Instituting a routine varicella vaccination program in Canada: an economic evaluation


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 main analysis compared varicella vaccination (VARIVAX) at 12 months of age with no vaccination. A secondary analysis considered the effects of adding a catch-up programme to vaccinate 12-year-old susceptible children who were older than 1 year when the programme was implemented.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
In the main analysis the study population comprised Canadian children aged 12 months. In the secondary analysis, to estimate the effects of adding a catch-up vaccination programme, the study population comprised susceptible children aged 12 years who were older than one year when the vaccination programme was implemented.

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

Dates to which data relate
The studies used to derive effectiveness dated from 1986 to 2001. The price year was 1998.

Source of effectiveness data
The effectiveness data were derived from a review of published studies and data, supplemented with authors’ assumptions.

Modelling
A model was developed to compare the outcomes of various varicella vaccination strategies. The model simulated the experience of cohorts of children susceptible to varicella infection. The model first calculated the number of infections expected each year given the annual age-specific infection rates and the proportion of the cohort alive and susceptible (i.e. uninfected). The age-specific annual hazards of infection were expressed in terms of varicella infections and the number of susceptible individuals (equation given).

Outcomes assessed in the review
The outcomes assessed in the review were:
annual varicella infections;
the number of individuals susceptible to varicella;
mortality caused by varicella;
hospitalisation rates due to varicella;
the proportion of hospitalisations for varicella as a result of encephalitis, and the proportion of these resulting in long-term disability;
the proportion of vaccinees who become immune to varicella after vaccination;
the proportion of vaccinees who experience waning of immunity over the course of 15 years;
the proportion of vaccinations estimated to result in adverse events requiring a doctor's visit;
the sensitivity and specificity for determining a person's varicella history through recall;
the vaccine coverage rate; and
the number of work days lost due to varicella.

Study designs and other criteria for inclusion in the review
No criteria were applied since a non-systematic review of the literature was conducted.

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
Approximately 18 primary studies were included in the review.

Methods of combining primary studies
The method used to combine the primary studies was not reported, even though in some instances this seems to have been relevant.

Investigation of differences between primary studies
The investigation of differences between primary studies reporting the same type of outcome was not reported.

Results of the review
The age-specific risks of varicella infection ranged from 0.035 cases per susceptible person-years in those aged less than one year, to 0.011 cases per susceptible person-years in those aged over 75 years.
The age-specific hospitalisation rate due to varicella ranged from 2.070 hospitalisations per 100 cases in those aged less than one year, to 5.730 hospitalisations per 100 cases in those aged over 75 years.

Mortality caused by varicella was calculated from reported data using a regression equation. The estimated case-fatality ranged from 0.74 deaths per 100,000 cases in 8-year-olds to 136 per 100,000 cases in 82-year-olds.

It was estimated that encephalitis resulted in 8.7% of hospitalisations for varicella in children and 2.6% in adults, and that 3% of these would suffer long-term disabilities. Thus, the estimated disability rate was 0.2% of hospitalisations in children and 0.1% in adults.

In the main analysis, the proportion of vaccinees completely immune to varicella was 90% initially. Over the course of 15 years, 15% of them would experience waning of immunity. Partial immunity (no risk reduction initially, but at risk of substantially milder break-through cases only) would be obtained in 8% of vaccinees, while the remaining 2% of vaccinees would have complete vaccine failure. In terms of safety, 0.3% of vaccinations would result in adverse events requiring a doctor's visit.

Sensitivity and specificity for determining a person's varicella history through recall were 97% (sensitivity) and 70% (specificity), respectively.

In the main analysis, the vaccine coverage rate was 85%.

Methods used to derive estimates of effectiveness
The authors supplemented the results derived from the review with their own assumptions, some of which were based on published literature.

Estimates of effectiveness and key assumptions
The authors assumed that, for 1-year old children, the determination of varicella history would be 100% accurate.

Based on the literature, the authors assumed that 90% of primary caregivers and 10% of secondary caregivers were female and that 89% of children had both.

Measure of benefits used in the economic analysis
The measures of health benefit used were the number of varicella cases prevented and the life-years gained due to the vaccination programme.

Direct costs
The resource quantities and the unit costs were not reported separately. The direct costs included in the analysis were those of the health service and those incurred by patients. The direct medical costs to the health service were for doctor and allied health care contacts, prescription medications plus tests and procedures for investigating uncomplicated cases of varicella, hospitalisation and the varicella vaccine. With the exception of the cost of the vaccine, there costs were based on published information from other studies. The costs borne by the patient or caregiver were derived from a study in Quebec. These consistsed of alternative childcare, transportation and non-prescription medications. Discounting was relevant since all the costs were incurred over a lifetime. The authors appropriately discounted all future costs at a rate of 3% per annum in accordance with current guidelines at the time of the study. The study reported the total and incremental costs. The price year was 1998.

Statistical analysis of costs
The costs were treated as point estimates (i.e. the data were deterministic).

Indirect Costs
The indirect costs included in the analysis were those due to work time lost, lost productivity resulting from premature death, and lost productivity resulting from severe disability. Work time lost was due to adults taking time off either to tend for children with varicella or because they had the disease themselves. Mean income and employment levels for Canadian adults were used to value work time lost for the care of children with varicella. Lost productivity results from premature death or severe disability were also calculated using age-specific employment rates and income levels. The authors appropriately discounted all future costs at a rate of 3% per annum in accordance with current guidelines at the time. The price year was 1998.

**Currency**
Canadian dollars (Can$).

**Sensitivity analysis**
To address uncertainty in epidemiological, cost and vaccine data, and to understand the importance of model assumptions, all inputs to the model were subjected to a sensitivity analysis.

**Estimated benefits used in the economic analysis**
The varicella vaccination programme would reduce the number of cases from 92,169 with no vaccination to 34,000 per 100,000 eligible children (i.e. a reduction of 58,169 cases per 100,000 children). With a catch-up programme, the number of further cases prevented would be 3,047 per 100,000 eligible children (i.e. a reduction of 61,215 cases per 100,000 children).

The immunisation programme would also reduce the number of deaths from 2.9 with no vaccination to 1.5 per 100,000 children (i.e. a reduction of 1.4 deaths per 100,000 children). With a catch-up programme, the number of further deaths prevented would be 0.6 per 100,000 children (i.e. a reduction of 2.1 deaths per 100,000 children).

**Cost results**
From the health system perspective, for the 11 cohorts of vaccinated children (the duration to complete a catch-up programme), the incremental cost of vaccination relative to no vaccination would amount to Can$21,245,145 without a catch-up programme. With a catch-up programme, the incremental costs for the 11 cohorts would be Can$22,686,280.

From the societal perspective, savings due to the vaccination programme were obtained regardless of whether there was a catch-up programme or not. For the 11 cohorts, the savings were Can$40,852,194 with a catch-up programme and Can$38,338,518 without.

**Synthesis of costs and benefits**
The costs and benefits were combined by calculating the cost-effectiveness ratios (additional cost required per extra case avoided, and the additional cost required for an extra life-year gained). From the health care system perspective, the cost-effectiveness of vaccination without the catch-up programme would be Can$42 per discounted case avoided (Can$38 undiscounted), or Can$84,515 per discounted life-year gained (Can$32,155 undiscounted). With a catch-up programme, the cost-effectiveness would be Can$43 per discounted case avoided (Can$39 undiscounted), or Can$79,391 per discounted life-year gained (Can$28,682 undiscounted).

From the societal perspective, vaccination was the dominant strategy (i.e. it had more beneficial effects and lower costs than non-vaccination). A programme with catch-up is also dominant over one without catch-up from this perspective.

The results from the sensitivity analysis demonstrated that, if the cost of the vaccine was halved, vaccination would lead to savings, even from the health system perspective. The threshold price estimated for the vaccine to result in no increase in health care costs was Can$35. Combination with other vaccines to eliminate vaccine administration costs would drop net health care costs only to Can$18.7 million (from Can$22.7 million). Other inputs to the model had a much smaller influence. However, the discount rate used in the model had a fairly strong impact on the net costs.
Authors' conclusions
Routine varicella vaccination would be likely to reduce the overall costs of varicella substantially, albeit resulting in an increase in health expenditures. In addition, the vaccination of 12-year-old children under an 11-year catch-up programme would not substantially change vaccination cost-consequences. However, the authors reported that the lack of conclusive data in several areas made precise estimates of the cost-effectiveness of vaccination impossible.

CRD COMMENTARY - Selection of comparators
Although no explicit justification was given for using no vaccination programme as the comparator, it would appear that the authors used this comparator because it was only after 1998 that varicella vaccination was licensed in Canada. You should decide if the comparator represents current practice in your own setting. The authors did, however, give a rationale for adding a catch-up programme to vaccinate those at age 12 who were older than 1 year when the programme was implemented. The rationale was to prevent these children from reaching adulthood still susceptible to infection because of reduced transmission resulting from widespread infant vaccination.

Validity of estimate of measure of effectiveness
The authors did not state that a systematic review of the literature had been undertaken to identify relevant research and minimise biases. The sources searched for relevant literature were not reported, and neither were the methods used to undertake the review. For example, the inclusion criteria, the methods used to judge relevance, how results from different sources were combined into a single measure of effectiveness (when appropriate), and how differences between the studies were investigated. The authors supplemented the results derived from the literature with their own assumptions, which, as they pointed out, make any precise estimates untenable. However, the authors appropriately investigated the impact of their assumptions in the sensitivity analysis.

Validity of estimate of measure of benefit
The estimate of benefits was modelled. The benefits were appropriately discounted at 3% per annum.

Validity of estimate of costs
For the societal perspective adopted, all the relevant categories of cost were included in the analysis. In addition, for each category of cost, all major relevant costs were included in the analysis, even though the authors reported that the costs of time lost from unpaid activities (e.g. housework) were not included. The authors also reported that the impact of vaccination on herpes zoster was not included. With evidence suggesting that zoster rates decline with vaccination, this omission, if anything, would bias the results in favour of no vaccination.

The costs and the quantities were not reported separately, which will limit the generalisability of the authors' results. The unit costs were generally derived from the literature. The exception was the cost of the VARIVAX vaccine, where the authors did not name the source from which the cost of one dose of the vaccine was derived. A sensitivity analysis of the prices was appropriately conducted, using ranges that appear to have been appropriate. The costs were appropriately discounted, as they were all incurred over a lifetime, and the rationale for the discount rate was reported. The price year was reported, which will assist possible reflation exercises.

Other issues
The results of the authors' analysis were, for the most part, consistent with those of other economic evaluations of varicella vaccination. The issue of generalisability to other settings was partially addressed in the sensitivity analysis. Even though the methodology of the review was not reported, it would appear that the results have not been presented selectively. The authors' conclusions reflected the scope of the analysis, although the authors warned readers about the limitations of their model and how these may make any precise estimates untenable. The authors reported a number of limitations of their study.

First, the analysis did not consider herd immunity, whereby there is a decreased opportunity for exposure given that the
population manifests fewer cases when large portions of the population are vaccinated. Even though herd immunity may lead to a reduction in cases, it will also lead to an upward shift in the age of infection, with unvaccinated individuals entering adulthood without any prior exposure and, hence, becoming infected when the disease has more serious consequences. However, simulations of herd immunity resulting from varicella vaccination suggested that, if coverage rates are reasonably high, herd immunity is unlikely to have a major impact on the overall results of the programme.

Second, there was a lack of long-term data on the efficacy of the varicella vaccine. The analysis made projections on efficacy that were well beyond the scope of available data.

Finally, even though the effectiveness of the varicella vaccine is widely accepted, the precise level of protection conferred remained uncertain, with the study producing effectiveness estimates that were somewhat different than those used in the base-case. However, a sensitivity analysis of these estimates demonstrated that the cost-effectiveness results did not differ notably.

**Implications of the study**

The authors reported that more complex modelling approaches attempting to dynamically model the impact of vaccination, although possibly yielding slightly more precise estimates, would still be unable to overcome the lack of long-term data. However, based on the results of their study and those from other studies, the authors recommended varicella vaccination on the basis that there would be substantial gains to society.

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**Other publications of related interest**


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