Cost-effectiveness of immunization strategies for the control of serogroup C meningococcal disease

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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

Four strategies for the control of serogroup C meningococcal disease (CMD) were examined. These were:

the "do nothing" strategy, implying no vaccination besides prophylactic measures for close contacts of CMD cases according to current Canadian guidelines;

surveillance and implementation of a mass immunisation campaign using meningococcal serogroup C conjugate (MenC-Con) after the beginning of an epidemic (usually in winter), targeting non-immunised persons aged 2 months to 21 years according to recommended age-specific schedules in Canada, and effective in the second epidemic year;

routine immunisation with three doses of MenC-Con administered at ages 2, 4 and 6 months when other childhood vaccines are administered; and

routine immunisation with one dose of MenC-Con given at age 12 months when another childhood vaccine is administered.

Type of intervention

Primary prevention.

Economic study type

Cost-effectiveness analysis and cost-utility analysis.

Study population

The study population comprised a hypothetical cohort followed from birth up to 24 years of age.

Setting

The setting was primary care. The economic study was carried out in Canada.

Dates to which data relate

The effectiveness data were obtained from studies published between 1995 and 2003. The resource use data and costs came from sources published in 2002 and 2003. The price year was 2002.

Source of effectiveness data

The effectiveness evidence was derived from a synthesis of completed studies and experts' opinions.

Modelling

A decision model was used to examine the costs and benefits of the alternative strategies under evaluation in 25 hypothetical cohorts of 75,000 births, which were followed for 25 years. Consequently, simulation extended over a 49-year period, from the year 2002 to the year 2050. Other details of the model were not reported.

Outcomes assessed in the review

The outcomes assessed from the literature were:

the age-specific mortality rates;

the quality weights used to calculate quality-adjusted life expectancy;

the incidence of endemicity;

the incidence of epidemic episodes;

the incidence of hyperendemicity;

the case-fatality rate;

the quality of life reduction in survivors with sequelae;

the productivity reduction in survivors with sequelae;

the initial vaccine efficacy rate;

the frequency of adverse reactions; and

vaccine coverage of target population in mass immunisation campaign and in routine infant programmes.

Study designs and other criteria for inclusion in the review

The authors did not state whether a literature review was undertaken to identify the primary studies. Some data were derived from official statistics. The design and characteristics of other studies were not reported.

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

Nine primary studies provided evidence.

Methods of combining primary studies

Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
The incidence of endemicity (annual rate) was 1.2 CMD cases per million person-years (range: 0.6 - 1.8).

The incidence of epidemic episodes (average annual rate during a 6-year period) was 12.6 CMD cases per million person-years (range: 6.3 - 18.9).

The incidence of hyperendemicity (annual rate) was 24.1 CMD cases per million person-years.

The case-fatality rate was 14% (range: 11 - 18).

The sequelae rate was 13%.

The quality of life reduction in survivors with sequelae was 28%.

The productivity reduction in survivors with sequelae was 20%.

The initial vaccine efficacy rate was 90%.

The frequency of adverse reactions was 1/3,000 doses.

The vaccine coverage rate was 84% in the mass immunisation campaign and 90% in routine infant programmes.

Methods used to derive estimates of effectiveness
A Delphi process was followed to derive some estimates used in the decision model. A group of 7 Canadian experts was contacted to define seven plausible epidemiological scenarios and their relative probability of occurrence during the 49-year study period.

Estimates of effectiveness and key assumptions
The following scenarios (and their probabilities) were considered:

a low incidence of endemicity, (p=0.03);

one 6-year outbreak in the middle of the study period, (p=0.16), two outbreaks, (p=0.23), three outbreaks, (p=0.28), four outbreaks, (p=0.18), and five outbreaks, (p=0.10); and

a high incidence of hyperendemicity, (p=0.02).

The decrease in vaccine efficacy was 1% per year (range: 0 - 2% per year).

Measure of benefits used in the economic analysis
The summary benefit measures were the number of CMD cases and quality-adjusted life-years (QALYs). Both were discounted at an annual rate of 3%. The utility values were derived from the literature.

Direct costs
Discounting was relevant since long-term costs were estimated. An annual discount rate of 3% was applied. The unit costs were not presented separately from the quantities of resources used for all items. The health services included in the economic evaluation were those related to vaccine acquisition and its administration, treatment of CMD cases (e.g. prophylactic measures, hospital care, and ambulatory care of acute infections and of permanent sequelae), and the

treatment of adverse reactions. The cost/resource boundary of the health care system was adopted in the analysis of the direct costs. The costs and resource use were estimated from published studies and estimates from the Quebec Ministry of Health. Other data came from experts' opinions. The price year was 2002. All prices anterior to 2000 were adjusted using the Canadian Price Index for health and personal care.

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

Indirect Costs
Indirect costs (i.e. productivity losses) were included in the economic evaluation because a societal perspective was adopted. Productivity losses from deaths and from disabilities when survivors reached workforce age were derived from data on gender-specific earnings of Canadians in 1998 and age- and gender-specific employment rates in 1999. The unit costs were not presented separately from the quantities of resources used. The price year was 2002. All of the costs were discounted at an annual rate of 3%.

Currency
Canadian dollars (Can$).

Sensitivity analysis
Sensitivity analyses were performed to examine the robustness of the cost-effectiveness of the four alternative strategies to variations in selected baseline model inputs. Experts set the ranges over which the inputs were varied. A Monte Carlo simulation using 1,000 iterations was also carried out in order to perform a multivariate sensitivity analysis.

Estimated benefits used in the economic analysis
The estimated QALYs were not reported.

The number of CMD cases depended on the epidemiological scenario. They ranged from 193 for low incidence endemicity to 3,007 for hyperendemicity with no vaccination, from 58 to 904 with routine vaccination with three doses, from 68 to 1,030 with routine vaccination with one dose, and from 283 to 289 with mass vaccination.

In general, the most effective strategy was a 3-dose vaccination programme. This resulted in approximately 70% prevention of CMD cases in comparison with no vaccination. A 1-dose programme was slightly less effective (approximately 65% prevention of CMD cases).

Cost results
In 25 cohorts of 75,000 births, the total undiscounted health system costs were Can$288,399 million for routine vaccination with three doses, Can$96,133 million for routine vaccination with one dose, and Can$90,031 million for one mass vaccination.

In all strategies, vaccine purchase represented the largest cost component. The health system costs for the no vaccination option ranged from Can$5,185 million to Can$80,666 million depending on the epidemiological scenario.

The indirect costs were reported only for the no vaccination option. These ranged from Can$33,525 million to Can$521,660 million depending on the epidemiological scenario.

Synthesis of costs and benefits
Incremental cost-utility and cost-effectiveness ratios were calculated to combine the costs and benefits.

Depending on the epidemiological scenario, the incremental (societal) cost per case of CMD averted in comparison with no vaccination ranged from Can$2,656,000 to Can$62,000 with routine immunisation with three doses, from Can$903,000 to dominant (lower costs and higher effectiveness) with routine immunisation with one dose, and from Can$302,000 to Can$453,000 with mass immunisation.

Depending on the epidemiological scenario, the incremental (societal) cost per QALY gained in comparison with no vaccination ranged from Can$598,000 to Can$14,000 with routine immunisation with three doses, from Can$203,000 to dominant (lower costs and higher effectiveness) with routine immunisation with one dose, and from Can$68,000 to Can$101,000 with mass immunisation.

Using the probabilities of occurrence of the different epidemiological scenarios in the routine 1-dose strategy, the weighted average cost per CMD case averted was Can$190,000, or Can$23,000 per life-year gained, or Can$42,000 per QALY gained.

The sensitivity analysis showed that vaccine acquisition cost and disease incidence were the variables with the greatest influence. For the routine 1-dose immunisation strategy, societal cost-neutrality was reached for a vaccine purchased at $12 per dose (base-case purchase cost $50). The population endemicity incidence resulting in a break-even between programme costs and societal benefits was 10.6 CMD cases per million per year for the 1-dose strategy, and 28.6 per million per year for the 3-dose strategy. In general, the 1-dose routine immunisation strategy appears to have been the most cost-effective in the most likely scenarios.

Authors' conclusions

A 1-dose routine programme was the most cost-effective strategy for the long-term control of serogroup C meningococcal disease (CMD) in Canada.

CRD COMMENTARY - Selection of comparators

The selection of the comparators reflected the choice of standard care (no vaccination) and the inclusion of three vaccination strategies that could be implemented in Canada. The authors noted that not all possible strategies were considered. For example, a 2-dose routine programme administered before one year of age was not taken into consideration. Similarly, programmes targeting school-age children were not considered. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness

The clinical data that were used in the decision model came from published studies and local sources. However, it was not stated explicitly whether a systematic review of the literature had been undertaken to identify the primary studies, which appear to have been identified selectively. A description of the design and characteristics of the primary studies was not provided. This limits the possibility of assessing the validity of the primary sources. Similarly, the issue of potential differences among the primary studies was not addressed. Some assumptions, based on a Delphi process, were also made. Some key model parameters were varied in the sensitivity analysis.

Validity of estimate of measure of benefit

Several summary benefit measures were used in the economic analysis. The use of QALYs was appropriate because they are comparable with the benefits of other health care interventions. Published quality weights were used to calculate the QALYs. However, limited information on the sources used was provided. Discounting was carried out, as suggested by Canadian guidelines.

Validity of estimate of costs

The analysis was carried out from a societal perspective, thus the indirect costs were included in the economic evaluation. The costs were also analysed from the more restricted perspective of the health care system, which could be relevant to decision-makers. However, limited details on the unit costs and quantities of resources used were given,

which reduces the possibility of replicating the cost analysis in other settings. The source of the data was reported. Experts' opinions were used when published or local data were not available. Probabilistic distributions were assigned to costs in the multivariate sensitivity analysis. The price year was reported, which aids reflation exercises.

Other issues

The authors did not make extensive comparisons of their findings with those from other studies, reporting results from only a few published economic evaluations on vaccination programmes. In terms of the generalisability of the study results to other settings, the authors stated that most of the data used in the model were specific to the Canadian context, although the conclusions of the analysis could be extrapolated to other industrialised countries. The authors noted that their analysis was conservative and did not consider other potential benefits of vaccination.

Implications of the study

The study results supported the implementation of a 1-dose routine vaccination programme against CMD. The authors suggested that more studies should be carried out to examine the long-term efficacy of the vaccine, which represented one of the most uncertain model inputs.

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Bibliographic details

De Wals P, Nguyen V H, Erickson L J, Guay M, Drapeau J, St-Laurent J. Cost-effectiveness of immunization strategies for the control of serogroup C meningococcal disease. Vaccine 2004; 22(9-10): 1233-1240

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Other publications of related interest

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Jodar L, Feavers IM, Salisbury D, et al. Development of vaccines against meningococcal disease. Lancet 2002;359:1499-508.

Miller E, Salisbury D, Ramsay M. Planning, registration, and implementation of an immunization campaign against meningococcal serogroup C disease in the UK: a success story. Vaccine 2002;20:S58-67.

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