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Benefits and costs of immunization of children with pneumococcal conjugate vaccine in Canada

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Abstract

To estimate cost-effectiveness of routine and catch-up vaccination of Canadian children with seven-valent pneumococcal conjugate vaccine, a simulation model was constructed. In base scenario (vaccination coverage: 80%, and vaccine price: $58 per dose), pneumococcal disease incidence reduction would be superior to 60% for invasive infections, and to 30% for non-invasive infections, but the number of deaths prevented would be small. Annual costs of routine immunization would be $71 million (98% borne by the health system). Societal benefit to cost ratio would be 0.57. Net societal costs per averted pneumococcal disease would be $389 and 125,000 per life-year gained (LYG). Vaccine purchase cost is the most important variable in sensitivity analyses, and program costs would be superior to societal benefits in all likely scenarios. Vaccination would result in net savings for society, if vaccine cost is less than $30 per dose. Economic indicators of catch-up programs are less favorable than for routine infant immunization.

Keywords: Cost-effectiveness; Pneumococcal vaccine; Canada

1. Introduction

Streptococcus pneumoniae remains an important cause of serious illness in children [1]. In Canada, the highest incidence of invasive pneumococcal infection is observed in those aged less than 2 years, and the case-fatality rate is 7% in children with pneumococcal meningitis and 44% in those presenting with septic shock [2]. Total costs of otitis media in Canadian children were estimated at $428 million in 1994 [3]. Antibiotic resistance is a matter of concern. In Quebec, only 3% of *S. pneumoniae* invasive strains were moderately susceptible or resistant to one or more of eight usual antimicrobial agents in 1984–1986 [4], and the proportion was 25% in the period 1996–1998 [5].

A seven-valent pneumococcal conjugate vaccine (Prevnar®) has been recently licensed for paediatric use [6]. The serotypes included in PCV-7 (4, 9V, 14, 19F, 23F, 18C, 6B) account for the large majority of invasive infections in children less than 5 years of age [7]. The safety and clinical efficacy of PCV-7 have been studied in randomized trials in the US [8,9] and Finland [10]. Decisions regarding inclusion of this new vaccine in routine immunization schedules for infants will have to be made by provincial/territorial health authorities, and economic evaluation is an important factor in these decisions. Results of economic analyses in the US [11] cannot be extrapolated validly to the Canadian context, due to differences in the composition of families, natural caregivers, employment rates, incomes, and costs of health services. In Canada, there is a comprehensive health insurance program in every juridiction offering gratuitousness of most medical and rehabilitation services. Publicly funded immunization programs are a provincial/territorial responsibility and free access to vaccines varies across the

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country [12]. The goal of this study is to estimate the effectiveness, cost and utility of a publicly funded immunization program against pneumococcal infections in Canadian children, using four doses of PCV-7 for routine vaccination of young infants, and 1, 2 or 3 doses for catch-up programs for older children.

2. Methodology

A simulation model representing mutually exclusive clinical outcomes and policy options was constructed for a cohort of 340,000 Canadian newborns followed up to the age of 106 years, the maximal life expectancy [13]. Pneumococcal disease included invasive infections: meningitis and bacteremia. Meningitis was supposedly always treated in hospital and could lead to death, deafness, other neurological disability, or no sequelae. Bacteremia was defined as any infection other than meningitis in which *S. pneumoniae* is isolated from blood. Non-invasive pneumococcal infections included pneumonia (excluding bacteremic pneumonia), and acute otitis media (AOM). Bacteremia and pneumonia could be treated in an outpatient clinic or in a hospital, and outcomes were either death or recovery with no sequelae. Acute otitis media may result in chronic serous otitis, requiring myringotomy with ventilation tube insertion (MVT). The "no vaccination" policy portrayed the present epidemiological situation. Under the "vaccination" policy, the probability of each outcome at each age was reduced in proportion to the expected population effectiveness of the immunization program. Perspectives of the health system, of the families, and of the society were considered in the analyses.

The net present costs (NPC) of pneumococcal immunization program was calculated as follows:

$$\text{NPC} = \sum \frac{\text{costs} - \text{benefits}}{(1+r)^t}$$

where 'costs' are the costs of vaccine purchase to the health system + vaccine administration costs for the health system and families, 'benefits' the costs of treatment of disease prevented to the health system and families + productivity gains from deaths prevented, 't' the time in years, 'r' the discount rate to take into account the differential timing of costs (at the time of vaccination) and of benefits (during the following 106 years).

In order to avoid double-counting, productivity gains were excluded in calculating cost-effectiveness and utility ratios: NPC per case of pneumococcal infection averted, per death averted, per life-year gained (LYG), and per quality-adjusted life-year gained (QALYG). All financial costs were expressed in year 2000 Canadian dollars. To handle inflation, all prices anterior to 1998 were adjusted using the Canadian price index for health and personal care [14]. Future costs were not inflated and a real discount rate was used (3% in the base model). Productivity losses and gains were calculated using sex-specific earnings of Canadians in 1998, and age- and sex-specific employment rates in 1999 [14].

Canadian health databases were used to estimate age-specific incidence rates of pneumococcal-related outcomes (Table 1). Details on the methodology are presented in another publication [15]. The proportion of pneumonia attributable to *S. pneumoniae* was set at 22% in the base model, based on published studies reporting values comprised between 13 and 37% [16–23]. The proportion of AOM attributable to *S. pneumonia* was assumed to be 19%, as estimated by an expert panel in the US [11]. Based on the work by Torrance [24], hearing loss was considered to be a mild disability state valued at 0.8, while neurological sequelae were considered to be a severe disability state valued at 0.6 (compared to healthy states).

Administrative health databases and results from a survey in a sample of patients in Quebec and Manitoba [15] were used to estimate average unit costs of pneumococcal-related outcomes (Table 2). Unit costs were multiplied by the frequency of episodes to estimate the economic burden of pneumococcal disease in the cohort of children between 6 months and 9 years of age.

Vaccine protection was assumed to begin after the third dose of PCV-7 at 6 months (routine program) and to continue up to 9 years of age. Short-term efficacy was that observed in the US trial for invasive pneumococcal infection (97.0%), for all causes pneumonia (10.7%), for all causes AOM (8.2%), and for MVT (24.9%) [8,9]. To estimate protection from routine and catch-up immunization up to 9 years of age, eight Canadian experts were consulted using a Delphi

Table 1
Incidence rate of pneurnococcal-related outcomes according to age (base model scenario)

Disease	Persons per	Years									
		0.5–1	1	2	3	4	5	6	7	8	9
Pneumococcal meningitis	100000	19.37	4.58	0.99	0.73	0.47	0.46	0.46	0.46	0.46	0.46
Pneumococcal bacteremia	100000	94.81	78.32	32.62	18.53	12.82	4.65	4.65	4.65	4.65	4.65
Hospitalized pneumonia all causes	1000	11.15	9.25	6.16	4.27	2.91	3.07	2.11	1.61	1.19	0.75
Non-hospitalized pneumonia all causes	1000	33.80	31.50	26.20	23.00	20.50	18.90	18.80	15.60	13.80	11.80
AOM all causes	1000	1178.60	925.10	560.50	449.00	390.80	356.40	289.80	220.10	170.00	138.50
MVT all causes	1000	11.35	21.89	11.79	10.19	10.06	10.52	9.20	5.98	3.67	2.20

AOM: acute otitis media; MVT: myringotomy with ventilation tube insertion.