Uptake of Pneumococcal Conjugate Vaccine: Methodological Issues in Measurement and Impact of Publicly Funded Programs

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ABSTRACT

Background: In Quebec, the pneumococcal conjugate vaccine was available on the private market as early as 2001 and has been included in the publicly funded immunization program since December 2004.

Objectives: To compare the advantages and limitations of two different sources for assessing vaccination coverage in the target population of children and to evaluate the impact of the public health program on uptake rates.

Methods: Data from a province-wide survey of a random sample of parents and from the Quebec City Immunization Registry were used to compute vaccination rates over time in different population groups.

Results: Data from the immunization survey and the regional registry were congruent regarding trends. Immunization rates were overestimated, more in the registry than in the survey. During the 2001-2004 period, uptake rates were low, and many children received fewer than the recommended number of doses. As soon as free vaccination was granted, uptake increased markedly and close to 90% of children received the recommended three doses, the level required for inducing herd effects. Delay in the administration of the third booster dose was observed.

Conclusions: Free vaccination is a major determinant of vaccine uptake and should remain a fundamental principle of the Canadian health system.

Key words: Evaluation study; immunization; pneumococcal vaccine

La traduction du résumé se trouve à la fin de l'article.

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A 7-valent pneumococcal conjugate vaccine (PCV7) was licensed in Canada in May 2001, and the vaccine was available on the private market soon thereafter.¹ It is an expensive product with a purchase price close to C\$100 per dose in a pharmacy and C\$70 for bulk purchase by the public sector. In the province of Quebec, free PCV7 was offered to high-risk children and those living in the two northern regions (Cree and Inuit) in October 2002, and four doses were recommended (respectively at 2, 4, 6 and 12-18 months of age).² In December 2004, PCV7 was included in the publicly funded immunization program, and three doses were recommended for low-risk children (respectively at 2, 4 and 12 months of age).³ At the same time, free vaccination was granted to all infants aged <5 years and offered during visits scheduled for the administration of other vaccines.

Measurement of vaccination coverage is important to evaluate the effectiveness of promotion programs and of vaccine delivery systems, and also to interpret epidemiologic data on pneumococcal-related outcomes. The objectives of this paper were to compare the advantages and limitations of immunization surveys and registries for assessing vaccination coverage in the target population of children, and to evaluate the impact of the public health program on uptake rates.

METHODS

Postal survey

In April-June 2006, a survey was conducted among two random representative samples of parents of children registered by the Quebec Provincial Health Insurance Board. The first sample comprised

600 children born between October 1, 2004, and January 31, 2005, and aged ≥ 2 months at the start of the universal 3-dose PCV7 program. The second sample comprised 600 infants born between December 1, 2003, and March 31, 2004, and eligible for the free PCV7 catch-up program. The sample size in each group was determined to achieve $\pm 4\%$ precision for proportions, assuming a response rate of 70%. Details of the methodology are presented in a previous report.⁴

A postal questionnaire was sent to parents, who were asked to provide dates of administration of PCV7 as recorded in the child's immunization chart. They were invited to return the questionnaire along with an authorization to contact the child's health care provider. An additional enquiry on the child's immunization status was performed when the immunization chart was not available or the number of doses administered was less than recommended. The design included two postal reminders followed by a telephone call for non-responders. The vaccination history of every child was

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reconstructed from the dates of PCV7 administration, and age-specific prevalence rates of vaccination in each of the two samples were computed.

Regional registry

Since 1990, all vaccinators in local public health units, private clinics and hospitals in the Quebec City area are invited to transmit individual immunization forms or electronic records to the Regional Public Health Board, which maintains a computerized registry. Records of children aged <5 years residing in Quebec City between January 1, 2001, and December 31, 2007, were selected for analysis. Denominators were generated from census data providing estimates of the number of residents by age category as of June 30 of each year, and linear inter/extrapolations were performed. The number of children aged <5 years in the study area fluctuated between 25,679 in 2001 and 25,089 in 2007. Dates of PCV7 administration were used to compute the prevalence of children who had received one to four PCV7 doses for every day of the study period, and to compute age-specific prevalence rates of vaccination in different birth cohorts.

RESULTS

Postal survey

Twenty-eight children were excluded from the province-wide survey because they were not living in the province. The overall response rate was 72.0% (844/1,172), and an authorization to contact the health care provider was received from 94.9% (799/844) of participants. Age-specific uptake rates according to the number of doses among children aged ≥ 2 months at the start of the universal PCV7 program are shown in Figure 1. By age 3 months, 80.0% of infants had received their first PCV7 dose, and uptake increased progressively up to age 18 months. By age 18 months, uptake was 97.5% for ≥ 1 dose, 97.2% for ≥ 2 doses and 89.6% for ≥ 3 doses. Only 5.1% of children had received 4 doses. The shape of the second and third dose curves indicates a substantial delay in vaccine administration, and only half of the children had received the booster dose at the recommended age of 12 months. Overall, 79.2% of children were considered as vaccinated as "per protocol" (at least two doses before 12 months and a booster dose between 12 and 15 months).

The vaccination history of children targeted by the catch-up program is shown in Figure 2. Before PCV7 was freely offered to all children, uptakes were in the 20%-30% range. Implementation of free PCV7 vaccination was followed by a substantial increase in the proportion of children who received one or two PCV7 doses, and catch-up doses were mostly administered during the second year of life.

Regional registry

Trends in uptake rates among children aged <5 years reported to the Quebec City registry are shown in Figure 3. PCV7 use started in the fall of 2001, and the proportion of vaccinated children increased slowly up to the end of 2004, although many children received fewer doses than recommended. As soon as free access to vaccination was granted in December 2004, uptake rates increased markedly, mainly as a result of catch-up vaccination. Coverage with ≥ 1 dose reached 97.0% by the end of 2007. The proportion of children who had received ≥ 3 doses increased at a slower pace as routinely vaccinated children entered the statistics. The proportion of

Figure 1. Cumulative vaccination rates according to age in a sample of children born between October 1, 2004 and January 31, 2005 in the province of Quebec

Figure 2. Cumulative vaccination rates according to age in a sample of children born between December 1, 2003 and March 31, 2004 in the province of Quebec

children who had received four doses remained low, at 4.2%, an indication of vaccinators' compliance with provincial guidelines.

To contrast the history of children exposed or not exposed to free vaccination, two birth cohorts were selected in Quebec City (Figure 4). A minority of children belonging to the non-exposed 2002 birth cohort were vaccinated, and only 16.9% had received ≥ 1 PCV7 dose by age 24 months. Vaccination rates were much higher among children born in 2005 and exposed to free vaccination. By age 24 months, almost all children had received ≥ 1 PCV7 dose (the actual estimate was 107.0%). However, only 83.5% of exposed children had received the recommended number of doses (≥ 3) by age 24 months, and many booster doses were administered later than at the recommended age of 12 months.

DISCUSSION

There is no perfect source for assessing vaccination coverage. A cross-sectional survey provides an instant photograph of the experience of a defined birth cohort, and the history of vaccination up to the time of the survey can be retrospectively reconstructed. The

Figure 3. Vaccination prevalence rates according to the number of doses in children aged less than 5 years residing in the Quebec City area from January 1, 2001 to December 31, 2007

Figure 4. Cumulative vaccination rates according to age in children born in 2002 and in 2004 in the Quebec City area

response rate in the present survey was high, and vaccination status was carefully assessed using parents' recollection and a review of children's immunization charts and health records.⁴ Parents who could not be contacted or who did not provide information may have characteristics associated with low vaccine uptake, and some "social desirability" in responses may also have occurred. As a consequence, vaccination coverage may be slightly overestimated in the survey results.

The main advantage of a population-based registry is to provide a continuous and dynamic view of vaccination in the entire target population. Trends in vaccination prevalence rates in Quebec City can be interpreted as a proxy of population immunity and used as an explanatory variable in time-series analyses of pneumococcal-related outcomes.^{5,6} The experience of particular birth cohorts could also be reconstructed. There is a belief among vaccinators in the Quebec City area that the distribution of vaccines by the public health authority is conditional on the transmission of immu-

nization forms, and compliance is apparently good. However, a low level of underreporting cannot be excluded, especially for PCV7 doses obtained on the private market. The Quebec City Immunization Registry is not linked with a population registry, and denominators were estimated from relatively imprecise census data. When a child immigrates into the study area, the immunization registry record may be updated at the time of the first vaccine administration. However, there is no system to trace emigrants. Yearly emigration/immigration rates among children ≤ 5 years in the Quebec City region were between 2% and 3% during the study period.⁷ As a consequence, uptake rates were overestimated, and the magnitude of this bias increased as age increased.

The Canadian Immunization Registry Network is one of the components of the National Immunization Strategy.⁸ Since its inception in 2001, the network has provided a forum for the creation of national data and functional standards, and the centralized coordination necessary to ensure that compatible electronic immunization registries are developed across Canada. In 2004, only five jurisdictions had fully functioning immunization registries (Manitoba, New Brunswick, Saskatchewan, Prince Edward Island and British Columbia). For this reason, national surveys of representative samples of the Canadian population are continued, and the latest published telephone survey was conducted in 2004, showing coverage rates between 70% and 94% for the eight childhood vaccines recommended in all provinces and territories.⁸ In Quebec, there is a provision in the *Law on Public Health* for establishing a population-based registry of immunization.⁹ Work is in progress, but until such a registry is fully operational and validated, surveys will have to be conducted at regular intervals for evaluating vaccination coverage and trends.

In the US, a systematic review of community-based interventions to improve vaccination coverage was published in 2000.¹⁰ Five studies of single-component interventions for reducing out-of-pocket costs for vaccine recipients, including free vaccine and/or administration, providing insurance coverage or reducing co-payment at the point of service, resulted in changes in coverage ranging from -1% to 20%, with a median value of 16%. In the province of Quebec, a quasi-experimental project was conducted in two health districts in 1997-1998, comparing promotion and free vaccination with promotion alone for the vaccination of adults aged ≥ 65 years with the 23-valent pneumococcal polysaccharide vaccine: uptake in public health clinics providing influenza shots was close to 100% in the free vaccination district and only 32% in the control group.¹¹

The results of the present study clearly show the impact of free access to vaccine on uptake in the Canadian context. Results from a survey in the Montréal region, province of Quebec, in March 2004 (before free program implementation) indicated that PCV7 was not available at all points of service, and that there were many restrictions on the administration of vaccines purchased in pharmacy and not shipped according to strict cold chain conditions.¹² At that time, the overall cost of a 4-dose PCV7 regimen (purchase + administration) for parents was between C\$304 and C\$784. Although health professionals in Canada are requested to offer all the vaccines recommended by national and/or provincial expert committees,¹³ the intensity of promotion may be higher for free vaccines than for those delivered under payment. Also, parents could consider a free vaccine as more important for their child than

a vaccine not included in the publicly funded program. In a survey in British Columbia in 2003, 59% of parents of children susceptible to varicella declared that they would have had their child vaccinated had the varicella vaccine been provided free (which was not the case at that time).¹⁴

In the US, uptake of ≥ 3 doses reached 40.8% among children aged 19-35 months as soon as PCV7 was recommended and funded through the federal Vaccines for Children program, and it increased to 87% in 2006.¹⁵ This was associated with a marked decrease in the incidence of invasive pneumococcal infections in young children but also in all other age groups, resulting from an indirect (herd) effect on carriage and transmission of pathogenic bacteria.¹⁶ Economic analyses incorporating herd protection against invasive infections caused by the *Streptococcus pneumoniae* serotypes included in PCV7 predicted a very favourable cost-effectiveness ratio of less than US\$3,000 per quality-of-life year gained in a societal perspective.¹⁷ Cost savings would probably have been found by including in the model herd effects against all-cause pneumonia and otitis media.¹⁸ In Quebec, uptake rates sufficiently high to induce herd protection were only achieved after the implementation of a publicly funded program providing easy and free access to PCV7. Free vaccination against diseases causing substantial mortality and/or morbidity is essential to reduce social inequities and health inequalities, and has to remain a fundamental principle of the Canadian health system.

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RÉSUMÉ

Contexte : Au Québec, le vaccin pneumococcique conjugué est disponible depuis 2001 sur le marché privé et a été inclus dans le programme public d'immunisation depuis décembre 2004.

Objectifs : Comparer les avantages et limites de deux sources différentes pour mesurer la couverture vaccinale de la population ciblée (les enfants) et évaluer l'impact du programme de santé publique sur les taux de couverture.

Méthodes : Des données provenant d'une enquête provinciale auprès d'un échantillon représentatif de parents et d'autres provenant du registre de vaccination de la région de Québec ont été utilisées pour estimer les taux de couverture au fil du temps dans différents groupes de population.

Résultats : Les résultats provenant de l'enquête provinciale et du registre régional de vaccination sont congruentes en ce qui concerne les tendances. Les taux de couverture sont surestimés, plus dans le registre régional que dans l'enquête. Durant les années 2001-2004, les taux de couverture sont restés bas et beaucoup d'enfants ont reçu moins que le nombre recommandé de doses. Dès que le programme de vaccination gratuite a été offert, la couverture vaccinale a augmenté de façon marquée et près de 90 % des enfants ont reçu les trois doses recommandées, un niveau de vaccination nécessaire à l'obtention d'une immunité de groupe. Des retards dans l'administration de la dose de rappel ont été constatés.

Conclusion : La vaccination gratuite est un déterminant majeur de la vaccination et devrait rester un principe fondamental du système canadien de santé.