Modelling cost effectiveness of meningococcal serogroup C conjugate vaccination campaign in England and Wales
Trotter C L, Edmunds W J

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 a meningococcal serogroup C conjugate (MenC) vaccination campaign for 0- to 17-year-olds. The analysis considered universal screening for 0- to 17-year-olds and also alternative vaccination strategies, defined according to the age class and delivery methods. The following alternative interventions were considered:

- vaccination of 0- to 4-month-olds by a general practitioner (GP) (3 doses);
- vaccination of 5- to 11-month-olds by a GP (2 doses);
- vaccination of 1- to 4-year-olds by a GP (1 dose);
- vaccination of 5- to 17-year-olds at school (1 dose); and
- vaccination of 16- to 17-year-olds not in education by a GP (1 dose).

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised individuals aged 0 to 17 years. The study groups differed according to the target population considered in each vaccination programme.

Setting
The setting was primary care and a school. The economic study was conducted in England and Wales.

Dates to which data relate
The effectiveness evidence was derived from studies published between 1993 and 2001. The data on resource use and costs came from studies published between 1996 and 2000. The price year was 2000.

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

Modelling
The authors stated that a model was used to assess the impact of the vaccination campaign, by following an imaginary
vaccine campaign cohort over a lifetime timeframe. Eighteen birth cohorts of people aged 0 to 17 years, who were offered vaccine in the first year of the campaign, were considered. Other details of the model, which was presumably an analytic calculation, were not provided.

**Outcomes assessed in the review**
The outcomes assessed from published studies were:

- the number of individuals in each cohort at birth;
- disease incidence (the data were adjusted to account for infections not confirmed by laboratories);
- case fatality ratios;
- the rate of long-term sequelae;
- vaccine efficacy; and
- vaccine coverage.

Average estimates, from ranges of values derived from published studies, were used for some of these model inputs.

**Study designs and other criteria for inclusion in the review**
Most of the outcomes were derived from official statistics, such as the Office for National Statistics, the Public Health Laboratory Service, the hospital episode statistics, and other published studies (including a meta-analysis).

**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**
The outcome measures were derived from approximately 7 published studies and 4 official statistics sources.

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

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

**Results of the review**
There were 658,800 individuals in each cohort at birth.

In the case of high estimates (based on 1998-99 values), the overall disease incidence (per 100,000) was 2.94. It was
also assessed for different age groups. The disease incidence ranged from 0.50 for individuals older than 64 years to 31.53 for children younger than 1 year.

In case of low estimates (based on 1989-94 values), the overall disease incidence (per 100,000) was 0.84. It ranged from 0.23 for individuals older than 64 years to 9.64 for children younger than 1 year.

Similarly, for low mortality estimates, the overall case fatality ratio was 7.8%. It ranged from 31.6% for individuals older than 64 years to 1.6% for individuals in the 5- to 9-year age class.

For medium mortality estimates, the overall case fatality ratio was 9.6%. It ranged from 36% for individuals older than 64 years to 2.8% for individuals in the 5- to 9-year age class.

For high mortality estimates, the overall case fatality ratio was 12.6%. It ranged from 30.6% for individuals older than 64 years to 3.4% for individuals in the 5- to 9-year age class.

The rate of long-term sequelae (including hearing impairment, skin scarring, amputation, neurological disorders, and so on) was 7% (range: 3 - 15).

Vaccine efficacy was 92% (95% confidence interval, CI: 65 - 98) for children younger than 2 years, 97% (95% CI: 77 - 99) for teenagers, and 95% for individuals in the 2- to 12-year age class.

Vaccine coverage was 89% in children under 1 year, 82% in 1- to 4-year-olds, 87% in 5- to 13-year-olds, 83% in 14- to 15-year-olds, and 65% in 16- to 17-year-olds in full time education.

Methods used to derive estimates of effectiveness
Some assumptions were also made to derive some effectiveness estimates. These were then combined with the outcomes estimated from the literature to calculate the life-year saved (LYS) with the vaccination strategy.

Estimates of effectiveness and key assumptions
It was assumed that patients died or acquired lifelong immunity to meningococcal disease and were removed from the susceptible pool. In addition, patients dying from MenC disease lost the average life expectancy for the age at which they died. It was also assumed that outbreaks would not occur after the start of the vaccination program. The vaccine coverage in 16- to 17-year-olds not in education was assumed to be 50%.

Measure of benefits used in the economic analysis
The summary benefit measures used were the number of meningitis C cases avoided, the number of deaths avoided, and the LYS in comparison with no vaccination. Only the number of meningitis C cases avoided and the LYS were combined with the cost estimates. Benefits occurring in the future were discounted at an annual rate of 3%.

Direct costs
An annual discount rate of 3% was applied as lifetime costs were estimated. The unit costs and the quantities of resources used were reported separately. The health services included in the economic evaluation were hospital stay in intensive care or ward, outpatient visits, GP and nurse consultations, treatment of meningococcal disease, treatment of sequelae, and management of an outbreak. These items were used to calculate the impact of the disease. The costs of the vaccination programme (vaccine, nursing, administration, consumables, GP services, wastage, television advertising and leaflet campaign, treatment of adverse events) were also calculated. Finally, the net costs (cost of vaccine campaign minus the costs saved due to the vaccination programme) were estimated. The cost/resource boundary of the NHS was used. Both resource use and costs were estimated on the basis of authors' assumptions and data derived from studies published between 1996 and 2000. The costs were presented in 2000 values using the hospital and community heath services pay and prices index.
Statistical analysis of costs
The costs were treated deterministically in the base-case.

Indirect Costs
The indirect costs were not considered.

Currency
UK pounds sterling ({}).

Sensitivity analysis
Univariate sensitivity analyses were conducted to assess the robustness of the estimated cost-effectiveness ratios to variations in all effectiveness and cost data. The parameters were varied one at a time, each within its given range. A multivariate sensitivity analysis (Monte Carlo simulation), using 500 iterations, was also carried out to simulate alternative scenarios.

Estimated benefits used in the economic analysis
With the overall UK vaccination campaign (0- to 17-year-olds), 7,880 cases of meningitis C were avoided, 845 deaths were avoided, and the number of LYS in comparison with no vaccination was 22,799.

For vaccination of 0- to 4-month-olds by a GP (3 doses), 365 cases of meningitis C were avoided, 30 deaths were avoided, and the number of LYS was 832.

For vaccination of 5- to 11-month-olds by a GP (2 doses), 512 cases of meningitis C were avoided, 42 deaths were avoided, and the number of LYS was 1,165.

For vaccination of 1- to 4-year-olds by a GP (1 dose), 2,422 cases of meningitis C were avoided, 212 deaths were avoided, and the number of LYS was 5,879.

For vaccination of 5- to 17-year-olds at school (1 dose), 4,432 cases of meningitis C were avoided, 539 deaths were avoided, and the number of LYS was 14,354.

For vaccination of 16- to 17-year-olds not in education, by a GP (1 dose), 149 cases of meningitis C were avoided, 22 deaths were avoided, and the number of LYS was 569.

Cost results
The net costs (cost of vaccine campaign minus cost-savings) relative to no vaccination were 142.8 million with the overall UK vaccination campaign (0- to 17-year-olds).

The corresponding net costs for the other strategies were:

12.2 million for vaccination of 0- to 4-month-olds by a GP (3 doses);
11.1 million for vaccination of 5- to 11-month-olds by a GP (2 doses);
34.3 million for vaccination of 1- to 4-year-olds by a GP (1 dose);
79.4 million for vaccination of 5- to 17-year-olds at school (1 dose); and
5.9 million for vaccination of 16- to 17-year-olds not in education, by a GP (1 dose).
Synthesis of costs and benefits
Incremental cost-effectiveness ratios (ICERs) were calculated to combine the costs and benefits of the vaccination strategies versus no vaccination.

The cost per case avoided was:

18,112 with the overall UK vaccination campaign (0- to 17-year-olds);
33,326 for vaccination of 0- to 4-month-olds by a GP (3 doses);
21,624 for vaccination of 5- to 11-month-olds by a GP (2 doses);
14,138 for vaccination of 1- to 4-year-olds by a GP (1 dose);
17,907 for vaccination of 5- to 17-year-olds at school (1 dose); and
39,341 for vaccination of 16- to 17-year-olds not in education, by a GP (1 dose).

The cost per LYS was:

6,259 with the overall UK vaccination campaign (0- to 17-year-olds);
14,630 for vaccination of 0- to 4-month-olds by a GP (3 doses);
9,493 for vaccination of 5- to 11-month-olds by a GP (2 doses);
5,826 for vaccination of 1- to 4-year-olds by a GP (1 dose);
5,529 for vaccination of 5- to 17-year-olds at school (1 dose); and
10,291 for vaccination of 16- to 17-year-olds not in education, by a GP (1 dose).

The sensitivity analysis showed that the estimated ICERs were sensitive to the incidence of disease, the case fatality ratio, and the vaccine cost and efficacy. The life-years gained were sensitive to the choice of the discount rate.

The multivariate analysis suggested that, in the base-case (3% annual discount rate, high incidence, medium case fatality ratio), 95% of the simulations resulted in an ICER of less than 10,000 per LYS.

With a low incidence, 25% (high case fatality ratios), 53% (medium case fatality ratios) and 75% (low case fatality ratios) of simulations resulted in an ICER higher than 30,000.

Authors' conclusions
The meningococcal serogroup C conjugate (MenC) vaccination was likely to be a cost-effective strategy in all age groups at high disease incidence values. Vaccination was also more cost-effective in children aged 1 to 4 years (administered by a GP) and those aged 5- to 17-years who were at school, than in infants under 12 months of age or young people aged 16 to 17 years who were not at school.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The study covered all possible vaccination strategies, which were defined according to the vaccine provider setting and age. The basic comparator was no vaccination, which represented the standard scenario before the 1999 UK Department of Health guidance. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used data derived from the literature and authors’ assumptions. A formal review of the literature was not conducted and the primary sources were identified selectively. Most of the sources were UK statistics. Little information on other studies was provided. However, data on vaccine efficacy were taken from early studies and should be considered with caution. The assumptions used appear to have been those of the authors and no external expert opinion was used to support them. The issue of uncertainty was addressed in the sensitivity analysis, which investigated all the assumptions and the robustness of the results to variations in all model inputs. This enhanced the validity of the analysis.

Validity of estimate of measure of benefit
The summary benefit measures were typical of vaccination programmes, but the use of LYS made the benefits of the current study comparable with those of other health care interventions. Discounting was relevant, owing to the long time horizon of the analysis, and was appropriately performed. The authors noted that quality of life issues were not considered, mainly because of the lack of available data.

Validity of estimate of costs
The authors explicitly stated the perspective adopted in the study. As such, it appears that all the relevant categories of costs have been included in the analysis. The unit costs, quantities of resources used and the price year were reported, in detail, thus it should be possible to replicate the study and perform reflation exercises in other settings. The source of the data was provided and the authors reported all the assumptions made in the analysis. All of these assumptions were investigated in the sensitivity analyses. Overall, the cost analysis appears to have been conducted satisfactorily.

Other issues
The authors did not compare their findings with those from other studies. They also did not address the issue of the generalisability of the study results to other settings. However, the fact that all the steps of the analysis (cost calculations, assumptions and efficacy data) were reported enhances the external validity of the study. The study referred to specific target populations and this was reflected in the conclusions. The authors admitted that the issue of herd immunity was not considered in the analysis, but its inclusion would further improve the cost-effectiveness of vaccination.

Implications of the study
The study results supported the implementation of meningococcal C vaccination in 0- to 17-year-olds, especially if school based.

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None stated.

Bibliographic details

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Other publications of related interest

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Subject indexing assigned by NLM

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