

RESEARCH PAPER



Cost-impact study of rotavirus vaccination programme in Scotland

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ABSTRACT

Aim: In July 2013, the Scottish Government introduced a rotavirus vaccination programme into the childhood immunisation schedule. The aim of this research was to estimate the cost-impact of this programme.

Methods: Data for rotavirus-related resource use were identified including laboratory reports, hospitalisations, attendances at accident and emergency departments (A&E), general practice consultations (GP), calls to the National Health Service telephone helpline (NHS24) and prescriptions for common rehydration treatments. We used an interrupted time series analysis approach to assess the impact on resource utilisation in all categories. Appropriate costs were added to the models and predicted pre-and post-vaccination mean annual costs were estimated. The cost of the vaccination programme was estimated using costs from the literature.

Results: The vaccination programme was associated with a reduction in utilisation in all measured healthcare resource categories. These reductions were all statistically significant (at the 95% level) with p-values less than 0.001. Reductions ranged from 18% in calls to NHS24 to 73% in positive laboratory reports. The vaccination programme was associated with a reduction in annual healthcare resource costs of 38% (£595,000 per 100,000 infants < 5 years old) in our measured categories (including £495,000 from a reduction in hospital stays). The annual overall cost-impact of the rotavirus vaccination programme (the cost of delivering the programme minus the reduction in resource costs) was estimated at approximately £435,000 per 100,000 infants < 5 years old.

Conclusion: The rotavirus vaccination programme was associated with a reduction in all measured categories of rotavirus-related resource use by infants < 5 years old.

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KEYWORDS

Rotavirus; cost-impact; vaccine

Introduction

Rotavirus is the leading cause of severe gastroenteritis in infants worldwide and results in approximately 500,000 deaths annually in infants < 5 years old.¹ Unlike in the developing world, rotavirus rarely causes mortality in the UK, however infection results in a high number of hospital admissions for severe dehydration in infants¹ and impacts on health related quality of life (HRQOL).² It has been estimated that rotavirus causes around 45% of hospitalisations for acute gastroenteritis in infants < 5 years old.² In addition, infections resulting in hospitalisation represent only a fraction of cases that occur in the community which cause substantial morbidity with consequent impact on healthcare providers such as general practitioners (GPs) and out-of-hours services.

In July 2013, the Scottish Government, along with the rest of the UK, introduced the GlaxoSmithKline (GSK) vaccine Rotarix®.³ The vaccine was made available to all infants born in Scotland on or after May 1st 2013 and delivered as part of the routine childhood immunisation programme. Over the first evaluation quarter 1st July – 30th September 2014, uptake of the rotavirus vaccine was 93%.⁴ The vaccine was made available to all infants at age 8 weeks (1st dose) and again at 12 weeks (2nd dose).

Routine surveillance carried out by Health Protection Scotland (HPS) found evidence of substantial reductions in rotavirus-related burden of disease in infants⁵ similar to that reported elsewhere.^{6–10} The aim of this research was to estimate the cost-impact of the rotavirus vaccination programme in Scotland, based on a retrospective analysis of routinely collected data on actual healthcare utilisation.



Results

Overall cost-impact

Table 1 shows the overall cost-impact of the rotavirus vaccination programme. Results are reported in terms of the cost of the programme, the monetary value of the reduction in resource use pre-and post-vaccination period, and the difference between the cost of the programme and the value of the reduction in resource use was estimated as the overall cost-impact of the programme.

Cost of vaccination programme

Based on the actual number of infants who received the vaccine over the evaluation period 1st July–30th September 2013, it was

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Table 1. Estimated annual cost-impact of the rotavirus vaccination programme introduced in Scotland in July 2013 (per 100,000 infants under 5 years).

	Cost of vaccination programme	Cost reduction from vaccination programme	Overall cost-impact
Overall cost-impact	£1,030,751	£595,470	£435,281

calculated that 18,575 infants received the vaccination in 2013, per 100,000 infants < 5 years old living in Scotland (note: the vaccine uptake rate was 92.7% however rates per 100,000 are calculated over the entire relevant population of infants < 5 years old).⁴ This figure is multiplied by the vaccine cost per 2 doses. On the assumption of a vaccine price of £23.91 per dose,¹¹ we estimated a total vaccine cost of £888,278 per 100,000 infants < 5 years old in Scotland in 2013/14. The additional administrative payment made to GPs of £7.67 per infant (per two doses)⁴ equates to £142,474 per 100,000 infants < 5 years old in Scotland. Taken together, this indicates that the cost of the vaccination programme was £1,030,751 per 100,000 infants < 5 years old in Scotland.

Sensitivity analysis

We undertook sensitivity analysis to estimate the impact of alternative vaccine prices on the overall cost of the vaccination programme. Table 2 presents the results based on a 50% increase or reduction from the price given in the base case. The results suggest that the overall cost of the programme is highly sensitive to the price of the vaccine.

Reduction in rotavirus-related resource use

Table 3 shows the reduction in rotavirus-related resource use associated with infants < 5 years old for the mean year pre- and post-vaccination programme. Data is presented as incident rate ratios (IRRs) which can be interpreted as representing a percentage reduction in resource use. For example, the IRR associated with vaccination for laboratory reports is 0.273 which equates to a reduction of 72.7% (1–0.273 expressed as a percentage). Also presented are the model predicted pre-and post-vaccination annual number of events, the 95% confidence intervals (CIs) and the p-value associated with the vaccination variable in the model. For each resource use appropriate cost data were attached and the resulting annual costs per 100,000 infants < 5 are presented.

All measured resource categories showed statistically significant reductions associated with the introduction of the rotavirus vaccination programme. These varied in magnitude according to the resource category with laboratory reports showing the highest reduction of 73% (IRR 0.273, $p < 0.001$) and the smallest reduction of 17% in calls to NHS24 (IRR 0.826, $p < 0.001$). Table 3 also presents the cost difference

Table 2. Sensitivity analysis of alternative vaccine price on overall cost-impact results.

Test cost (per dose)	£11.96	£23.91 (base case)	£35.87
Overall cost-impact (annual)	£586,798	£1,030,751	£1,475,076

estimated from the predicted pre-and post-vaccination mean costs. The reduction in hospital stays forms the largest part of the cost difference. Figures 1 and 2 present the actual and predicted counts for laboratory reports and hospital stays respectively. Equivalent figures for the other resource categories are presented in the Supplementary Material. These figures were selected for presentation in the main body of the article as they illustrate the model fit achieved in the most specific measure of rotavirus (positive laboratory reports) and the largest cost category (hospital stays).

Discussion

Our study found statistically significant reductions in all rotavirus-related health-care resource categories examined following the introduction of the vaccination programme. However, the range of the reductions varied from 17% to 73%. The size of the reduction is driven by the ability of the data source to accurately capture cases of rotavirus. The highest reduction was found in the most specific data source, positive laboratory reports and the lowest in the least specific areas of NHS24 calls and prescriptions for rehydration treatments. We found a 40% reduction in hospital stays, which are the main cost driver among health-care resource categories.

Our findings are in line with the extensive literature across diverse geographies finding that the introduction of a rotavirus vaccination programme leads to reductions in a broad range of health-care resource categories.^{12,13} Prior to the introduction of the rotavirus vaccination programme, the Scottish Government predicted that such a programme could reduce the number of rotavirus-related hospital stays by approximately 70%.¹⁴ Forrest et al (2017) found a reduction of 85% and 91% in rotavirus related admissions and bed-days, respectively, in a paediatric hospital setting in Lothian, Scotland.¹⁵ This study used a highly specific definition of rotavirus-based admissions based on positive laboratory reports so is comparable with the 73% reduction suggested by our study. In undertaking this study, we gave much consideration to the issue of how best to capture the impact of rotavirus on hospital resources. When we considered the changes in solely those hospital admissions and bed-days which were coded for rotavirus specific (ICD10 code “A080” in either 1st and 2nd diagnostic position), we observed higher reductions in hospital admissions for rotavirus and rotavirus-related hospital stays similar to the reductions found by Forrest et al.¹⁴ However, many hospital admissions relating to rotavirus are coded as generic viral enteritis, particularly when specific organism testing is not required for clinical management. As the aim of this study is to estimate the cost impact we chose to increase the sensitivity of our measure by including viral enteritis unspecified (possible rotavirus) “A083”, “A084” and “A085” as well as the specific rotavirus code “A080”. This would have the effect of increasing the volume of cases in both the pre-and post-vaccination periods as well as reducing the percentage differences between the periods. It is likely that using these codes will miss a proportion of rotavirus cases as they are likely to be coded under general acute gastroenteritis codes.¹⁵ Our finding of

Table 3. Adjust incidence rate ratios (IRRs) for the association between vaccination and rotavirus-related annual events and costs, for infants < 5 years old in Scotland.

Effects	Pre-vaccination mean events	Post-vaccination mean events	Incident rate ratio for association (IRR) between introduction of vaccination and resource use (IRR 95% CIs) (p-value)
Laboratory reports	515	105	0.273 (0.266, 0.279), p < 0.001
Hospitalisation days (length of stay)	1,169	631	0.599 (0.589, 0.601), p < 0.001
A&E visits	2,177	1,791	0.655 (0.652, 0.658), p < 0.001
GP consultation	3,301	2,672	0.736 (0.729, 0.743), p < 0.001
NHS24 calls	2,725	2,208	0.826 (0.820, 0.833), p < 0.001
Prescriptions	N/A	N/A	0.798 (0.788, 0.808), p < 0.001
Costs	Pre-vaccination mean cost	Post-vaccination mean cost	Cost difference
Laboratory reports	£10,825	£2,211	£8,615
Hospitalisation days (length of stay)	£1,075,510	£580,624	£494,886
A&E visits	£232,973	£191,662	£41,311
GP consultation	£119,653	£96,871	£22,782
NHS24 calls	£56,913	£46,113	£10,800
Prescriptions	£71,117	£54,041	£17,076
Total costs	1,566,992	£971,522	£595,470

Notes: CI – confidence intervals. IRR–Incidence Rate Ratio. An IRR below 1 indicates a reduction in events and costs associated with the vaccination programme. P-value is a measure of statistical significance and a result under 0.05 is considered statistically significant for the purposes of this study. All models were adjusted for seasonality and underlying trend. The mean costs are estimated by applying a unit cost to the event rates predicted by the model.

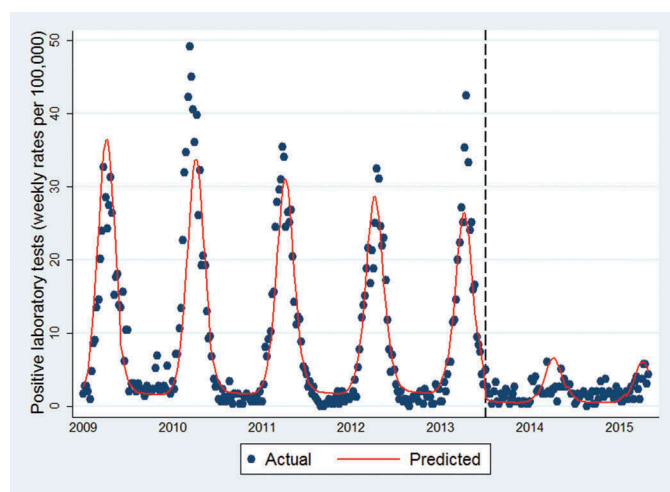


Figure 1. Positive laboratory reports for rotavirus (weekly rates per 100,000), for infants < 5 years old in Scotland – 2009 to 2015.

Notes: $R^2 = 0.86$. Dashed line represents introduction of vaccination programme

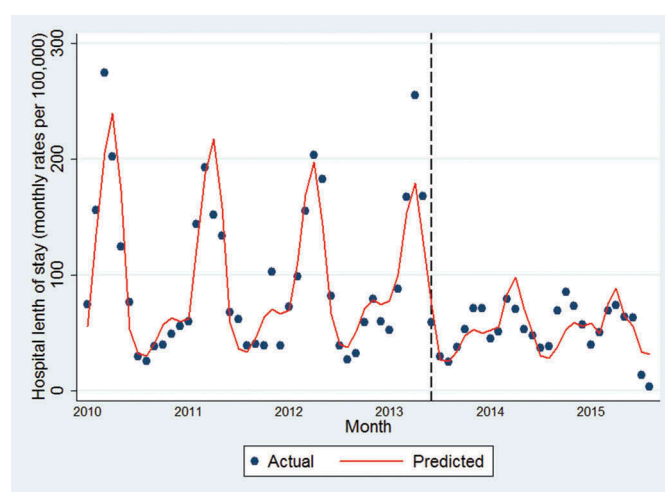


Figure 2. Hospital length of stay for rotavirus (weekly rates per 100,000), for infants < 5 years old in Scotland – 2010 to 2015.

Notes: $R^2 = 0.83$. Dashed line represents introduction of vaccination programme

a 40% reduction in hospital admissions is in line with the 44% reduction found in a study of five local authority areas in Merseyside, England over the period 2013–2016 (consisting of five hospitals with emergency and secondary care facilities and a paediatric hospital).¹⁶

We found that the impact of the vaccine in primary care was lower than that predicted by Jit et al (2007), with a substantial proportion of overall reduction in healthcare cost due to a decrease in GP consultations.¹¹ Data were available on consultations for diarrhoea, vomiting and all gastrointestinal illness, however due to possible double counting and for consistency with other data analysed for this study, we decided only to include the impact from consultations for diarrhoea. This may therefore represent an underestimate, which may explain the 32% reduction in prescriptions during the rotavirus season, despite only a 16% reduction in consultations. Lack of adherence to the use of appropriate Read codes may also help to explain this underestimate.

The impact of childhood rotavirus infection and the vaccine on nonmedical costs was not included in this study, however it is likely that there are significant costs associated with productivity loss (or “time-off” work) of the parent(s). Different studies give different estimates of the number of work days lost – typically ranging from around two to five days.¹⁷ The typical UK worker earns a median daily wage of £103.6.¹² Hence, 2 days (5 days) forgone work on behalf of the caregiver results in £207.2 (£518) in lost earnings per childhood rotavirus case. Some estimates suggest that the loss in productivity to the economy is the difference between a rotavirus vaccination programme being, not only cost-effective, but cost saving in the UK.¹³

This study only considers costs and does not value the improved quality of life which a reduction in rotavirus incidence would deliver. Jit and Edmunds (2007) report a quality of life (QALY) loss due to rotavirus of 0.0022 for a child and 0.00184 for an adult per case of rotavirus.¹¹ In our study, there

was a mean of 472 laboratory confirmed cases of rotavirus pre-vaccination programme, compared with 110 cases post-vaccination programme, per 100,000 infants < 5 in Scotland. If we use this as a proxy for the mean number of rotavirus cases pre- and post-vaccination, then we estimate the QALY loss averted per family (2 adults, 1 infant) as 2.13 QALYs per 100,000 infants < 5 years old in Scotland between the mean year pre-and post-vaccination period.

Since completion of our analysis, the first full year of data became available for calendar year 2015 (infants born Jan-Dec 2014). These indicate 53,013 infants (18,141 infants per 100,000) received rotavirus vaccine in 2015. This is comparable with the estimate used in our analysis (18,575 infants, per 100,000).

Strengths and limitations

At time of publication, this is the only study the authors are aware of which attempts to estimate the cost-impact of the rotavirus vaccination programme for the whole of Scotland, based on observational data.

The challenge with using indicators of gastrointestinal illness such as reporting of symptoms of diarrhoea as a proxy for rotavirus is that it also captures changes in the prevalence of other gastrointestinal illnesses unrelated to rotavirus. As a result, there are uncertainties in the estimates of resource use both pre-and post-vaccination and these differ depending upon the type of resource-use considered. In comparing our results with other studies it is, therefore, important to note the precise definitions included in the analysis.

We obtained data on the number of prescriptions made per-day per-patient population, however, we did not have a further breakdown of composition of these prescriptions (i.e. which hydration drugs were given). Hence, it was not possible to calculate the change in mean prescriptions and then attach unit costs. Rather, we calculated the change in the mean gross cost of prescriptions pre-and post-vaccination programme. A detailed breakdown of the prescriptions given would have provided a more accurate estimate of the cost-impact, however it is not clear whether an absence of this breakdown suggests an over or underestimate of the overall cost-impact. The data we obtained was based on prescriptions for rotavirus in primary care. However, there is the possibility that these prescriptions, which are mainly rehydration drugs, could have been prescribed for alternative conditions requiring rehydration.

Due to duplication concerns, it was not possible to use calls relating to vomiting and diarrhoea, combined, from NHS24 data. Hence, data on calls citing diarrhoea in infants < 1 year old and < 5 years old were used as a proxy for rotavirus. It is acknowledged that this is likely to be an underestimate of the true total cost associated with NHS24. Similarly, for duplication concerns, only GP consultations for diarrhoea were included. This is also likely to represent a considerable underestimate of the cost.

The overall cost-impact of the vaccination programme was highly sensitive to the cost of the vaccine, which we were not able to confirm. Our analysis relies on an estimate from the literature which we varied in sensitivity analysis.

Conclusion

In this study we have estimated the mean change in rotavirus-related resource use before-and-after the introduction of the Scottish Government's rotavirus vaccination programme in 2013. In doing so, we have observed reductions in the burden placed on rotavirus-related; laboratory reports; hospitalisations; GP consultations; A&E attendances; and NHS24 calls. Our analysis showed a reduction in the mean number of rotavirus-related hospital bed-days of 40%. This reduction accounted for 83% of the overall cost reduction associated with the implementation of the rotavirus vaccination programme. This study found that the overall cost-impact of the rotavirus vaccination programme (that is, the cost of delivering the programme minus the reduction in resource costs) was £435,000 increase (2013 prices) per annum per 100,000 infants < 5 years.

Methods

Statistical analysis

In line with previous research¹⁸ and European Centre for Disease Prevention and Control (ECDC)¹⁹ guidance, this study adopted a "before-and-after" approach with the pre-vaccination period serving as a reference point from which to compare the post-vaccination period.

This study defined the net cost-impact of the programme as being the cost of the vaccination programme minus cost reductions in resource use. As such, the net cost-impact was defined as follows:

$$\begin{aligned} \text{Net cost impact} &= (\text{cost of vaccine} + \text{administration payment}) \\ &- (\text{cost reductions from lab reports, hospitalisations,} \\ &\text{A\&E attendances, GP consultations,} \\ &\text{prescriptions and NHS24 calls}) \end{aligned}$$

To investigate the impact of the rotavirus vaccination programme, in terms of the change in resource use and cost-impact, we used an interrupted time series analysis.²⁰

To estimate the overall cost-impact of the rotavirus vaccination programme, we first estimated the rotavirus-related resource utilisation for each resource pre- and post-vaccination programme, in units determined by how the data were collected (i.e. resource use per week or per month). We attached unit costs to resource use to estimate the cost of this resource over each time period for which the data were collected. Mean resource use in the pre-and post-vaccination periods were assessed using a range of modelling approaches. We selected a Generalised Linear Model (GLM) with a Poisson family and log link as this reduced autocorrelation and provided the best model fit. We assessed goodness of fit of alternative models using the Akaike and Bayesian Information Criteria²¹ Underlying trend was accounted for within the regression framework and seasonality were modelled by including Fourier terms (sine and cosine terms)²⁰ and a dummy variable representing the peak rotavirus season (January-May). We also included an interaction term between the seasonality variables and the relevant period variable (week or month) to allow seasonality to vary in different

time periods. We hypothesised that the rotavirus vaccination programme would result in a permanent level change in resource use.²⁰ We therefore included a single binary variable to represent the intervention which was coded '0' in the period prior to the vaccination programme and '1' in the period following the introduction of the programme.

Population data for all infants < 5 years old living in Scotland over the study period were obtained from the National Records of Scotland and used as an offset variable.²² Incidence rates per 100,000 were calculated as the number of incidents (i.e. days in hospital or GP consultations) divided by the study population (number of infants < 5 years old living in Scotland) per year multiplied by 100,000. The same approach was used to estimate the cost of the programme, hence cost per 100,000 represents the cost of providing the vaccination to eligible infants (age 8 weeks and again at 12 weeks) to realise the benefits over the population of all infants < 5 years.

One-way sensitivity analysis was undertaken to estimate the impact on the cost of the vaccination programme of alternative vaccine prices. Vaccine price was varied \pm 50% of the base case price. The results are presented in the supplementary material.

Perspective

This study takes the perspective of the UK National Health Service (NHS) and includes resource use associated with laboratory reports, hospitalisations, A&E attendances, GP consultations, prescriptions and NHS24 calls. This is the only study at present to take such a wide perspective in estimation of the economic benefits from a national rotavirus vaccination programme in Scotland.

Measurement of resource use

Data available for each resource were; 2009–2014 for laboratory reports; 2010–2014 for hospitalisations; 2010–2014 for NHS24 calls; 2010–2014 for prescriptions; 2011–2014 for A&E; and 2011–2014 for GP consultations.

Laboratory confirmed reports

All laboratory confirmed cases of rotavirus infection in Scotland are reported to HPS via the Electronic Communications of Surveillance in Scotland (ECOSS) system.²³ A positive laboratory sample was detected using a real-time PCR and were only counted for the first sample from any patient episode and repeated laboratory tests for the same episode were not included. Laboratory reports for infants < 5 years old in the pre- and post-vaccination years were used.

Hospitalisation data

All hospitalisations for infants < 5 years were extracted using Scottish Morbidity Records (SMR01) database using predefined International Classification of Diseases 10 (ICD10) codes Rotavirus enteritis "A080" and Viral enteritis unspecified (possible rotavirus) "A083", "A084" and "A085".²⁴ This aimed to capture admissions for rotavirus, which are not laboratory confirmed due to the relatively short length of stay and which are coded under the more general term of viral enteritis. Due to

concerns of possible double counting of patients only data with the relevant ICD10 code as main diagnosis were included.

When a patient is discharged from hospital or transferred between hospitals, specialties or to the care of a different consultant, an episode is generated. Episode data were grouped together to identify continuous inpatient stays (CIS) and it is this level of analysis that was used to monitor hospital admissions and length of stay in this study.

Accident and emergency (A&E) data

Age specific monthly data on attendances at A&E data for symptoms associated with gastrointestinal illness was available from Information Services Division (ISD). These data are based on a combination of ICD10 codes and, where coding was not used, free text analysis. Data were analysed for infants aged < 5 years.

GP consultation data

Data on GP consultations, who provide all primary care for infants in Scotland, recorded for all infants < 5 years old for diarrhoea were obtained as the best proxy for rotavirus-related GP attendances. Weekly aggregate data are received by HPS from approximately 50% of General Practices (GP) across Scotland on the number of consultations based on defined Read codes, which are currently the standard clinical classification terminology system used in GPs in the United Kingdom.²⁵ Data were obtained from a broad geographical spread of Scotland and were considered representative of Scotland as a whole. Data were scaled to account for 100% of GP practices.

NHS24 syndromic surveillance data

HPS monitor trends in calls made to the NHS24 telephone helpline in Scotland. NHS24 is also the route to out-of-hours general practice care. Data gathered on the number of calls relating to vomiting and diarrhoea give an indication into the incidence of gastroenteritis in the community. Due to duplication concerns, it was not possible to use data relating to vomiting and diarrhoea combined. Hence, data on calls citing diarrhoea in infants < 5 years old were used as a proxy for rotavirus.

Prescription data

Data on rotavirus-related drug prescriptions were collected by the Prescribing Information System (PIS) provided by ISD Scotland and based on prescriptions administered in the primary care setting. Treatment for rotavirus typically involves the prescription of oral rehydration drugs. Data on prescription of the following drugs, listed in local formularies, were used as a proxy for rotavirus and viral enteritis: Dioralyte; Dioralyte Relief; Electrolade; O.R.S Oral, Peach. Data were provided in terms of the gross ingredient cost (£) per month for infants < 5 years old over the period 2010–2015. Hence, change in gross cost pre- and post-vaccination were reported, rather than change in resource use (i.e. unit costs were not necessary).

Vaccine price

The Joint Committee on Vaccination and Immunisation (JCVI) carried out a review of the published literature on the cost-effectiveness of rotavirus vaccines on behalf of the

Scottish Government.²⁶ The JCVI statement on rotavirus vaccine assumes a vaccine unit price of £35 per dose (2006 prices), based on the work of Jit & Edmunds.¹¹ At the price of £35 per dose, the incremental cost per QALY gained would be £61,000 and hence unlikely to be considered cost-effective. Further modelling by the authors suggested that the vaccine would have to be priced at £19 per dose for the cost of the programme to be less than £30,000 per QALY gained and hence deemed cost effective, given the current UK threshold. For this reason, we chose to assume a vaccine price of £19 per dose.¹¹ Inflating this to 2014 prices equates to £23.91 per dose and this was used as our base case price. Due to commercial sensitivities, there is no published price for the vaccine other than the JCVI statement.

The local health board pay each relevant GP an administrative payment of £7.67 per child receiving the rotavirus vaccination (one payment for two doses.²⁷ This payment was therefore included as a direct cost of providing the service.

Valuation of resource use

All prices are expressed in 2013/14 prices and have been inflated (where necessary) using the Hospital and Community Health Services (HCHS) Index which uses an inflation rate specific to the UK health service (PSSRU, 2014).

Any stool sample taken from an infant suffering from diarrhoea and vomiting would undergo a full screening for a range of gastrointestinal pathogens, rather than for one specific causative agent. Hence, the unit cost of a routine enteritis laboratory report was given by Lorgelly et al as £15.08 per report (in 2001/02 prices, £20.99 in 2013/14 prices).²⁸

The unit cost estimate for hospitalisations in 2013/14 was obtained from ISD. Using their new patient-level costing data, they were able to estimate the cost per day of hospital treatment for rotavirus (based on ICD10 code A080). The unit cost per day for rotavirus was estimated at £920 (2013/14). This unit cost is applied to both incidents of rotavirus coded as “rotavirus” and “viral enteritis” in SMR01 hospitalisation data.

A standard unit cost of £107 per attendance at A&E was obtained from ISD’s annual Scottish Health Service Costs.²⁹

The unit cost of a GP consultation was obtained from the Personal Social Services Research Unit 2014 publication.³⁰ The unit cost was £37.50, per GP visit lasting 11.7 minutes (excluding qualification costs).

The unit cost per call to NHS24 was reported by Munro et al as £15 (2001 prices). Inflating this to 2014, provides a unit cost of £20.88.³¹

Highlights

- The Rotavirus vaccination programme for infants < 5 years old in Scotland was associated with a reduction in healthcare resource utilisation.
- The Rotavirus vaccination programme was associated with a reduction in healthcare resource costs of 38% (approximately £595,000 per 100,000 infants < 5 years old) before accounting for the cost of the programme.
- 83% of the reduction in costs associated with rotavirus-related resources use came from reduced hospitalisations.

- Based on our assumed costing of vaccine at £23.91 per single dose the cost of the vaccination programme is estimated at approximately £1,031,000 per 100,000 infants under five years old, resulting in an overall annual cost of the programme of approximately £435,000 per 100,000 infants under five years old.

Disclosure of potential conflicts of interest

No potential conflict of interest was reported by the authors.

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