Impact of transmission dynamics on the cost-effectiveness of rotavirus vaccination
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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
This study examined the cost-effectiveness of a universal rotavirus vaccination programme in children aged five years or younger. The authors concluded that vaccination was cost-effective from the perspectives of society and the US health care system, when considering the child and one caregiver. The methods appear to have been appropriate and generally well reported. The authors’ conclusions appear to be appropriate for the selected cost-effectiveness threshold, which might or might not be relevant in other settings.

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

Study objective
The objective was determine the cost-effectiveness of a national programme of immunisation against rotavirus in US infants less than five years old.

Interventions
A strategy of no rotavirus vaccination was compared with universal rotavirus vaccination, using RotaTeq administered in three doses, according to the schedule recommended by the Centers for Disease Control and Prevention (CDC).

Location/setting
USA/primary care.

Methods
Analytical approach:
The analysis used a dynamic transmission model that accounted for herd immunity and had a time horizon of 20 years. The model tracked the rotavirus-related epidemiological status of individuals in five age-dependent states, which were susceptible; severely infected; mildly infected; temporarily recovered; and vaccinated. The authors stated that the perspectives of both society and the health care system were taken.

Effectiveness data:
The authors used their judgement to select the most appropriate estimates of age-group-specific incidence rates (10 groups) for mild and severe rotavirus infections, any rotavirus-related gastroenteritis, and mortality due to rotavirus from the available evidence in published literature. The authors stated that the vaccine efficacy for mild rotavirus infections and severe rotavirus infections, including those leading to hospitalisation and death, were based on the findings of RotaTeq clinical trials (Clark, et al. 2004, see ‘Other Publications of Related Interest’ below for bibliographic details). Assumptions were made for vaccine coverage and some other parameters.

Monetary benefit and utility valuations:
The utility weights were from published studies, which used questionnaires completed by parents on behalf of their children, who were infected with rotavirus. The utilities were derived for both infected children (requiring hospitalisation, or emergency department, out-patient, or general practitioner visit) and the primary caregiver.

Measure of benefit:
Disability-adjusted life-years (DALY), quality-adjusted life-years (QALYs), life-years saved (LYS), and averted infections or deaths were the summary benefit measures. These benefits were discounted at an annual rate of 3%.
Cost data:
The analysis included the direct medical costs of vaccination (acquisition, administration, and vaccine-related adverse events) and the treatment of rotavirus infections (hospital in-patient and out-patient, and emergency care). The direct non-medical costs were included for episodes of rotavirus infection (travel, nappies, oral hydration solution, and child care), as were the indirect costs of work productivity lost by caregivers and due to the premature death of the child. The cost of the vaccine was the manufacturer’s price at the time. The costs of vaccine administration, hospital treatment for vaccine-related adverse effects, and treatment for mild or severe infections were from a published US study of rotavirus vaccination (Widdowson, et al. 2007, see ‘Other Publications of Related Interest’ below for bibliographic details). The costs of work productivity lost, special foods, nappies, travel, and child care were based on authors’ opinions or other published US sources (Widdowson, et al. 2007). All costs were in US dollars ($) and were discounted at an annual rate of 3%. The price year was 2007.

Analysis of uncertainty:
One-way sensitivity analyses were carried out on the vaccine coverage, price, and efficacy against severe or mild rotavirus infections, using published ranges of values or alternative estimates defined by the authors. A breakeven analysis was performed, on the vaccination price, to determine the price at which the cost of the vaccination programme equalled the expected savings to the health care system (due to adverted cases of rotavirus infections). The authors used a cost-effectiveness threshold defined by a World Health Organization report in 2002, where interventions were cost-effective if the cost per additional DALY or per QALY gained was less than three times the gross domestic product (GDP). The cost-effectiveness ratios were presented graphically for variations in a few of the parameters.

Results
The expected total cost of the vaccination programme was $407 million from the health care perspective or $966 million from the societal perspective. In total, vaccination cost an additional $245 million from the health care perspective and resulted in cost savings of $216 million from the societal perspective. The breakeven vaccine price was $147 from the health care perspective and $347 from the societal perspective, per child completing a vaccine course.

From the health care perspective, the incremental cost per QALY gained per child vaccinated was $192,100 considering the child only or $104,610 considering the child and one caregiver. At the threshold for cost-effectiveness of three times the $43,800 GDP per capita in the USA, rotavirus vaccination, with RotaTeq, could be considered to be cost-effective. Vaccination using Rotarix resulted in a cost per QALY gained of $148,270 for the child only or $80,740 for the child and one caregiver.

From a health care perspective, the cost of RotaTeq vaccination was $77.30 per case prevented, $318.22 per serious case prevented, or $7,482,000 per LYS. From a societal perspective, vaccination resulted in cost savings of $80.75 per case prevented, $144.85 per serious case prevented, or $7,815,000 per LYS.

Sensitivity analysis on vaccine coverage showed that the cost-effectiveness ratios increased markedly when the coverage was over 75%. Ratios increased exponentially as the efficacy declined, if the efficacy for either severe or mild rotavirus was relatively low.

Authors’ conclusions
The authors concluded that infant rotavirus vaccination in the USA, using RotaTeq, was cost-effective from the perspectives of society and the health care system, when considering the costs of one caregiver as well as the child.

CRD commentary
Interventions:
The selection of the comparators was appropriate and reflected the situation in the authors’ setting.

Effectiveness/benefits:
It was unclear if the best available evidence was used, as a systematic review to identify this data was not reported. The authors stated that the model inputs were derived from the published findings of RotaTeq clinical trials, but they reported limited details, such as their sample size and design, which makes it difficult to fully assess the validity of this data. QALYs were an appropriate benefit measure. The authors reported the methods used and the source for the utility...
values. There was a lack of US data for the utility values and so these were from an Australian and Canadian study and they might not have represented the US population. The additional measures of benefit, such as cases averted, and life-years saved, were appropriate and might be useful to some readers.

Costs:
Those cost categories and costs relevant to the two perspectives appear to have been included. These categories and the unit costs were clearly reported, as were the price year and discounting. The assumptions were justified and they were tested in the sensitivity analyses. In general, the cost analysis was conducted satisfactorily.

Analysis and results:
The analytic approach used to synthesise the costs and benefits was well described and, in general, the results were well presented, but detailed information on the QALYs with and without vaccination was lacking. The issue of uncertainty was addressed by focusing on the most influential model inputs (vaccine efficacy, price, coverage), but no sensitivity analyses were performed on the utilities, even though QALYs were the main benefit measure. The authors acknowledged that their estimates of the actual reduction in rotavirus incidence might differ from clinical trial efficacy estimates because trials measure the direct effects of vaccination only and do not take into account herd immunity. They compared their findings with those from other studies (using the cost per case prevented), and discussed the potential explanations for different results (for example, the use of a static cohort versus a dynamic transmission model).

Concluding remarks:
The methods appear to have been appropriate and generally well reported. The authors' conclusions appear to be appropriate for the selected cost-effectiveness threshold, which might or might not be relevant in other settings.

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