Potential cost-effectiveness of annual influenza immunization for infants and toddlers: experience from 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
The study examined influenza immunisation with two doses for healthy infants and toddlers aged 6 to 23 months for the introductory year, and then immunisation with two doses for infants aged 6 to 12 months in every following year.

Type of intervention
Primary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The authors conducted two analyses. In the first analysis, the study population comprised a hypothetical cohort of 500,000 healthy children aged between 6 and 23 months. In the second analysis the children were aged between 6 and 12 months.

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

Dates to which data relate
The studies that provided the effectiveness evidence were published between 1969 and 2004. The studies providing the cost data were published between 2000 and 2004. The price year was 2004.

Source of effectiveness data
The evidence was derived from a review or synthesis of published studies.

Modelling
Two models were produced for the two analyses described. Each model was a decision tree, populated by a cohort of 500,000 children. The model was used to evaluate the cost-effectiveness of influenza immunisation. In the base-case, the analytical horizon was a single influenza season.

Outcomes assessed in the review
The authors clearly reported all the clinical parameters used in the model. Perhaps the most important clinical parameter was the effectiveness of the inactivated influenza vaccine in infants and toddlers. Several population and prevalence parameters were reported.
Study designs and other criteria for inclusion in the review
Not reported.

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 46 primary studies provided the effectiveness evidence.

Methods of combining primary studies
A narrative method was used to combine the results of the individual primary studies.

Investigation of differences between primary studies
Not reported.

Results of the review
The parameters were well reported in the paper but there were too many to report in this abstract.

The effectiveness of the inactivated influenza vaccine in infants and toddlers was 66% (range: 39 to 91).

Methods used to derive estimates of effectiveness
Some authors’ assumptions were used.

Estimates of effectiveness and key assumptions
Key model assumptions are reported in full detail in the paper. They included the following.

The risk of illness and complication was assumed to be uniform across the age range.

Infection is only spread by infants and toddlers in day care and to caregivers (parents). That is to say, sibling illness was not included.

Measure of benefits used in the economic analysis
The measures of health benefits used in the economic analysis were:

- infant/toddler influenza illness averted;
- days of infant/toddler influenza illness averted;
- cases of acute otitis media (AOM) averted;
prescriptions averted;
physician visits averted;
hospitalisations averted;
life-years (LYs) gained; and
deaths averted.
The LYs gained were discounted at a rate of 3%.

Direct costs
The estimation of the direct costs included costs incurred by the third-party payer (social insurance system), such as immunisation, medical visits, prescriptions and hospitalisation. The unit costs were estimated from government sources. The cost of vaccination and administration was assigned by the authors, but was tested in the sensitivity analysis. The quantities and the costs were not analysed separately.

The price year was 2004, and estimates from other years were converted into 2004 Canadian dollars using the Consumer Price Index. Discounting was not required in the analysis of the first year. It appears that the costs estimated for the second year were assumed to have been the same for each of the following years. The authors estimated what the annual cost would be without calculating the total present value of these costs. Hence, no discounting was performed. The authors stated that some minimal costs were not included in the analysis, but no further details were given.

Statistical analysis of costs
No statistical analysis of the costs was reported.

Indirect Costs
The estimation of indirect costs included loss of income due to a physician visit for immunisation, childhood illness or transmission to an adult. The value of lost income was derived from government publications. The quantities and the costs were not analysed separately. The price year was 2004, and estimates from other years were converted into 2004 Canadian dollars using the Consumer Price Index. Again, there does not appear to have been any discounting because the analysis calculated only the annual costs.

Currency
Canadian dollars (CAD).

Sensitivity analysis
A univariate sensitivity analysis was conducted. The cost of the vaccine, incidence rate, vaccine effectiveness, rate of AOM, proportion of physician visits, proportion of antibiotics, hospitalisation rate, parental time loss, transmission from infant to parent, and cost of hospitalisation were varied. The parameters were varied over the ranges presented. These parameters were also subject to a break-even analysis to determine when the total cost of the vaccination programme was equal to the total cost of no vaccination programme.

Estimated benefits used in the economic analysis
Per year, the infant/toddler influenza vaccination was found to avert 82,500 cases of illness, 20,625 cases of AOM, 45,375 physician visits, 26,565 antibiotic prescriptions, 825 hospitalisations, 1.65 deaths and 129.03 (undiscounted) LYs lost.
Cost results
Introducing a vaccination programme would cost society CAD 12 million in the first year, of which CAD 10.5 million was direct costs. In subsequent years, the programme would cost society CAD 2 million per year, with direct costs to the third-party payer of CAD 5.5 million.

From the third-party perspective, the vaccination programme with 100% of children receiving two doses cost CAD 34.66 per child, compared with no vaccination which cost CAD 13.72 per child. The vaccination programme resulted in an incremental cost of CAD 20.94 per child.

From the third-party perspective, the vaccination programme with one in three children receiving two doses cost CAD 24.61 per child. The vaccination programme resulted in an incremental cost of CAD 10.89 per child.

From the societal perspective, the vaccination programme with 100% of children receiving two doses cost CAD 81.14 per child, compared with no-vaccination which cost CAD 56.23 per child. The vaccination programme resulted in an incremental cost of CAD 24.01 per child.

From the societal perspective, the vaccination programme with one in three children receiving two doses cost CAD 60.36 per child. The vaccination programme resulted in an incremental cost of CAD 4.13 per child.

Synthesis of costs and benefits
The authors calculated incremental cost-effectiveness ratios for the first year of vaccination and each year of vaccination thereafter from each of the two perspectives. Only the results for the first year of vaccination are reported in this abstract.

In the first year (assuming 100% vaccination coverage), it would cost the third-party payer CAD 126.94 per illness averted, CAD 230.80 per physician visit averted, CAD 12,694 per hospitalisation averted and CAD 863,855.92 per LY gained. It would cost society CAD 150.99 per illness averted, CAD 274.53 per physician visit averted, CAD 15,099.20 per hospitalisation averted and CAD 1,027,143 per LY gained.

The sensitivity analysis showed that the cost-effectiveness ratio was most sensitive to the incidence rate, hospitalisation rate and cost of immunisation. Cost-savings were possible from the societal perspective when the cost per dose was CAD 10, the hospitalisation rate was 2%, and parental time off work for vaccination was less than 1.5 hours.

Authors' conclusions
A fully implemented immunisation programme could prevent 825 hospitalisations and 1.65 deaths per year. Introducing a vaccination programme would cost society CAD 12 million in the first year, and CAD 2 million per year in subsequent years. In the base-case, infant/toddler influenza immunisation was not cost-saving but could become more cost-effective in settings of higher attack rate and lower immunisation cost.

CRD COMMENTARY - Selection of comparators
This paper was not written clearly. It required detailed reading to establish that, (1), the vaccination of infants and toddlers aged 6 to 23 months in the introductory year of vaccination was compared with no vaccination in one analysis and, (2), the vaccination of infants and toddlers aged 6 to 12 months in each subsequent year was compared with no vaccination in another analysis.

The authors did not explain why the age range of vaccination differed from the first year to the subsequent years, although one could guess that vaccinating infants and toddlers aged 6 to 12 months would be adequate to protect them until a certain age and that the first year was needed to capture all those below that certain age.

Validity of estimate of measure of effectiveness
The authors referenced several studies, including a systematic review. However, they reported the methods used to identify the clinical literature and did not state that a systematic review of the literature had been undertaken. Although
this is common practice with models, it does not always ensure that the best data available are used and it restricts the confidence one can have in the estimates. The authors do not appear to have used data from the available studies selectively.

There appears to have been an implicit assumption in the study that the vaccine effectiveness was the same in the second year (and subsequent years) as it was in the first year. The authors stated at the end of the paper that "herd immunity has not been demonstrated with infant/toddler vaccination". If there were a herd immunity effect then the benefits would be quite different, and the effect of vaccinating infants/toddlers in the previous year would have to be taken into account.

The estimates were investigated in sensitivity analyses using ranges derived from the included literature.

**Validity of estimate of measure of benefit**
The measures of benefit used in the economic analysis included influenza illness averted, hospitalisations averted and LYS gained. Other outcomes were mentioned and it was not clear how one would interpret the value of an incremental cost-effectiveness ratio such as the cost per prescription averted. The authors employed a simple static decision model to estimate events, costs and benefits. Given that influenza is an infectious disease, if there were a possibility of herd immunity then it might have been more appropriate to have employed a model of a dynamic nature: a model with a time horizon of several years from the start of immunization.

**Validity of estimate of costs**
The perspectives of the analysis were clearly reported. As such, it appears that all the relevant costs have been included. The costs were taken from published sources. These costs were clearly stated in the paper and this adds to its generalisability. Although no statistical analysis of the costs was undertaken, a sensitivity analysis was conducted. The price year was reported.

**Other issues**
The authors made some comparisons of their findings with those from other childhood vaccines. The issue of generalisability to other settings was addressed. The authors do not appear to have presented their results selectively and their conclusions reflected the scope of the analysis. The authors acknowledged a number of further limitations to their study. First, some parameters were derived by extrapolation. Second, they did not consider the cost or benefit of immunising other household contacts. Finally, they did not consider sibling transmission or serious morbidity in adults.

**Implications of the study**
Integrated economic evaluation is an essential part of strategic influenza programme design.

**Source of funding**
None stated.

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