



## Determinants of under-immunization and cumulative time spent under-immunized in a Quebec cohort



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### ABSTRACT

**Background:** Under-immunization refers to a state of sub-optimal protection against vaccine preventable diseases. Vaccine coverage for age may not capture intentional or non-intentional spacing of vaccines in the recommended provincial immunization guidelines. We aimed to identify factors associated with coverage and under-immunization and to determine the number of days during which children were under-immunized during their first 24 months of life.

**Methods:** Secondary analysis of children  $\leq 3$  years recruited through active surveillance for gastroenteritis from three Quebec pediatric emergency departments from 2012 to 2014. Vaccination status for children at least 24 months of age was determined using provincial immunization guidelines. Cumulative days under-immunized were calculated for DTaP-VPI-Hib, PCV, MMR, and Men-C-C. Factors associated with up-to-date (UTD) status at 24 months of life and for under-immunization  $\geq 6$  months were analyzed using logistic regression.

**Results:** Of 246 eligible children, 180 (73%) were UTD by 24 months of life. The mean cumulative days under-immunized for MMR was 107 days, for PCV 209 days, for Men-C-C 145 days, and for DTaP-VPI-Hib 227 days. Overall, 149 children (60%) experienced delay for at least 1 vaccine. Factors associated with both an UTD status at 24 months and concurrently associated with being under-immunization  $\geq 6$  months, included timely initiation of immunization (OR = 5.85; 95% CI: 2.80–12.22) and (OR = 0.13; 95% CI: 0.07–0.24), failure to co-administer 18-month vaccines (OR = 0.15; 95% CI: 0.10–0.21) and (OR = 3.29; 95% CI: 2.47–4.39), and having a household with  $\geq 3$  children under 18 years ((OR = 0.50; 0.28–0.86) and (OR = 2.99; 1.45–6.22), respectively).

**Conclusion:** Paired with an unexpected low level of coverage at 24 months of life, the majority of our cohort also experienced a state of under-immunization for a least one vaccine. Estimates of coverage do not capture intentional or non-intentional gaps in protection from vaccine preventable illnesses. Timely preventive care should be prioritized.

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**Abbreviations:** AGE, acute gastroenteritis; CLSC, Centre local de services communautaires; CMA, Census Metropolitan Area; cNICS, childhood National Immunization Coverage Survey; FSA, forward sortation area; PIQ, Quebec Immunization Protocol; UTD, up to date.

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## 1. Introduction

Evaluation of vaccination coverage is a key health indicator that is crucial to ensure that vaccination programs are reaching their objectives. In jurisdictions lacking a regional vaccine registry, studies that evaluate changes in coverage and timeliness, provide valuable information for targeted immunization strategies among specific groups [1]. Under the provincial immunization program,

all recommended childhood vaccines are offered free of charge in public health clinics (CLSC), hospitals, and in physicians' offices. More than 75% of vaccinated children 0–4 years are vaccinated by public health nurses [2,3]. Proof of vaccination or vaccination exemption is not required in Quebec to enter the education system. When looking at the most recent Canadian childhood National Immunization Coverage Survey (cNICS), vaccination uptake by vaccine type at age 2 years in 2013 varied from 72% to 91%. A 2014 proportionally representative survey study from Québec estimated full coverage at 24 months to be between 71% and 85% [2].

Vaccination coverage is the standard measure to assess if recommended threshold for herd immunity has been met, by vaccine type. Coverage often does not consider the timeliness of doses and may underestimate periods of sub-optimal protection or absence of protection against vaccine preventable diseases, leaving children susceptible to illness in the event of an outbreak [4–9]. Age-appropriate vaccination can be assessed by determining the age at vaccine dose, while the measure of delay may be categorized by cumulative time under-immunized [10]. Finally, coverage seldom distinguishes unvaccinated from undervaccinated children. This lack of distinction ignores the refusal of all vaccines, having received some, but not all, age-appropriate vaccines, and those who are fully vaccinated for age, but experienced serious delays [11]. Arguably, children who are not up-to-date (UTD) when coverage is assessed or who are under-immunized by spacing vaccines beyond recommended timing, represent a more important group to target than those who receive no immunization at all, and likely represent entirely different population [2,12].

Several factors have been found to influence an UTD immunization status. Maternal age, marital status, low level of education, and large family size have been associated with a delay in complete vaccine coverage [4,11,13–34]. In contrast, higher levels of education and daycare attendance have been positively associated with complete immunization for age [13,35]. Additionally, variables that relate to parental choice or parents' ability to organize, such as timely initiation of immunization and failure to co-administer 18 months vaccines (2nd dose MMR and 4th dose DTaP-IPV-Hib) are associated with a future immunization status [2,17,36–39].

Behaviours of individuals or communities who delay vaccination are complex and determinants of these choices, context specific [15]. Without a vaccine registry, the unique opportunity to analyze the localized determinants of UTD immunization status and describe vaccination coverage at 24 months of age in preschoolers in two metropolitan areas in the province of Quebec, will provide valuable information to regional public health decision makers [15,40]. To challenge the standard measure of vaccine coverage, our secondary objective was to evaluate the average number of days under-immunized for four vaccines: diphtheria and tetanus toxoids, acellular pertussis vaccine, poliovirus vaccine and *Haemophilus influenzae* type b vaccine (DTaP-IPV-Hib), pneumococcal conjugate vaccine (PCV-7, 10 or 13), Measles, Mumps, and Rubella with one containing varicella (MMR (v)), and Meningococcal type C vaccine (Men-C-C). Finally, we determined factors associated with a cumulative delay of more than 6 months for one or more vaccines.

## 2. Methods

### 2.1. Study design

This was a secondary analysis of a prospective, active surveillance study of children 8 weeks to 3 years of age, presenting to the emergency department for acute gastroenteritis (AGE) at 3 tertiary pediatric hospitals in the province of Quebec [1,41,42]. The

aim of the original study for which the data was collected, was to examine the relative burden of pediatric gastroenteritis by etiology, compare the clinical severity of rotavirus and norovirus cases, and evaluate the rotavirus vaccine effectiveness after the implementation of a publicly funded rotavirus vaccination program in Quebec. Recruitment and data collection took place between February 2012 and December 2014 with a total of 937 patients recruited. All recruited patients with immunisation records were included in the current study.

### 2.2. Data collection and variables

Participant demographics, medical information and vaccination history were systematically collected via phone interview with the child's caretaker. Vaccination history (vaccine type and date) was collected from the participant's immunization booklet. If the booklet was not available, parental permission was sought to contact vaccination provider to review records. History of prematurity (<37 weeks gestation) and presence of underlying conditions were coded as binary variables. The number of children in the home under the age of 18 years, in addition to the index child, was categorized as only index child, 2 children (index + 1) and,  $\geq 2$  (at least 2 + index). The age of parents at index child's birth was categorized into three groups, based on distribution, <26, 26–39, and >39 years as the reference. Parents' highest level of education was coded as <12 years of education, college, university and, graduate degree, the latter was used as the reference category.

We selected covariates for our model based on factors found in the literature to be associated with immunization practice in high-income countries. The first three characters (forward sortation area, FSA) of the residential postal code were used to determine the median household income using 2006 census data. Two hospitals were located in the Montreal Census Metropolitan Area (CMA) with a population  $\sim 4$  million and in the Sherbrooke CMA, with a population of >200,000. Two binary variables were created to assess initiation of vaccination at 2 months (with one month grace period) and to assess whether co-administration of the two recommended 18-month vaccines were associated with an UTD status at 24 months in accordance with the Quebec Immunization Protocol (PIQ) [2,14,17,36–38,43–46].

To allow all children equal time to receive vaccinations, only children 24 months and older were included. Patient's age was determined at phone call date, when immunization data was collected or if missing, at consent date. Patients were excluded if they reported underlying inherited immunodeficiency and neoplasm of any kind past or present, as this population's immunization needs differs from those of the healthy preschool population. We also excluded children with complete vaccination refusal, as they were likely to represent a different population.

### 2.3. Outcome ascertainment

The two outcome variables were UTD for age for all recommended vaccines at 24 months of life and delay of  $\geq 6$  months for one or more vaccines [4]. We examined the UTD status regardless of timeliness of 4 vaccines during the first 24 months of life. Children were defined as being UTD by 24 months if they received the recommended number of vaccine doses, as per the PIQ during the study time frame (4 doses of DTaP-IPV-Hib, 3 doses PCV 13, 2 doses MMR(v), and 1 dose Men-C-C). The Hepatitis B vaccine was not included in our analysis, as newborn vaccination was added to the PIQ after our study time frame. Rotavirus vaccine was not included, as it was introduced during our study. Results of uptake from this cohort have been previously described [42]. The influenza vaccine was also excluded due to its nonspecific timing in

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