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Cost and cost-effectiveness of childhood vaccination against rotavirus in France☆

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Summary
Objectives: To assess the effectiveness and cost-effectiveness of routine childhood vaccination by new vaccines against rotavirus in France.
Methods: We constructed a Markov decision tree to compare two alternatives: ''no vaccination'' and ''vaccination''. A hypothetical birth cohort of 750,000 children was followed until 3 years of age. First, the disease burden without vaccine was estimated using data from French databases and medical literature. Incidence rates in unvaccinated children were modelled as a function of age and seasons. Next, using data from the medical literature, the vaccine's protective effect on rotavirus diarrhoea was considered.
Results: A routine universal rotavirus immunization programme was estimated capable of annually avoiding 89,000 cases of diarrhoea, 10,500 hospitalizations, and 8 deaths. At a vaccination cost of €150/course, assuming 75% vaccine coverage, the programme would cost €95 million and involve a net loss of €68 million to the health care system. The vaccination programme would cost €298,000/year of life saved, and €138,000/QALY saved. Key variables affecting the results were disease incidence, mortality rates and vaccine price.
Conclusion: In France, childhood rotavirus vaccination with new antirotavirus vaccines would reduce the morbidity burden of rotavirus infection, but would not be cost-effective unless the price of vaccine decreased considerably.

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Introduction

Rotavirus has been recognized as the main cause of severe acute diarrhoea in young children [1]. In tropical countries, rotavirus infection is associated with high mortality [2]. In temperate countries rotavirus infection is associated with low mortality, but is responsible for high morbidity. In a previous study, we found that in France, rotavirus infection is responsible, annually, for 300,000 episodes of acute diarrhoea among children under 5 years of age [3].

To reduce the burden of rotavirus infection, huge efforts have been made to develop a vaccine. In 1998, the first oral reassortant tetravalent rotavirus vaccine was licensed in the United States [4–8]. However, its use was stopped after an association between the vaccine and the risk of intussusception was detected [9]. A monovalent vaccine based on an attenuated human rotavirus strain (RotaRix®) and a human-bovine reassortant rotavirus vaccine (RotaTeq®) were recently licensed in many countries throughout the world [10,11]. Several randomized clinical trials have been conducted to evaluate and demonstrate the efficacy of these new vaccines [12–15]. However, the decision whether or not to integrate a new vaccine into the routine immunization schedule increasingly requires cost and cost-effectiveness analysis, in order to optimize the allocation of limited financial resources and establish health intervention priorities on the basis of concrete evidence. The objective of this study was to compare the results of routine infant rotavirus vaccination versus no intervention, in terms of life years saved, costs and cost-effectiveness ratios. This study was performed as part of an ''expert advice'' provided by the French Advisory Board on Immunization to the Ministry of Health, in order to participate in the decision-making process regarding universal infant rotavirus vaccination in France.

Materials and methods

Study design

We estimated the impact of rotavirus vaccination performed during the first 4 months of life [12–15] as part of routine infant immunization, and compared this impact to that of the absence of rotavirus vaccination, which is the current situation in France. A Markov decision tree of the risk of various rotavirus-related outcomes was constructed to compare the two alternative strategies. The analysis was applied to a hypothetical French birth cohort of 750,000 children (the average number of annual births, 1997–2001) which was followed up until the age of 35 months. Model outcome measures included the number of symptomatic cases and hospitalizations, life expectancy, quality-adjusted life expectancy, lifetime costs, and incremental cost-effectiveness ratio [16]. We adopted a societal perspective, and in the base-case analysis, discounted both costs and clinical benefits at 3% per year [16].

Model structure

The model structure has been detailed in Fig. 1. In brief, the root of the decision tree is a decision node with two branches representing the two alternatives of vaccination and no vaccination. During the follow-up we considered rotavirus age-specific infection or reinfection rate, depending on the child's history of infection, birth cohort, and rotavirus vaccination. Mortality related to rotavirus infection and age-specific overall mortality were considered. We classified rotavirus diarrhoea episodes as mild or severe [17,18]. The second episode of rotavirus diarrhoea was always assumed to be mild [19–24]. Different scenarios regarding rotavirus management were considered.

Input data

Rotavirus diarrhoea incidence, diarrhoea management and mortality rates (Table 1)

The probability of the events in the decision tree was derived from the French Communicable Diseases Computer Networks [25], the National Hospital Discharge Database, a medical prescriptions evaluation database from a private network (IMS Health) [26], the National Deaths Notification Database [27] and the data available in the medical literature.

First we estimated the age-specific rotavirus diarrhoea incidence rate in France [3,25,28]. To obtain this, in the population of children under 3 years old, we began by determining the annual number of cases of rotavirus diarrhoea seen by general practitioners, by paediatricians, by practitioners in emergency rooms without previous consultation, and the number of children with rotavirus diarrhoea who did not consult at all. These numbers were then summed and divided by the total number of children of less than 3 years of age in France to estimate the annual rotavirus diarrhoea incidence rate.

To determine the number of rotavirus diarrhoea cases seen by general practitioners, we used data from the French Communicable Diseases Computer Network [25]. We first used data on number of acute diarrhoea cases per month for different age groups from 1992 to 2002. Five age groups were studied: 0–2 months, 3–5 months, 6–11 months, 12–23 months and 24–35 months. Next, using data from a community-based prospective study of diarrhoeal diseases carried out within the same surveillance network [28], we considered that in children under 3 years of age seen by a general practitioner between November and April, the proportion of cases of acute diarrhoea due to rotavirus was 27%. From April to November, this proportion was considered to be zero, and we postulated that it remained constant in all age groups. Of the total number of rotavirus diarrhoea cases, the proportion seen by paediatricians was estimated at 28%, using data from the IMS health medical prescriptions evaluation database [26]. The respective proportions of rotavirus diarrhoea cases seen in an emergency room without previous consultation (3%), and of cases for which there was no consultation (51%) were determined using published data on acute diarrhoea management [18,29].

Next, on the basis of data from a longitudinal follow-up of 336 infants from birth to 24–32 months of age, we estimated at 53 per 100 cases the probability of severe rotavirus illness among those with an initial episode of rotavirus diarrhoea [17,18]. The hospitalization rate for patients with acute diarrhoea due to rotavirus was then