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
Polysaccharide vaccine against Neisseria meningitidis, which can cause meningitis, septicaemia and severe complications, was examined. Three vaccination options using different target populations were examined in 15 to 19-year-olds.

Option 1 was the vaccination of students in secondary school (years 10 - 12) and first-year university from a defined regional population with a high incidence of disease.

Option 2 was the vaccination of all year 12 students in a larger population, approximating a state or territory with a lower incidence (and which contains the regional area).

Option 3 comprised both options 1 and 2.

Type of intervention
Primary prevention (vaccination).

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

Study population
The hypothetical study population comprised 15 to 19-year-olds in the general population.

Setting
The setting was the community. The economic study was carried out in Australia.

Dates to which data relate
The effectiveness data were derived from studies published between 1995 and 1999. No dates for resource use were reported. The price year was 1999.

Source of effectiveness data
The effectiveness data were derived from a review of published and unpublished studies, augmented by the authors' assumptions.

Modelling
A decision tree model was constructed to model the costs and benefits of the vaccination options over 5 years, the baseline duration of vaccine efficacy. Vaccine administration occurred at the commencement of the programme (year
1. The model allowed for the transition into the next age cohort.

Outcomes assessed in the review
The model inputs estimated from the literature were vaccine efficacy, time to averting disease, incidence of vaccine side effects, and disability weights for acute episode, after-effects and long-term sequelae.

Study designs and other criteria for inclusion in the review
Not stated.

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 effectiveness data were obtained from seven primary studies.

Methods of combining primary studies
The primary studies were combined using narrative methods.

Investigation of differences between primary studies
Not stated.

Results of the review
Vaccine efficacy was 90%.

The time to averting disease was 2 weeks.

The incidence of vaccine side effects was 1 case per 100,000 vaccinated.

The disability weights were 0.913 for acute episode, 0.226 for after-effects and 0.133 for long-term sequelae.

The model assumed that aversion of disease occurred 2 weeks after vaccination.

Methods used to derive estimates of effectiveness
The authors made some assumptions and derived data from unpublished studies to identify other model inputs.

Estimates of effectiveness and key assumptions
The defined regional area included 10,000 individuals while the larger population comprised 50,000 teenagers. Both areas included a total of 58,000 potential patients.
In terms of disease incidence without vaccination, there were 20 cases per 100,000 population among high-risk 15 to 19-year-olds (regional area) and 7 cases per 100,000 population among high-risk 20 to 24-year-olds. There were 6 cases per 100,000 population in the general population of 15 to 19-year-olds, and 1.2 cases per 100,000 population in the general population of 20 to 24-year-olds.

Vaccination coverage was 90% for high-school students and 60% for first-year university students.

These data were mainly derived from personal communications based on the 1999 Victorian measles vaccination campaign and 1997 Higher Education Office data.

Measure of benefits used in the economic analysis
The main benefit measures used in the cost-effectiveness analysis were the disability-adjusted life-years (DALYs) and life-years saved (LYS). The disability weights used to calculate the DALYs were derived from published studies. Other benefit measures derived from the decision model were the number of cases of disease averted. The benefit measure used in the cost-benefit analysis was avoided lost earnings due to morbidity and premature mortality from meningitis. These were calculated using the human capital approach, and although this was not explicitly stated as the methodology used by the authors, the approach was consistent with conventional cost-benefit analysis. A 5% discount rate was applied to events occurring after the first year.

Direct costs
A 5% discount rate was applied to the costs incurred after the first year, as the time horizon of the model was 5 years. The unit costs were reported separately from the quantities of resources. Only vaccination costs were included in the economic evaluation. These costs referred to the vaccine itself, vaccine administration (staff, travel and equipment), treating side effects of the vaccine, and campaign promotion. The costs of disease treatment and public health follow-up costs (arising from training and providing chemoprophylaxis to close contacts) were also included in the analysis to calculate cost-savings. The cost/resource boundary adopted in the analysis reflected the societal perspective of the study. The direct costs were estimated from the point of view of the Department of Human Services (DHS) in Victoria, Australia. The costs and quantities were mainly estimated on the basis of actual data derived from the DHS. The price year was 1999.

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

Indirect Costs
Since a societal perspective was adopted, the cost-effectiveness analysis included the avoided lost earnings due to morbidity and premature mortality from meningitis, in order to calculate the indirect cost-savings. The indirect costs were obtained from the Australian Bureau of Statistics. The price year was 1999 and a 5% discount rate was applied.

Currency
Australian dollars (Aus$).

Sensitivity analysis
Several sensitivity analyses were conducted on the outcome cost per DALY, to assess the robustness of the study conclusions to variations in some model inputs. One-way sensitivity analyses were performed by varying the vaccine efficacy, incidence rates, duration of protection, case fatality rate (CFR) and discount rate. Two-way sensitivity analyses were conducted by simultaneously varying the incidence rates in the high-risk group and the general population, the CFR and the duration of vaccine efficacy, and the discount rate and the duration of vaccine efficacy.
**Estimated benefits used in the economic analysis**

The number of people vaccinated was 8,250 with option 1, 45,000 with option 2 and 51,450 with option 3.

The number of discounted (undiscounted) cases averted was 5.6 (6.1) with option 1, 8.5 (9) with option 2 and 13.0 (13.9) with option 3.

The number of deaths averted was 0.7 with option 1, 1.0 with option 2 and 1.5 with option 3.

The number of discounted (undiscounted) LYS was 12.2 (40.3) with option 1, 18.6 (60.5) with option 2 and 28.4 (92.8) with option 3.

The number of discounted (undiscounted) DALYs averted was 13.7 (43.1) with option 1, 20.8 (64.6) with option 2 and 31.8 (99.2) with option 3.

In the cost-benefit analysis, the total undiscounted lost earnings avoided were Aus$1,118,164 with option 1, Aus$1,672,006 with option 2 and Aus$2,570,727 with option 3.

The total discounted lost earnings avoided were Aus$393,644 with option 1, Aus$592,414 with option 2 and Aus$908,500 with option 3.

**Cost results**

The total costs of the vaccination programme were Aus$288,724 with option 1, Aus$1,550,177 with option 2 and Aus$1,771,534 with option 3.

The total undiscounted direct cost-savings (due to treatment cost-savings and public health follow-up cost-savings) were Aus$289,462 with option 1, Aus$334,849 with option 2 and Aus$369,424 with option 3.

The total discounted direct cost-savings (due to treatment cost-savings and public health follow-up cost-savings) were Aus$259,221 with option 1, Aus$299,619 with option 2 and Aus$338,345 with option 3.

Consequently, the net discounted (undiscounted) cost of the programmes was Aus$24,953 (-Aus$739) with option 1, Aus$1,243,651 (Aus$1,215,327) with option 2 and Aus$1,433,189 (Aus$1,402,110) with option 3.

**Synthesis of costs and benefits**

Average and incremental analyses were performed to combine the costs and benefits of each of the three vaccination options in comparison with no vaccination.

When no cost-savings were deducted, the average cost per person vaccinated was Aus$35 with option 1, Aus$34.45 with option 2 and Aus$34.43 with option 3;

the average discounted (undiscounted) cost per case averted was Aus$51,725 (Aus$47,672) with option 1, Aus$182,959 (Aus$171,705) with option 2 and Aus$136,603 (Aus$127,465) with option 3;

the average discounted (undiscounted) cost per LYS was Aus$23,623 (Aus$7,162) with option 1, Aus$83,477 (Aus$25,643) with option 2 and Aus$62,443 (Aus$19,082) with option 3;

the average discounted (undiscounted) cost per DALY averted was Aus$21,097 (Aus$6,704) with option 1, Aus$74,554 (Aus$24,006) with option 2 and Aus$55,766 (Aus$17,863) with option 3.

When all the direct costs were deducted, option 1 was cost-saving in undiscounted terms for all outcome measures and cost Aus$1,823 per DALY averted. The undiscounted (discounted) cost per DALY averted was Aus$59,812 (Aus$18,821) for option 2 and Aus$45,115 (Aus$14,138) for option 3.

When options 2 and 3 were compared with option 1, the incremental discounted (undiscounted) cost per DALY averted...
was Aus$177,494 (Aus$58,647) for option 2 and Aus$82,007 (Aus$26,427) for option 3, when no cost-savings were
deducted. When cost-savings were deducted, the values were Aus$171,478 (Aus$56,537) for option 2 and Aus$77,883
(Aus$25,002) for option 3.

The cost-benefit analysis, comparing the net cost of the vaccination programme (cost of vaccination less direct cost-
savings) with the lost earnings avoided, showed that all three options led to benefits in excess of the costs in
undiscounted terms. However, in discounted terms, only option 1 had a positive net benefit (lost earnings avoided
exceed vaccination costs) regardless of whether or not the direct cost-savings were deducted. With option 1, the break-
even incidence rate for 15 to 19-year-olds (the rate at which discounted costs and benefits are equal or net benefits are
zero) was 14/100,000 with no direct cost savings deducted and 1/100,000 with cost-savings deducted. The sensitivity
analyses showed that the estimated cost-effectiveness and cost-benefit ratios were sensitive to variations in the
incidence rate in the general population, discount rate, CFR and duration of vaccine efficacy.

Authors’ conclusions
Polysaccharide vaccination of students in secondary school (years 10 to 12) and first-year university, from a defined
regional population with a high incidence of disease, was a cost-effective vaccination strategy against Neisseria
meningitidis. Under some circumstances, this vaccine option may be cost-saving.

CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. No vaccination was selected as the basic comparator, as the
aim of the study was to assess the active value of each of the three vaccination strategies, which represented feasible
alternatives for vaccination against Neisseria meningitidis. You should decide whether this represents a valid
comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used data derived from published studies and from the authors’ assumptions. In terms of
the data derived from the literature, a formal review was not undertaken. The primary studies were combined using
narrative methods. The authors did not state whether they took into account potential differences between the primary
studies when estimating the effectiveness. The authors’ assumptions were based on unpublished data and personal
communications relating to official statistics for Australia. The sensitivity analyses investigated variability around most
of these assumptions.

Validity of estimate of measure of benefit
DALYs and LYS were used as the principal benefit measures in the cost-effectiveness analysis. The values of disability
weights in the calculation of DALYs were derived from published studies, but uncertainty around these data was not
investigated. The structure of the decision model used to estimate the benefits of the vaccination options was clearly
reported and the benefits were appropriately discounted. The lost earnings avoided were used as monetary benefits in
the cost-benefit analysis. However, the authors did not explicitly state the method used to quantify the value of a life
lost, although the human capital approach appears to have been used. A more detailed discussion of the results from the
cost-benefit analysis would have been helpful.

Validity of estimate of costs
The cost analysis was conducted from a societal perspective. It appears that all the relevant categories of costs have
been included in the analysis. The unit costs were reported separately from the quantities of resources and the price year
was appropriately given. These factors enhance the reproducibility of the study in other settings. A detailed breakdown
of the costs was reported. Both the costs and quantities were treated deterministically. No sensitivity analyses were
conducted on the cost side of the analysis.

Other issues
The authors did not compare their findings with those from other studies. The issue of the generalisability of the study results to other settings was not addressed. Sensitivity analyses were performed, and were reported clearly, but only for the cost per DALY measure. The fact that the costs and quantities were reported separately, and the price year was given, enhances the external validity of the analysis. The study referred to the general population of 15 to 19-year-olds and this was reflected in the conclusions of the analysis.

Implications of the study
The authors highlighted the economic convenience of strategy 1 for vaccination of Neisseria meningitidis among teenagers aged between 15 and 19 years. They noted that "policy decision-making for use of vaccination also requires consideration of non-economic factors, including feasibility of implementation and community risk perception".

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