less than that following all four doses (90%). Since the new meningococcal OMV vaccine was to be administered as part of an existing immunisation programme, it was assumed that the vaccination rate for this new extended programme would be the same as that for the current one (95%). The authors assumed that the duration of the vaccine efficacy was 3 years after the final dose.

**Measure of benefits used in the economic analysis**
Two measures of benefits were used in the economic analysis, the QALYs and the life-years gained. The QALYs were evaluated using specific weighting factors for diseases in The Netherlands (see Other Publications of Related Interest), which assigned a value between 0 and 1 according to the severity of the disease. The impacts of neurological and physical sequelae on quality of life were obtained from the EuroQol EQ5D+ (codes 212111 and 112112). The number of deaths and cases of severe long-term sequelae averted were also reported. The benefits were discounted at a rate of 4%.

**Direct costs**
The costs were discounted at a rate of 4% since the timeframe for the analysis was 76 years. The quantities of resource use and the costs were analysed separately. The resources used were GP visits, hospitalisation with intensive or standard care treatment, inpatient paediatric consultation (and during intensive care treatment), paediatrician follow-up after recovery, parenteral antibiotics, extra medical assistance with septic shock, diagnostic procedure, outpatient contact with paediatrician, treatment for scars (including hospitalisation), treatment for amputations (including hospitalisations), institutional lifetime care for mentally and physically disabled, and special education needs. The cost of the vaccine, and the promotional and administrative costs of introducing the vaccine, were also included. The unit costs were obtained for each category of resource use.

Data on resource utilisation were obtained from PRISMANT Healthcare (for 1993 to 1997), international literature and expert panels. Resource use was estimated for patients with meningitis and also those with septic shock. The unit cost information was derived from published sources, expert panels, data from the University Hospital Groningen, and through personal communications with the Dutch departments of health and education. The price year was 1998.

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

**Indirect Costs**
The indirect costs were discounted at the same rate as the direct costs. This was necessary to express the costs incurred at some future stage over the 76 years of the model in terms of their present value. The quantities and the costs were analysed separately. Using the friction cost method, the authors measured the lost productivity arising from the number of days parents would take off work to look after their children. This was converted into a monetary value using the average production value of one hour of work per parent. The time off work and lost productivity were calculated using actual data from published sources. The number of days taken off work was calculated on the basis of an allowance contained in work contracts in The Netherlands. However, it was unclear for what year the average days off work were calculated. The price year was 1998.

**Currency**
Euros (Euro).
Sensitivity analysis
One-way sensitivity analyses were conducted on the costs for lifetime treatment of sequelae, and the price and efficacy of the vaccine.

Estimated benefits used in the economic analysis
The incremental benefits from the vaccine were 526 QALYs per year and 386 life-years gained. It was unclear whether the side effects of vaccination were included in the analysis. The benefits were discounted at a rate of 4%.

Cost results
The total costs of the meningococcal vaccination amounted to Euro 11,601,356.

In the absence of such a vaccine, the annual costs consisted of the acute phase of illness (Euro 1,426,634), the treatment of sequelae (Euro 3,801,121) and lost productivity (Euro 21,389).

As a result of the vaccination programme, a substantial amount of these costs were prevented. The acute medical costs fell by Euro 972,850, the cost of treating sequelae was reduced by Euro 2,339,813 and there was no productivity loss.

The incremental costs of the vaccination programme amounted to Euro 8,267,304.

These costs were accumulated throughout the 76 years of the model. It was unclear whether the costs of side effects were included.

Synthesis of costs and benefits
The estimated costs and benefits were combined in cost-effectiveness and cost-utility analyses. An incremental analysis was performed.

The incremental cost-effectiveness ratio (ICER) was Euro 15,721 per QALY and Euro 21,415 per life-year gained.

As a consequence of the sensitivity analysis, three parameters in particular were found to have important impacts on the results. These parameters were the vaccine price, the coverage rate and the quality of life.

If efficacy were reduced by 50%, the ICER would increase by 53%.

In the sensitivity analysis, the price of the vaccine was varied from Euro 7 to Euro 14. A change in the price of the vaccine of 50% led to a change in the ICER of the same order of magnitude.

The results were less sensitive to changes in the indirect costs or the costs of lifetime care for sequelae.

Authors' conclusions
The meningococcal B outer-membrane vesicle (OMV) vaccine is a potentially cost-effective intervention.

CRD COMMENTARY - Selection of comparators
The authors justified the choice of the comparator on the grounds that it was current practice in The Netherlands. You should decide if this is appropriate 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. It was not clear how the authors combined estimates of effectiveness when two or more sources were cited for these parameters. Further, the authors did not specifically address the issue of differences between the primary studies used to estimate effectiveness. The authors justified some of their assumptions with reference to evidence from other vaccination programmes and medical
literature. Some of these estimates were investigated by sensitivity analyses.

**Validity of estimate of measure of benefit**
The estimate of the benefits was obtained directly from the effectiveness analysis, and the choice of estimates appears justified. The measures of quality of life included in the model only took account of neurological and physical sequelae arising from meningococcal infection. The impact of the acute phase of meningococcal disease or septic shock on quality of life was omitted. Consequently, the benefits from the vaccination programme may have been underestimated.

**Validity of estimate of costs**
Most of the categories of cost relevant to the perspective adopted were included in the analysis. However, some relevant costs were omitted. For example, the indirect costs were restricted to the lost productivity associated with parents visiting hospitalised infants. The authors acknowledged that the indirect costs did not include the costs borne by parents who provide lifetime care for their child. Similarly, future productivity losses arising from the patients' disability were not included. Consequently, the cost-effectiveness of the vaccination programme may have been underestimated. In addition, it was unclear whether the costs of treating side effects of the vaccine were incorporated in the analysis. However, the authors stated that these effects were likely to be mild and, therefore, may not require treatment. Further, in their model, the authors focused only on amputations, scars and neurological sequelae leading to long-term care (i.e. seizures, spasticity and mental retardation). The exclusions of other complications and sequelae may have understated the cost-savings associated with the vaccine.

The costs and the quantities were reported separately. A sensitivity analysis of the quantities was not conducted and this may limit the interpretation of the study findings. A sensitivity analysis of the price of the vaccine was conducted.

**Other issues**
The authors did not make appropriate comparisons of their findings with those from other studies. However, the issue of generalisability of the study to other countries was addressed. The authors argued that their assumptions and the costs were likely to be similar in other countries with living standards comparable to those in The Netherlands. The authors do not appear to have presented their results selectively. Their conclusions reflected the scope of the study. The authors acknowledged that, in general, their estimates for several parameters were conservative. If, in practice, these assumptions are invalidated, they will impact on the cost-effectiveness of the vaccine. In addition, the authors also recognised that the use of expert opinion may have increased the uncertainty.

**Implications of the study**
The authors acknowledge that the decision to introduce this vaccination programme should not be determined solely by the results of their study. Instead, other budgetary, social and physiological factors should also be taken into consideration. If the vaccine is introduced, the authors suggest using their model to continue to assess its cost-effectiveness.

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None stated.

**Bibliographic details**

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11567765
Other publications of related interest

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Subject indexing assigned by NLM

MeSH
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