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Beyond expectations: Post-implementation data shows rotavirus vaccination is likely cost-saving in Australia

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ABSTRACT

Background: Universal vaccination against rotavirus was included in the funded Australian National Immunisation Program in July 2007. Predictive cost-effectiveness models assessed the program before introduction.
Methods: We conducted a retrospective economic evaluation of the Australian rotavirus program using national level post-implementation data on vaccine uptake, before-after measures of program impact and published estimates of excess intussusception cases. These data were used as inputs into a multi-cohort compartmental model which assigned cost and quality of life estimates to relevant health states, adopting a healthcare payer perspective. The primary outcome was discounted cost per quality adjusted life year gained, including or excluding unspecified acute gastroenteritis (AGE) hospitalisations.
Results: Relative to the baseline period (1997–2006), over the 6 years (2007–2012) after implementation of the rotavirus program, we estimated that ~77,000 hospitalisations (17,000 coded rotavirus and 60,000 unspecified AGE) and ~3 deaths were prevented, compared with an estimated excess of 78 cases of intussusception. Approximately 90% of hospitalisations prevented were in children <5 years, with evidence of herd protection in older age groups. The program was cost-saving when observed changes (declines) in both hospitalisations coded as rotavirus and as unspecified AGE were attributed to the rotavirus vaccine program. The adverse impact of estimated excess cases of intussusception was far outweighed by the benefits of the program.
Conclusion: The inclusion of herd impact and declines in unspecified AGE hospitalisations resulted in the value for money achieved by the Australian rotavirus immunisation program being substantially greater than predicted by pre-implementation models, despite the potential increased cases of intussusception. This Australian experience is likely to be relevant to high-income countries yet to implement rotavirus vaccination programs.

1. Introduction

Rotavirus is the most frequent cause of severe dehydrating diarrhoea in young children worldwide [1], resulting in substantial health care utilisation, quality of life impact, and productivity loss in caregivers. The introduction of rotavirus vaccination in many high-income settings led to an almost immediate impact on the burden of rotavirus disease, especially in preventing substantial numbers of hospitalisations in young children [2–5].

Prior to introduction of universal vaccination against rotavirus for infants to the Australian National Immunisation Program (NIP) in July 2007, there were an estimated ~19,000 annual hospitalisations for acute gastroenteritis (AGE) in children less than 5 years of which ~10,000 were attributable to rotavirus infection [6]. Since program implementation, marked declines in both rotavirus and all-cause AGE hospitalisations [7–13] as well as presentations to an emergency department (ED) [14] were observed for children less than 5 years, in both vaccinated cohorts and in other young children [10]. Assessment of risk of intussusception (IS)

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following rotavirus vaccination in Australia [15–17] found evidence of a small increased risk of IS in the first 1–21 days after receipt of doses 1 and 2 for both vaccines [15,16].

Public funding of vaccines in Australia requires confidential economic evaluations by the respective vaccine manufacturers submitted to the Pharmaceutical Benefits Advisory Committee (PBAC) [18,19]. For rotavirus vaccination in Australia, there was also an academic-led cost-effectiveness analysis [20,21] suggesting borderline cost-effectiveness of the program at the manufacturer-listed price. Since this time, Australian surveillance data captured effects across a broad range of rotavirus disease indicators and provided evidence of herd immunity effects not anticipated in earlier evaluations [5,11,22,23].

We have previously outlined the value of retrospective cost-effectiveness analyses for vaccination programs, through methodological advice and an evaluation of the 7-valent pneumococcal conjugate vaccine in Australia [24,25]. In this study, we expand on our previous research to evaluate the value for money achieved by the Australian rotavirus vaccination program using post-implementation data on vaccine coverage, program impact, and adverse events following immunisation.

2. Methods

2.1. Study design and model

We designed an age-specific static multi-cohort compartmental model to examine the impact of the Australian rotavirus program. While the program was implemented (in July 2007 for children born from 1 May 2007) using two different vaccine brands, we examined the vaccination program as a whole, not as individual brands of the vaccine. We adopted a healthcare payer perspective with costs and benefits discounted at 5% per annum as recommended in Australian PBAC guidelines [26]. We calculated the incremental cost-effectiveness ratio (ICER) for different scenarios (see below Program impact) and report results from the base case model and use the median when reporting results from the probabilistic sensitivity analyses.

2.2. Data sources and rates of health outcomes

We included potential rotavirus-associated AGE health outcomes, including hospitalisations, deaths, ED presentations, general practitioner (GP) consultations, rotavirus infections not requiring medical care, and intussusception cases. Rates of health outcomes were estimated using observational data over the years 1997–2012, where available. For each of these outcomes, we converted the data to annual age-specific rates using population data from the Australian Bureau of Statistics (ABS) [27]. Specific details are reported in Supplementary File 1. Where possible, we considered the following age stratifications: 0–<6 months, 6–<12 months, 1–<2 years, 2–<3 years, 3–<4 years, 4–<5 years, 5–<10 years and 10–<15 years. The available observational data was divided into two main categories: either ***'coded' rotavirus (coded-RV)*** using rotavirus-specific diagnostic codes or ***'unspecified' acute gastroenteritis (unspecified AGE)***. Studies prior to vaccination have shown that a high proportion of unspecified AGE in young children was due to rotavirus infection [6]. The coded-RV data was determined using rotavirus-specific diagnostic codes. Any change in this category is likely to underestimate the program impact since not all cases of AGE due to rotavirus are coded as such (e.g. due to a lack of laboratory testing [13]). For coded-RV hospitalisations we used ICD-10-AM A08.0 (Rotaviral enteritis), while for unspecified AGE hospitalisations we combined ICD-10-AM A08.4 (Viral intestinal infection, unspecified) and A09 (Infectious gastroenteritis and colitis, unspecified) as used previously [6]. For GP consultations and non-admitted ED presentations, we focused on syndromic AGE presentations since rotavirus is rarely tested for in these settings. Details of the calculation of annual rates and changes in non-medical care as well as intussusception cases as are provided in Supplementary File 1. The annual rates used in the model are illustrated in Figs. S1.1 and S1.2.

2.3. Program impact

We established two different scenarios on the period 2007–12: the "with vaccine" scenario which was based on the observed data, and the hypothetical "no vaccine" scenario which was estimated based on an average of the pre-implementation rates in the data available prior to 2007 (see Supplementary File 1) in each of the outcomes. The impact of the vaccination program was calculated by taking the difference between estimates for the numbers of cases from the "with vaccine" scenario and those from the "no vaccine" scenario. For projections of the "with vaccine" scenario beyond the observed data, we applied the average rate in the last 3 years of available post-implementation data (see Supplementary File 3, Future benefits).

We considered two main scenarios for the impact on hospitalisations, including either changes in ***coded-RV*** hospitalisations only or in both ***coded-RV + unspecified AGE*** hospitalisations. Impacts using observed changes were presented separately in order of increasing uncertainty (in hospitalisations, deaths, ED presentations, GP consultations and excess IS cases in infants <1 year old) in children (i) <5 years, (ii) <15 years, and (iii) <15 years with the addition of non-medical care. We excluded impacts on persons aged 15 years and above due to a lack of supportive evidence of effect.

2.4. Costs and quality of life

Costs and QALY losses used in the model are shown in Table 1 and details of their estimation are provided in Supplementary File 1. Hospitalisation costs in Australia were estimated using Australian Refined Diagnosis-Related Groups (AR-DRG) codes associated with corresponding ICD-10-AM hospitalisation codes [28,29]. Costs of ED presentations were calculated in the same way using the ED component of this data [28,29]. GP consultation costs were estimated as in Newall et al. [20], using costs of consultation and bulk-billing service fee in 2007 [30]. No costs were included for non-medical care.

While the negotiated price for rotavirus vaccines in Australia is confidential, an estimated program cost was listed in Australian budget papers [31] in 2008. We used this to estimate a cost per completed schedule set to the same value for each vaccine based on the PBAC recommendations [18,19]. The total cost of program implementation between 2007 and 2012 was calculated using annual data on vaccine uptake from the Australian Childhood Immunisation Register (ACIR) (see Supplementary File 1). Vaccine administration costs were applied as in Newall et al. [20].

QALY loss estimates were taken from Brisson et al. [32] and are assumed to be the same for all cases with medical care. The QALY loss for non-medical care was assumed to be half that associated with medical care as assumed by Bilcke et al. [33]. As inclusion of QALY loss for caregivers (not ill from rotavirus) remains controversial, it was only included in additional scenario analyses.

2.5. Sensitivity analyses

One-way (varying each parameter by ±25% from base case) sensitivity analyses were conducted to explore which parameters were most influential in the model. Probabilistic sensitivity