The cost-utility of rotavirus vaccination with Rotarix (RIX4414) in the Netherlands
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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 estimate the cost-utility of mass rotavirus (RV) vaccination of children from birth to four years. The authors concluded that mass vaccination against RV in children might be a cost-effective strategy from the perspective of Dutch society. The analysis appears to have been based on valid methodology, therefore the authors’ conclusions are likely to be valid.

Type of economic evaluation
Cost-utility analysis

Study objective
The aim was to estimate the cost-utility of mass rotavirus (RV) vaccination of children from birth to four years old.

Interventions
The study examined a mass immunisation strategy against gastroenteritis (GE) induced by RV, using the human live-attenuated oral vaccine Rotarix (RIX4414) for the active immunisation of infants from the age of six weeks. The vaccination course consisted of two oral doses administered at two months, and four weeks later. This mass vaccination strategy was compared with the standard treatment in the Netherlands, which was no vaccination.

Location/setting
Netherlands/primary care.

Methods
Analytical approach:
A Markov model, which resembled a published model, was developed to estimate the clinical and economic impact of the two strategies. A lifetime horizon was considered and the authors stated that a societal perspective was adopted.

Effectiveness data:
The clinical data appear to have been derived from a selection of known, relevant studies. The data on RV-induced diarrhoea, probability of general practitioner (GP) visits, and risk of hospitalisation due to RV-induced diarrhoea were obtained from epidemiological data in the Netherlands. Vaccine effectiveness was derived from the European 036 study which included 3,994 patients. Other details on these sources were not provided. Some assumptions were also made and justified. The key clinical outcomes were the reduction in episodes of RV-induced diarrhoea and its consequences with the vaccine.

Monetary benefit and utility valuations:
The utility valuations were derived from a British sample of GPs and paediatricians who completed the EQ-5D questionnaire.

Measure of benefit:
Quality-adjusted life-years (QALYs) were used as the summary benefit measure. QALYs were calculated by means of the decision model and using a 1.5% annual discount rate.

Cost data:
The health service costs included in the analysis were vaccine (acquisition and administration), GP visits, hospitalisations, treatment of RV infection (community-acquired and nosocomial), travel (to hospital and GP office),
and productivity losses. The resource use data for RV-induced diarrhoea were obtained from national studies. GP visits were estimated using three different approaches and the arithmetic means of these were used in the base-case analysis. A range of prices for vaccine acquisition was considered. The costs were, in general, taken from national sources. The approach used to derive the costs of work absenteeism was described and the potential elasticity of productivity was considered, as recommended by Dutch guidelines (the friction-cost method). All costs were in Euros (EUR) and a 4% annual discount rate was applied to future costs. The price year was 2005 and, where necessary, costs were updated to the reference year using the price index.

Analysis of uncertainty:
A deterministic and a probabilistic sensitivity analysis were carried out to deal with the issue of uncertainty. In the former, individual model inputs were varied using published ranges of values. In the latter, a second order Monte Carlo simulation was performed by varying all model inputs simultaneously and generating cost-effectiveness acceptability curves.

Results
In the birth cohort of 187,910 children born in 2005, vaccination was expected to lead to a reduction of 58,388 community-acquired infections, 808 nosocomial infections, 21,954 GP consultations, and 2,940 hospitalisations. The expected gain in QALYs with vaccination over no vaccination was 276, for the lifetime of the whole cohort. The additional costs were EUR 18,228,304 assuming a vaccination cost of EUR 100 (for two doses plus administration).

The incremental cost per QALY gained with vaccination over no vaccination at a vaccine price of EUR 100 was EUR 28,488 (EUR 21,900 at a vaccine price of EUR 90, and EUR 35,076 at a vaccine price of EUR 110).

The univariate sensitivity analysis indicated that the probability of being hospitalised was the most influential model input where a 33% reduction in the probability led to a 45% increase in the cost-utility ratio, while a 33% increase in the probability resulted in a 35% reduction in the cost-utility ratio. Other relatively influential model inputs were the rate of diarrhoea, the probability of a GP visit, the utility scores, and the hospital costs.

The results of the probabilistic analysis were only presented in graphical form, and showed that, at a willingness to pay of EUR 50,000 per QALY, the probability of being cost-effective for mass vaccination was around 83% (assuming a vaccine cost of EUR 100).

Authors’ conclusions
The authors concluded that mass vaccination against RV in children might be a cost-effective strategy from the perspective of Dutch society.

CRD commentary
Interventions:
The selection of the comparator, namely no vaccination, was appropriate and reflected the situation in the authors’ setting.

Effectiveness/benefits:
The clinical data were identified selectively from published sources and this approach should have ensured the selection of the most relevant sources. The use of national data was appropriate in terms of simulating the Dutch epidemiological setting, although the authors did not address the issue of homogeneity among these sources. Vaccine effectiveness was taken from a large European study, but details of this study were not provided. The approach used to derive the benefit measure was clearly reported and discussed. QALYs are an appropriate and validated measure, which can be compared with the benefits of other health care interventions.

Costs:
The analysis of costs was consistent with the viewpoint. Resource use data reflected the national health care context and most costs were valued using reference prices and national guidelines. The assessment of specific cost items was clearly described. The methods used to calculate productivity costs reflected the Dutch guidelines. The price year and the use of discounting were reported.
Analysis and results:
The synthesis of costs and benefits was appropriately performed. The results from the base-case analysis and the
sensitivity analysis were clearly presented and discussed. Discounting, and other aspects of the analysis, were performed
in accordance with Dutch guidelines. The authors noted some potential limitations of their analysis, which mainly arose
from the uncertainty of some of the epidemiological parameters of the model. Nevertheless, it was pointed out that,
when required, conservative assumptions were made in order to bias the analysis against the vaccination strategy. The
authors reported the findings from other studies and discussed the different results.

Concluding remarks:
On the whole, the analysis appears to have been based on valid methodology, therefore the authors’ conclusions are
likely to be valid.

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Other publications of related interest
Jit M, Edmunds WJ. Evaluating rotavirus vaccination in England and Wales. Part II. The potential cost-effectiveness of

Widdowson MA, Meltzer MI, Zhang X, et al. Cost-effectiveness and potential impact of rotavirus vaccination in the

Ruiz-Palacios GM, Perez-Schael I, Velazquez FR, et al. Safety and efficacy of an attenuated vaccine against severe

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