Cost-effectiveness and potential impact of rotavirus vaccination in the United States
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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 a pentavalent human-bovine reassortant rotavirus vaccine (PRV) administered to children at 2, 4 and 6 months. The vaccine was compared with no vaccination.

Type of intervention
Primary prevention (vaccination).

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised a hypothetical cohort of children aged 0 to 59 months.

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

Dates to which data relate
The clinical data and most resource use information were derived from studies published between 1981 and 2006. The price year was 2004.

Source of effectiveness data
The clinical data used in the model were;
- estimates of rotavirus gastroenteritis requiring medical care;
- hospitalisations, emergency department and hospital outpatient visits, and physician office visits due to rotavirus gastroenteritis;
- the age distribution for rotavirus hospitalisations;
- rotavirus-related deaths;
- the number of rotavirus gastroenteritis cases not requiring medical care; and
- vaccine efficacy and compliance with vaccination.

Modelling
A probabilistic model was used in a hypothetical cohort of 4,010,000 children who were monitored from birth to 59
months of age. Thus, the time horizon of the analysis was 5 years. No details on the structure of the decision model were given. The model was populated with data derived from the literature. The probabilistic distributions given to all inputs and the methods used to derive these data were extensively described.

**Sources searched to identify primary studies**
The rate of rotavirus gastroenteritis requiring medical care was derived by applying codes for gastroenteritis to data from the National Health Care Survey for each year from 1993 to 2002. Data on hospitalisations came from the National Hospital Discharge Survey. Data on emergency department and hospital outpatient visits, as well as physician office visits, came from the Hospital Ambulatory Medical Care Survey. Rotavirus-related death data were taken from two US studies for which no details were reported. The number of rotavirus gastroenteritis cases not requiring medical care came from two longitudinal studies. Vaccine efficacy was derived from a large clinical trial. Vaccine compliance was obtained from the US National Immunization Survey. Some assumptions on compliance were also made.

**Methods used to judge relevance and validity, and for extracting data**
No systematic search for data was reported, thus the primary studies might have been identified selectively. Vaccine efficacy was appropriately taken from a clinical trial with a large sample size.

**Measure of benefits used in the economic analysis**
The summary benefit measures used were the life-years (LYs) saved, any case of rotavirus gastroenteritis averted, and serious cases (hospitalisations, emergency department visits, or death) averted. No discounting appears to have been applied.

**Direct costs**
The analysis of the costs included the direct medical costs associated with rotavirus gastroenteritis (hospitalisations, emergency department visits, hospital outpatient visits, physician office visits, drugs) and the vaccination programme (3 doses of vaccine, its administration, and treatment of intrassusception). The direct costs borne by families of children with rotavirus (e.g. special foods, diapers, travel and child care) were also considered. The unit costs were not presented separately from the quantities of resources used. The resource use data were mainly derived from national databases. The unit costs were obtained from a national database (MarketScan), which includes more than 500 million claim records on inpatient and outpatient health care services from 45 large employers, health plans and public organisations, and from almost 100 different payers. The quantities and costs borne by families came from an outpatient study. The cost of the programme was based on the official list price for PRV. Discounting was relevant, as the costs were incurred during more than 2 years, and an annual rate of 3% was used. All costs were updated to 2004 values using the medical component of the Consumer Price Index.

**Statistical analysis of costs**
Probabilistic distributions were assigned to the costs and quantities.

**Indirect Costs**
Since a societal perspective was adopted, productivity losses for parents of children with gastroenteritis and lifetime productivity losses attributable to death were included. These costs were derived from published tables with Bureau of Labor Statistics. The number of workdays lost came from published studies. The price year was 2004 and an annual discount rate of 3% was used. The unit costs and the quantities of resource use were not presented separately.

**Currency**
US dollars ($).
Sensitivity analysis
Probabilistic distributions were assigned to all clinical and economic inputs of the model. Details of the type of distribution associated with each model parameter were given. A tornado diagram was constructed, though stepwise regression procedures, to investigate the importance of the input distributions. The break-even cost of vaccination (where net savings are as likely as net costs) was calculated. Finally, the impact of changes in workday losses was specifically investigated.

Estimated benefits used in the economic analysis
In comparison with no vaccination, rotavirus vaccination prevented 63% of all cases of rotavirus gastroenteritis and 79% of all serious cases. Specifically, vaccination resulted in a reduction of 60% of office visits, 48% of episodes with home care, 66% of hospitalisations, 64% of emergency department visits, 60% of hospital outpatient visits and 44% of deaths. The change in LYs was not reported.

Cost results
The total direct medical costs were $318,501 thousand with no vaccination and $833,363 thousand with vaccination (difference $514,862 thousand).

The total non-medical costs were $574,381 thousand with no vaccination and $275,368 thousand with vaccination (difference - $299,013 thousand).

The total costs were $892,882 thousand with no vaccination and $1,108,731 thousand with vaccination (difference $215,849 thousand).

From the health care perspective, the break-even total cost of rotavirus vaccination was approximately $12 per dose, while the probability that vaccination was cost-saving was above 95% at a dose price of $1.

Vaccination would be unlikely to be cost-saving at more than $12 per dose and would incur net costs at more than $38 per dose.

From the societal perspective, rotavirus vaccination would be very likely to be cost-saving at a price of $26 per dose, with a break-even point of $42 per dose.

Synthesis of costs and benefits
Incremental cost-effectiveness ratios were calculated in order to combine the costs and benefits of the two strategies.

From the perspective of the health care system, the incremental cost per case prevented with vaccination over no vaccination was $336 (5th to 95th percentiles: 165 to 436), the incremental cost per serious case prevented was $3,024 (5th to 95th percentiles: 1,498 to 4,460), and the incremental cost per LY gained was $470,729 (5th to 95th percentiles: 218,710 to 738,949).

From the perspective of society, the incremental cost per case prevented with vaccination over no vaccination was $138 (5th to 95th percentiles: 44 to 247), the incremental cost per serious case prevented was $2,636 (5th to 95th percentiles: 1,108 to 4,043), and the incremental cost per LY gained was $197,190 (5th to 95th percentiles: 67,298 to 406,933).

The sensitivity analysis showed that the cost of hospitalisations, emergency department visits and extra child care were the most important variables of the model. Similarly, the number of parental days lost had a strong influence on the results: a 50% increase in the number of workdays lost increased the best-estimate, break-even total cost per vaccine (3 doses plus administration) from $156 to $187 using a societal perspective (total cost per vaccination of $217 in the base-case), while a 50% decrease in days decreased this cost to $123 per child vaccinated.

Authors' conclusions
A rotavirus vaccine programme was not likely to be cost-saving from the perspectives of the health care system and
society unless the price of the vaccine was reduced. However, rotavirus vaccination might be a cost-effective preventive intervention.

CRD COMMENTARY - Selection of comparators
The choice of comparing the new vaccine with no immunisation was appropriate in order to evaluate the active value of the new campaign. The PRV had been recently licensed and recommended in the USA. You should decide whether they are valid comparators in your own setting.

Validity of estimate of measure of effectiveness
The clinical data came from several published sources. The authors did not describe a systematic review of the literature, thus the primary studies might have been identified selectively. Some information on the characteristics of the primary sources was given. The effectiveness of vaccination was derived from a large clinical trial, which is usually associated with high internal validity. However, in general, it is not easy to judge the validity of the clinical data given the lack of detail.

Validity of estimate of measure of benefit
Several benefit measures were used in the cost-effectiveness analysis. Some of these were disease-specific, whereas LYs can be compared with the benefits of other health care interventions. Discounting was not applied. The impact of the disease on quality of life through the use of quality-adjusted life-years was not considered, owing to the lack of data on the psychological costs of gastroenteritis of relatively short duration among young infants and parents.

Validity of estimate of costs
The analysis of the costs was consistent with the stated perspectives. All the relevant categories of costs appear to have been included. A breakdown of the cost items was given. However, information on the unit costs and quantities of resources used was not reported, which could limit the possibility of replicating the analysis in other settings. The sources of the costs were reported, and should be representative of US national tariffs given the choice of large databases. However, the authors noted that the national database used to provide the costs might not reflect poorer segments of society that are at greater risk of severe rotavirus disease. The impact of using alternative cost estimates was investigated only for some items. The price year was reported, thus aiding reflation exercises in other time periods.

Other issues
The authors stated that their findings differed from those of other published studies in several respects. They provided some possible justifications for these discrepancies, such as the use of assumptions around workdays lost that were less favourable to the vaccination strategy. The issue of the generalisability of the study results to other settings was not addressed. Some limitations of the analysis were also pointed out. For example, the model did not take either nosocomially acquired rotavirus gastroenteritis or rotavirus disease in adults, or the subsequent effect of herd immunity, into account.

Implications of the study
The study results suggest that a mature rotavirus immunisation programme would prevent serious rotavirus disease but, at the current manufacturers’ list price, would result in net costs to the health care system. The authors stated that post-licensing surveillance data on adverse reactions and impact of vaccination on disease would be required to judge the actual cost-effectiveness of rotavirus immunisation.

Source of funding
Funded by the Centers for Disease Control.

Bibliographic details

PubMedID
17403839

DOI
10.1542/peds.2006-2876

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AccessionNumber
22007006198

Date bibliographic record published
30/11/2007

Date abstract record published
30/11/2007