Budget impact and cost-utility analysis of universal infant rotavirus vaccination in Spain

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ABSTRACT

Rotavirus is not included in the Spanish mass infant vaccination schedule but has also not been economically evaluated for its inclusion. We analysed cost-utility of the universal infant rotavirus vaccination using RotaTeq® versus no vaccination in Spain. We also carried out a budget impact analysis and determined the effect on results of different variables introduced in the model. A deterministic Markov model was built considering loss of quality of life for children and their parents, and introducing direct and indirect costs updated to 2011.

The introduction of the vaccination using RotaTeq® as a universal infant vaccination would increase the annual health care budget in 10.43 million euro and would result in a gain of an additional Quality Adjusted Life Year at a cost of 280,338€ from the healthcare system perspective and 210,167€ from the societal perspective. The model was stable to variable modifications.

To sum up, according to our model and estimates, the introduction of a universal infant rotavirus vaccination with RotaTeq® in Spain would cause a large impact on the health care budget and would not be efficient unless significant variations in vaccine price, vaccine efficacy and/or utilities took place.

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Introduction

Rotavirus is a major cause of acute gastroenteritis in children worldwide (CDC, 2011). Although deaths due to rotavirus occur mostly in less-developed countries (Parashar et al., 2009), a substantial burden of Rotavirus Gastroenteritis (RVGE) has been reported in European countries (Giaquinto et al., 2007). In Spain, RVGE entails important morbidity and considerable resource utilization across all health care settings, as well as for families of patients and their employers (Diez-Domingo et al., 2010). It has been estimated that 181,626 episodes of acute gastroenteritis occur per year among children under 5 years of age in Spain (Díez-Domingo et al., 2010), which translates into 14,342 hospitalizations, 41,701 emergency department visits and 48,320 primary care visits with important implications for families, and society as a whole. Spanish parents miss, on average, 4.6 workdays when their child is hospitalized due to a rotavirus infection (Giaquinto et al., 2007).

Vaccination has proven to be effective in preventing rotavirus infections and limiting their impact (Vesikari et al., 2006). Although there are two rotavirus vaccines authorized for use in the European market, RotaTeq® and Rotarix®, our study has focused only on RotaTeq®, as it is the only vaccine available in Spain (Agencia Española de Medicamentos y Productos Sanitarios, 2010a, 2010b, 2010c). Currently the rotavirus vaccination is not included within the Spanish universal infant vaccination schedule, so RotaTeq® has to be purchased at market prices, as an out of pocket expense, if so desired.

The introduction of a new vaccine into the public immunization schedule would require a high resource investment and significant costs, taking into account that public vaccination programmes are, currently, completely publicly funded.

Cost-utility studies have been performed in some European countries, though not in the Spanish setting, estimating the costs of adding a Quality Adjusted Life Year (QALY) with mass vaccination versus no vaccination and adopting time dependence models. The assessments have differed in their assumptions, choice of model, contextual information, and other parameters, but also in their results. Some of them have concluded in favour of the introduction of the universal rotavirus vaccination (Atkins et al., 2012; Jit et al., 2009). However, most of them have come to the conclusion that the introduction of the vaccine would not be efficient with the current conditions, although a lower vaccine price could achieve a cost-effective result(Bilcke et al., 2009; Mangen et al., 2010; Melliez et al., 2008; Rozenbaum et al., 2011; Tilson et al., 2011).

An economic evaluation of rotavirus vaccination has recently been published for a specific region in Spain, "Castilla y León" (Pérez-Rubio et al., 2011). The study estimates the cost–utility ratio based on a decision tree that does not take into account time evolution and second episodes. Our study tries to overcome these limitations, using a Markov model, to compare the cost–utility of the universal infant rotavirus vaccination in Spain using RotaTeq® versus no vaccination. In addition, we assessed the effect on these results of varying different variables that feed the model.

Methods

A deterministic static Markov cohort model, adopting both the Spanish National Health System (SNHS) and the societal perspective, was developed for a hypothetical cohort of 500,000 newborns, which represents the approximate annual birth rate in Spain (INE, 2012). The model was built using the Tree Age Pro Suite 2011.

Two strategies were compared: one considering a fully publicly funded universal rotavirus vaccination with RotaTeq®, and the other considering no vaccination. In the vaccination strategy, children are vaccinated with RotaTeq®, at 2, 4 and 6 months. A 96% vaccination adherence rate was assumed, which corresponds to the average adherence rate reported for the Spanish infant vaccination programme in previous years (Ministerio de Sanidad, 2012).

The following health states were included in the model as represented in Fig. 1: 1) no previous infection (being at risk for rotavirus infection for the first time), 2) first rotavirus infection, 3) post first-infection (being at risk for a second rotavirus infection), 4) second rotavirus infection, 5) post second-infection, 6) rotavirus death, and 7) non-rotavirus death (death by causes other than rotavirus).

The model's time horizon was five years with one month time cycles. In each monthly cycle, children in the cohort have a risk of getting rotavirus-induced diarrhoea. Diarrhoea may lead to consultation of a General Practitioner (GP), visit to an emergency service, not seeking any medical attention or death. The GP may send patients to the emergency service or home. Once a patient seeks emergency service attention, they can be hospitalized or sent home. A child can be confronted with a second episode, but this one is assumed not to be severe and never lead to death by rotavirus infection. We also assume that the child is fully immune after two rotavirus infections. Only severe consequences were assumed for a first infection as rotavirus immunity acquisition has been reported (Velázquez, 2009; Ward et al., 1994).

Clinical parameters

The probabilities of getting a rotavirus infection were derived from the Spanish epidemiological data included in the REVEAL study (Van Damme et al., 2007) (Table 1). This is a broad sample of Spanish rotavirus infection incidence data, from 2 hospitals, 3 emergency departments and 23 primary care centres that registered rotavirus infections between October 2004 and September 2005, for children under the age of 5. These data were based only on community-acquired infections, excluding nosocomial ones.

Mortality rates for children under the age of 5 were derived from the 2009 mortality data reported by the Spanish Statistical Institute (INE, 2012) (Table 1). Transition probabilities regarding natural history and health care utilization after episodes of rotavirus infection are displayed in Table 2. Due to the lack of available Spanish data, we assumed the transition probabilities of risk reduction after a first rotavirus infection reported in a rotavirus vaccine trial conducted along two years in the USA (Ward and Bernstein, 1994). We assumed the same transition probabilities regarding health care utilization as those found in the French and Finnish economic evaluations (Melliez et al., 2008; Takala et al., 1998).

Regarding efficacy of RotaTeq® to avoid rotavirus infection among children, we used data from the Rotavirus Efficacy and Safety Trial (REST) (Vesikari et al., 2006). To the best of our knowledge, this is the only randomized trial that evaluates the efficacy of the vaccine among children of developed countries with a long follow-up period. This randomized controlled trial studied nearly 70,000 children from eleven, mostly developed, countries, reporting 74% higher efficacy for RotaTeq® vaccination compared to placebo in preventing first rotavirus episodes (CI 95%: 66.8–79.9). Our base case used the efficacy in the REST trial for all rotavirus infections, regardless of severity. We assumed no herd immunity and no-waning vaccination efficacy during the five year period.

Costs and utilities

The analysis was performed both from the societal and the national health care payer (SNHS) perspectives. The societal perspective analysis included both direct (health care and non-health care) and indirect costs (Table 3), but the SNHS perspective included only direct medical costs. Costs are described in Table 3 and derive from the estimations for Spain included in the REVEAL study (Giaquinto et al., 2007), and were updated to 2011 using the Laspeyres index, recommended by the Spanish Statistics Institute (INE, 2012).

GP visits, emergency visits, telephone consultations, medication, home assistance, diagnostic and therapeutic procedures during hospitalization were included as direct medical costs. The SNHS perspective included only the direct medical costs reimbursed. However, the societal perspective included both reimbursed and non-reimbursed direct medical costs. Costs of hospitalization procedures were estimated using Diagnostic Related Groups. Medication consumption was estimated based on the average consumption for Spanish patients in the REVEAL study.

Caregiver expenses, extra nappies and transport-related costs were included as direct non-medical costs. Working days lost by parents or caregivers under the age of 65 were also included as indirect costs.
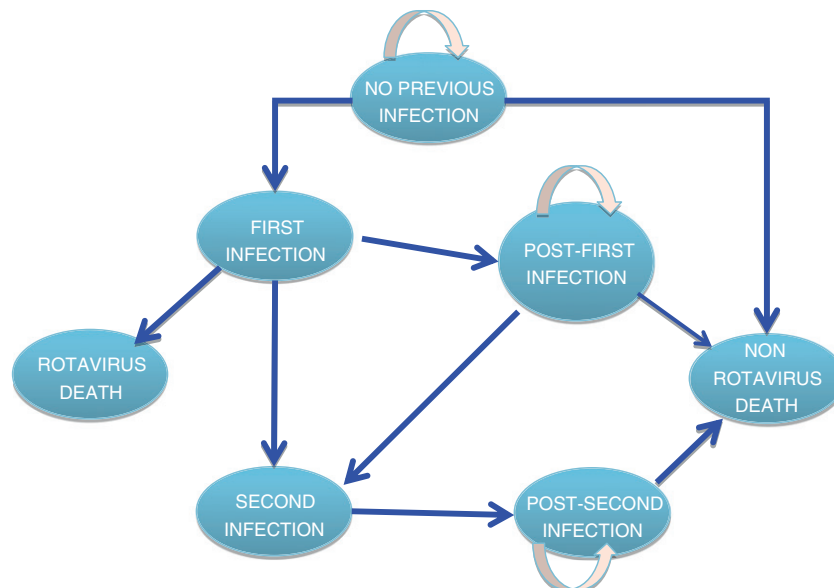

Fig. 1. Markov model representing the natural history of rotavirus infection.