Effectiveness and cost-effectiveness of pediatric rotavirus vaccination in British Columbia: a model-based evaluation

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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.

CRD summary
The objective was to assess the cost-effectiveness of RotaTeq and Rotarix vaccinations for the prevention of rotavirus gastroenteritis in children. The authors concluded that Rotarix was highly cost-effective. The study appeared well conducted but it suffered from limited reporting on identification and selection of data to inform the model. The authors' conclusion seems appropriate but some uncertainty surrounds the results.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
To assess the cost-effectiveness of RotaTeq and Rotarix vaccinations for prevention of rotavirus gastroenteritis in children.

Interventions
Three strategies were considered: universal childhood immunisation with RotaTeq (Merck Frosst Canada Ltd); universal childhood immunisation with Rotarix (GlaxoSmithKline Inc); and no immunisation. Two doses were administered for each of the vaccination strategies. Dosage timings were in accordance with the Canadian National Advisory Committee on Immunization recommendations: first dose given between six and 15 weeks (14 weeks plus six days) of age, a recommended four-week between-dose interval and a recommended maximum age for the last dose of eight months.

Location/setting
Canada/outpatient

Methods
Analytical approach:
A Markov model was developed to allow for age and seasonally dependant costs and outcomes for a Canadian infant cohort (birth to five years of age) to be simulated. Model parameters were derived from the literature. The authors stated that the analysis was performed from a healthcare perspective within the context of a publicly subsidised healthcare system.

Effectiveness data:
The main effectiveness parameter was incidence of rotavirus gastroenteritis. The cumulative baseline five-year incidence of rotavirus gastroenteritis was taken from various sources that included National Advisory Committee on Immunization (NACI) documents and published studies. Other parameters included relative risk of rotavirus gastroenteritis for the two vaccines (first and second doses), natural immunity after infection rates, vaccine coverage and adverse events. These were derived from published and national sources. Waning and herd-immunity were not accounted for.

Monetary benefit and utility valuations:
Illness associated with rotavirus gastroenteritis was associated with a loss of quality-adjusted survival equivalent to approximately 0.75 quality-adjusted life-days in both affected children and their parents. This value was used to generate cost-utility estimates associated with vaccination.
Measure of benefit:
The measure of benefit was the quality-adjusted life-year (QALY). Future benefits were discounted at an annual rate of 3%.

Cost data:
Direct costs included those associated with vaccination (including material costs, operational costs, wastage, vaccine shipping costs, cold chain maintenance costs, delivery costs, promotion and advertising costs and additional human resources and training costs), adverse drug reaction costs and healthcare utilisation costs (including hospitalisation, emergency department visit and general practitioner/paediatrician visit costs). Costs of Rotarix and RotaTeq were based on contract prices between the manufacturer and other Canadian provinces, government expert information and authors' assumptions. Total immunisation programme delivery costs were based on those associated with human papillomavirus vaccination in British Columbia. Phase III trial and post-licensing surveillance data were used to estimate adverse events. Hospitalisation costs were derived using sources specific to British Columbia. Utilisation of hospital resources was obtained from NACI data and a Canadian Institutes of Health Information dataset. All costs were inflated to 2007 Canadian dollars ($) using the health care component Canadian consumer price index. Future costs were discounted at an annual rate of 3%.

Analysis of uncertainty:
Uncertainty was assessed using univariate, multivariate and probabilistic sensitivity analysis. In the base case, probabilities were sampled from triangular distributions for all major model parameters. Threshold analysis was performed to evaluate the effect of varying costs of both vaccine preparations on model projections over different willingness-to-pay thresholds.

Results
The projected number of rotavirus gastroenteritis episodes without vaccination was 111 for every 100 children at a mean cost of $66 per episode. For every 100 children vaccinated with RotaTeq, the projected number of rotavirus gastroenteritis episodes was 48 at a mean cost of $103 per episode. For every 100 children vaccinated with Rotarix, the projected number of episodes was 30 at a mean cost of $74 per episode.

Incremental analysis showed that compared with no vaccination, RotaTeq avoided 63 rotavirus gastroenteritis episodes for every 100 children and Rotarix avoided a further 18 episodes per 100 children. Rotarix dominated RotaTeq (Rotarix was less expensive and more effective than RotaTeq).

The incremental cost-effectiveness ratio (ICER) for Rotarix was $10 per rotavirus gastroenteritis episode averted and the ICER for the cost per QALY gained was $2,400 per QALY. Were Rotarix not available, the ICER for RotaTeq versus no vaccination would be $62.50 per infection averted and $14,300 per QALY gained.

In the sensitivity analysis, model projections were most sensitive to assumptions about vaccine costs and risks of rotavirus gastroenteritis. Assuming a willingness-to-pay threshold of $10,000 per QALY ($40 per infection averted) rotavirus gastroenteritis vaccination provided positive net health benefits across the full range of healthcare probabilities, costs and utility estimates evaluated.

In the threshold analysis, immunisation with Rotarix was projected to be cost-saving in 50% of simulations. Beyond a threshold willingness to pay of approximately $24 per rotavirus gastroenteritis prevention (approximately $6,000 per QALY) vaccination with Rotarix was the preferred strategy in more than 90% of simulations.

One-way sensitivity analysis found that the no vaccination strategy would be preferred if the year-round rotavirus gastroenteritis risk were similar to that seen in the summer in British Columbia.

The authors stated that their findings were consistent with the results of other health economic analyses of rotavirus gastroenteritis vaccines performed in high-income countries.

Authors' conclusions
The authors concluded that Rotarix was highly cost-effective.
CRD commentary

Interventions:
The interventions appeared appropriate; the authors stated that the two interventions were the only live rotavirus vaccines approved for use in Canada at the time of the study. The authors did not report details of current practice but current practice should be included as a comparator in order to obtain accurate cost-effectiveness results.

Effectiveness/benefits:
The effectiveness estimates and sources used to derive them were reported clearly. Most sources were specific to Canada and USA and were relevant to the setting. However, methods used to identify and select data were not reported and none of the studies used were presented in sufficient detail to judge their validity. The utility value used in the analysis was reported but not the methods used to derive it. Overall, the methods around identification and selection of data to inform the model were limited. On the whole they appeared relevant to the setting and the population but it was not possible full assessment of their validity was not feasible.

Costs:
Costs were clearly reported and appropriate for the perspective. The sources used to derive estimates costs were clearly stated and were specific to Canada. It was not always clear what assumptions were used in deriving resource use estimates such as for hospitalisation and emergency room visits. There were appropriate adjustments for inflation and discounting.

Analysis and results:
The Markov model was clearly described with a diagram supplied. The authors justified the choice of model time horizon by stating that most of the disease burden from rotavirus occurred in individuals aged under five years. The results were reported clearly and appropriate diagrams were used. For the deterministic sensitivity analyses the range of values over which parameters were altered was reported clearly. But no justification for the choice of range values was reported so it was unclear whether these ranges accurately reflected uncertainty around parameter values. Probabilistic sensitivity analysis helped to characterise the uncertainty but use of triangular distributions limited the analysis. It was unlikely that the probabilistic results provided an accurate evaluation of uncertainty in the model.

The authors stated that they were unable to state with certainty that any strategy was cost-effective given the lack of willingness-to-pay benchmarks for rotavirus gastroenteritis and the limited information on health utilities associated with childhood rotavirus gastroenteritis. The authors suggested that an area for future research should concern establishing a societal willingness-to-pay threshold for rotavirus gastroenteritis prevention.

Concluding remarks:
The study appeared well conducted but it suffered from limited reporting on identification and selection of data to inform the model. The authors’ conclusion seems appropriate but some uncertainty surrounds the results.

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