The cost-effectiveness of varicella vaccination in Canada

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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
Three vaccination strategies for varicella were examined:

- routine vaccination at 1 year of age (infant strategy);
- infant strategy plus vaccination of 5- and 11-year-old children for the first 5 years of the programme (catch-up strategy); and
- routine vaccination at 12 years (preteen strategy).

Type of intervention
Other vaccination.

Economic study type
Cost-effectiveness analysis.

Study population
The study comprised the general population of children, as relevant in the different vaccination strategies.

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

Dates to which data relate
The effectiveness and resource use data were obtained from studies published between 1997 and 2001. The costs were reported in 1997 to 1998 values.

Source of effectiveness data
The effectiveness evidence was derived from published studies, augmented by the authors' assumptions.

Modelling
Two age-structured deterministic models were used to assess transmission patterns of the disease, with and without the three vaccination strategies. The first model was constructed to assess the impact of vaccination on varicella, while the second was elaborated to investigate the impact of vaccination on breakthrough varicella and zoster. The full details of the models used were published elsewhere (see Other Publications of Related Interest).

Outcomes assessed in the review
The outcomes estimated from the published studies were:
vaccine coverage,
the rate at which temporarily protected individuals become partially susceptible to varicella,
the percentage of individuals who become temporarily protected after vaccination,
the percentage of individuals for whom vaccine fails completely,
the rate of varicella acquisition of vaccinees compared with non-vaccinees,
the proportion of temporarily protected individuals who become immune due to contact with varicella,
the rate of varicella infectiousness of vaccinees compared with non-vaccinees,
the percentage of cases that visit a physician,
the number of consultations per episode,
the percentage of hospitalisation per case,
the mean inpatient days per hospitalisation, and
the deaths per 100,000 cases.

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 evidence was derived from five primary studies.

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

Investigation of differences between primary studies
Not carried out.

Results of the review
The vaccine coverage was 90% (range: 50 - 95) in infants and 80% (range: 50 - 90) in children.
The rate at which temporarily protected individuals become partially susceptible to varicella was 0.031 (worst case: 0.085; best case: 0.021).

The percentage of individuals who become temporarily protected after vaccination was 93% (worst case: 83%; best case: 95%).

The percentage of individuals for which vaccine fails completely was 4% (worst case: 6%; best case: 1%).

The rate of varicella acquisition of vaccinees compared with non-vaccinees was 73% (worst case: 100%; best case: 50%).

The proportion of temporarily protected individuals who become immune due to contact with varicella was 91% (worst case: 50%; best case: 100%).

The rate of varicella infectiousness of vaccinees compared with non-vaccinees was 50% (worst case: 100%; best case: 20%).

The percentage of cases that visit a physician was 38% (range: 24 - 100% for both natural varicella and breakthrough varicella, depending on the class age of the patient).

The average number of consultations per episode was 1.37 for natural varicella and 1.38 for zoster.

The percentage of hospitalisation per case was 0.5% (range: 0.2 - 7) for natural varicella and 4.9% (range: 0.8 - 10.4) for zoster.

The mean inpatient days per hospitalisation were 6.4 (range: 4.3 - 18) for natural varicella and 17.5 (range: 4.2 - 20) for zoster.

The deaths per 100,000 cases were 2.6 (range: 0.5 - 1.236.1) for natural varicella and 10.8 (range: 0.5 - 35.9) for zoster.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions that were used in the analytic model.

**Estimates of effectiveness and key assumptions**
The percentage of cases that visit a physician was assumed to be 100% for zoster.

The number of consultations per episode of breakthrough varicella was assumed to be 1.

The percentage of hospitalisations per case of breakthrough varicella was 0.1%.

The mean inpatient days for hospitalisation due to breakthrough varicella were 1.3.

There were no deaths per 100,000 cases of breakthrough varicella.

**Measure of benefits used in the economic analysis**
The benefit measure used in the economic analysis was the life-years gained, which were calculated using the decision model. A 3% discount rate was used, as the time horizon of the analysis was 30 years. The number of cases of natural varicella, breakthrough varicella and zoster were also reported, as were the number of physician consultations, hospitalisations and deaths.

**Direct costs**
A 3% discount rate was used as the costs were incurred over 30 years. The unit costs were reported separately from the
quantities of resources. The health services included in the analysis of the direct costs were physician visits (for uncomplicated varicella), hospitalisation (for complicated varicella) and vaccination costs. The cost/resource boundary adopted for the direct costs was that of the health payer. The quantities of resources and unit costs were both estimated from published studies. The expected costs were calculated using modelling. The costs were inflated to 1997 to 1998 values using the Canadian Consumer Price Index for Health.

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

**Indirect Costs**
A 3% discount rate was used as the costs were incurred over 30 years. The unit costs were reported separately from the quantities of resources. The health services included in the analysis of the indirect costs were only available for varicella. These were for non-medical costs and work and leisure time lost due to varicella. Work loss was measured using the human capital approach, while leisure time lost was estimated to be equal to what could be earned in the labour force (opportunity cost method). The cost/resource boundary for the indirect costs was that of society. The unit costs and quantities of resources were derived from published studies. The costs were expressed in 1998 values.

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

**Sensitivity analysis**
Several sensitivity analyses were performed to assess the robustness of the estimated cost-effectiveness ratios to variations in the parameter estimates used in the models. Alternative scenarios, such as assumptions on zoster and breakthrough varicella, discount rate and time horizon of the analysis, were also varied.

**Estimated benefits used in the economic analysis**
The number of cases of natural varicella was 8,156,780 with no vaccination, 2,272,030 with the infant strategy, 1,047,608 with the catch-up strategy, and 7,195,659 with the preteen strategy.

The number of physician consultations was 4,204,976 with no vaccination, 154,629 with the infant strategy, 792,678 with the catch-up strategy, and 3,506,566 with the preteen strategy.

The number of hospitalisations was 40,733 with no vaccination, 11,999 with the infant strategy, 6,823 with the catch-up strategy, and 35,135 with the preteen strategy.

The number of deaths was 208 with no vaccination, 100 with the infant strategy, 78 with the catch-up strategy, and 184 with the preteen strategy.

In the analyses assessing the impact of breakthrough varicella and zoster following mass vaccination, there were 2,272,039 cases of varicella, 426,266 cases of breakthrough varicella, 1,774,892 physician consultations, 12,375 hospitalisations, and 100 deaths.

The number of discounted life-years gained was 0 with no vaccination, 3,415 with infant vaccination, 3,868 with catch-up vaccination, 1,013 with preteen vaccination, 3,415 with infant breakthrough varicella vaccination, and 2,809 with infant zoster vaccination.

**Cost results**
The total discounted direct medical costs (in millions) were Can$365.6 with no vaccination, Can$511.7 with infant vaccination, Can$562.3 with catch-up vaccination, Can$383.3 with preteen vaccination, Can$519.8 with infant vaccination.
breakthrough varicella vaccination, and Can$519.8 with infant zoster vaccination.

The total discounted indirect medical costs (in millions) were Can$2,435.1 with no vaccination, Can$618.6 with infant vaccination, Can$312.8 with catch-up vaccination, Can$2,173.9 with preteen vaccination, and Can$667.2 with infant breakthrough varicella vaccination.

The total discounted costs (in millions) were Can$2,800.7 with no vaccination, Can$1,130.3 with infant vaccination, Can$1,437.4 with catch-up vaccination, Can$2,557.2 with preteen vaccination, and Can$1,187 with infant breakthrough varicella vaccination.

The total zoster direct medical costs (in million) with no vaccination were Can$812.4 and, for infant zoster, Can$985.2.

**Synthesis of costs and benefits**
The costs and benefits of the screening strategies were combined using both the discounted benefit-cost ratio (BCR) and the cost per life-year gained.

From the societal perspective, the BCR (dollar saved per dollar invested in the vaccine programme) was 5.24 with infant vaccination, 4.90 with catch-up vaccination, 4.44 with preteen vaccination, and 5.09 with infant breakthrough varicella vaccination. From the health payer's perspective, the BCR was 0.61 with infant vaccination, 0.60 with catch-up vaccination, 0.73 with preteen vaccination, 0.59 with infant breakthrough varicella vaccination, and 0.16 with infant zoster vaccination.

The cost per life-year gained from the health payer's perspective was Can$44,503 with infant vaccination, Can$50,866 with catch-up vaccination, Can$18,508 with preteen vaccination, Can$46,896 with infant breakthrough varicella vaccination, and Can$118,188 with infant zoster vaccination.

The break-even vaccine cost per course (health payer's perspective) was Can$37 with infant vaccination, Can$35 with catch-up vaccination, Can$59 with preteen vaccination, Can$35 with infant breakthrough varicella vaccination, and Can$10 with infant zoster vaccination.

The estimated cost-effectiveness ratios were sensitive to the cost per vaccine course, the efficacy of the vaccine, the discount rate of benefits, and time loss due to uncomplicated cases of varicella. The unknown relationship between varicella and zoster had the strongest impact on the results of the analysis.

**Authors' conclusions**
If the threshold value of $25,000 per life-year gained was selected, then only routine preteen screening for varicella would be cost-effective from the healthcare payer's perspective in Canada. All three strategies were cost-saving from the perspective of society when the indirect costs were included in the analysis.

**CRD COMMENTARY - Selection of comparators**
The rationale for the choice of the comparators was clear. All three-vaccination strategies represented feasible vaccination options. The "no vaccination" option was selected to assess the active value of each strategy. You should decide whether they represent valid comparators in your own setting.

**Validity of estimate of measure of effectiveness**
The effectiveness analysis used data derived from published studies. However, no formal review of the literature was undertaken and the primary study estimates were combined using narrative methods. It was unclear whether the authors considered the impact of differences between the primary studies when estimating the effectiveness. It was necessary for the authors to make several assumptions in the analysis, although most relied on published estimates. Extensive sensitivity analyses were conducted to take into account the uncertainty surrounding the effectiveness estimates and, as a result, highlight problematic variables within the model.
Validity of estimate of measure of benefit
The benefit measure used in the economic analysis was the life-years gained. These were calculated using an analytic model. Appropriate discounting was performed and the impact of different discount rates was assessed. The authors commented that the use of quality-adjusted life-years would have been more appropriate, but no relevant validated methodology was found in the literature.

Validity of estimate of costs
The analysis of the costs was carried out from two different perspectives. It would appear that all the relevant categories of costs were included in the analysis. The authors stated that start-up costs were not included in the analysis, but that their impact on the study findings was not substantial. The price year was appropriately reported and several statistical analyses were conducted on the quantities and unit costs. The unit costs were reported separately from the quantities of resources, and a complete breakdown of the costs was given. The authors noted that a potential limitation of the analysis was related to the difficulties in measuring the indirect costs.

Other issues
The authors made several comparisons of their findings with those from other studies. In terms of the generalisability of the study results to other settings, the authors noted that both the unit costs and age-specific epidemiology data may vary across countries, thus caution is required when extrapolating the study findings. However, the external validity of the analysis remains high, as all components of the analysis were made explicit.

Implications of the study
The main implication of the study is that mass varicella vaccination campaigns may have the potential for cost-effectiveness in Canada. Further analyses should focus on the precise assessment of productivity losses and the mechanism of re-activation in the relationship between varicella and zoster.

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Other publications of related interest

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