# Trends in severe gastroenteritis among young children according to socio-economic characteristics before and after implementation of a rotavirus vaccination program in Quebec

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## ABSTRACT

**OBJECTIVES:** Following implementation of a publicly funded rotavirus immunization program in Quebec (Canada) in 2011, its impact on gastroenteritis hospitalization rates, a proxy for severe gastroenteritis, was assessed.

**METHODS:** Using a tertiary hospital database and a regional vaccination registry, temporal trends in rates of hospitalization for acute gastroenteritis (AGE) and rotavirus gastroenteritis before the age of five years and rotavirus vaccine coverage were examined from June 2004 through May 2014 in a large retrospective birth cohort in the Eastern Townships region. The mean annual AGE hospitalization rate in post-program years (2011/2012–2013/2014) was compared with that in pre-program years (2004/2005–2010/2011) overall and according to the characteristics of the children, families and residential neighbourhoods at birth.

**RESULTS:** The AGE hospitalization rate significantly decreased from 81/10,000 in the pre-program period to 46/10,000 in the post-program period (relative reduction = 43%). Following implementation of the program, vaccine coverage rapidly increased and reached 81%. All socio-economic categories showed a reduced hospitalization rate in the post-program period, but the lowest relative reductions were observed in children living in neighbourhoods with higher rates of unemployment, low-income families and single mothers. However, these disadvantaged subgroups did not have lower vaccine coverage.

**CONCLUSIONS:** Three years following its introduction in a universal vaccination program, rotavirus vaccine significantly reduced severe gastroenteritis in young children. Despite similar vaccine coverage among all children, disadvantaged socio-economic groups appeared to have a less pronounced AGE reduction, suggesting that factors other than vaccination could partially influence the reduction of gastroenteritis morbidity in young children.

KEY WORDS: Rotavirus infections; rotavirus vaccines; immunization programs; gastroenteritis; child; socio-economic

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

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R otavirus is the main cause of acute gastroenteritis (AGE) among children under five years of age worldwide.<sup>1</sup> In developed countries, hospitalizations related to rotavirus gastroenteritis (RVGE) generate important costs for society.<sup>2</sup> Before the arrival of rotavirus vaccines in Canada, there were on average 7,500 to 10,500 estimated hospitalizations for RVGE annually.<sup>3,4</sup> Rotavirus infections were responsible for up to 72% of AGE hospitalizations during winter months.<sup>5</sup> Rotavirus season started in December and ended in May, with a peak incidence observed in March and April.<sup>4</sup>

In Canada, two rotavirus vaccines, RotaTeq<sup>®</sup> and Rotarix<sup>®</sup>, were approved in 2006 and 2007, and were recommended by the National Advisory Committee on Immunization in July 2010 to prevent RVGE in young children.<sup>6</sup> Both vaccines showed high clinical efficacy in upper-middle and high-income countries, reducing RVGE hospitalizations by 85%–100%.<sup>7,8</sup> On November 1, 2011, the monovalent rotavirus vaccine Rotarix<sup>®</sup> (RV1), offered to all infants in two doses and administered orally at two and four months of age, was introduced into the publicly funded vaccination program in Quebec. This program primarily aims at reducing gastroenteritis morbidity in the general population, including vulnerable subgroups.

After implementation of rotavirus vaccination programs, many studies from the US, Australia and the European Union documented significant declines in AGE and RVGE hospitalization rates.<sup>9–11</sup> Globally, they observed a 30%–60% decline in AGE hospitalization rates. Only two studies from Mexico analyzed relative reductions according to socio-economic status.<sup>12,13</sup> They found lower, but still significant, reductions in diarrhea-related hospitalizations and deaths in states with low socio-economic status. To date, no studies have assessed the impact

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of the rotavirus immunization program in Quebec since its implementation in 2011. In Canada, where people benefit from the universal health care system, an impact study could be highly relevant in describing the burden of severe rotavirus infections over time, before and after implementation of universal rotavirus immunization, and could therefore assess its public health benefits in the general population as well as in socio-economic subgroups.

The aim of this study was to assess the impact of the rotavirus routine immunization program on gastroenteritis morbidity and health inequalities among young children living in the Eastern Townships (QC, Canada). More specifically, AGE and RVGE hospitalization rates in post-program years were compared with those of the pre-program years, overall and according to individualand neighbourhood-level socio-economic characteristics. Rotavirus vaccine coverage was also examined in the post-program period overall and according to the same characteristics.

### **METHODS**

## **Study setting**

The Eastern Townships, a southern region of Quebec with 320,000 residents in 2014 (4% of the Quebec population), is composed of a mix of urban, semi-urban and rural communities.<sup>14</sup> One central city, named Sherbrooke (Quebec's sixth largest city), has half of the regional population. This city contains one central tertiary hospital, the Centre hospitalier universitaire de Sherbrooke (CHUS), where 95% of deliveries in the Eastern Townships occur and where nearly 100% of pediatric beds for acute care in the region are held.<sup>4</sup> Therefore, the vast majority of children living in the Eastern Townships requiring hospitalization for AGE attend the CHUS.

## **Data sources**

Data on all births and hospitalizations occurring at the CHUS were obtained from CIRESSS (Centre informatisé de recherche évaluative en services et soins de santé), which is a local data warehouse based at the CHUS that has contained exhaustive data since 1991. Vaccination data were obtained from LOGIVAC, an immunization registry unique to the Eastern Townships in which all births in the region and all vaccines administered to the residents have been recorded since 1998, even for those born outside the region. Thus, all children born in the region, regardless of their vaccination status, are included in LOGIVAC.

# **Study population**

This longitudinal descriptive study included all children born at the CHUS between June 1999 and May 2014 and living in the Eastern Townships at birth, in order to assess gastroenteritis hospitalization rates among children younger than five years from 2004 to 2014. This birth cohort, extracted from the hospital database CIRESSS, was followed up from birth (or from the start of the study for children born before June 2004) to the age of five years (or until the end of the study for children born after May 2009) with respect to all AGE hospitalizations. Data were then linked to LOGIVAC to obtain the rotavirus vaccination status of newborns. After the pairing, all data were denominalized. The final cohort consisted of 37,757 newborns.

## Variables

## Dependent Variables

In this study, three dependent variables were examined: 1) AGE hospitalization rates among children younger than five years (a proxy for severe gastroenteritis), 2) RVGE hospitalization rates among children younger than five years and 3) rotavirus vaccine coverage. Hospitalizations for AGE that occurred between June 1, 2004 and May 31, 2014, were identified in CIRESSS using the following International Classification of Diseases, 9th Revision and 10th Revision, Canada (ICD-9/10-CA) codes: AGE of determined etiology (bacterial [003.0, 004, 005, 008.0-008.5/A02.0, A03-A05], parasitic [006.0-006.1, 007/A06.0-A06.3, A07] and viral [008.6-008.8/A08, including rotavirus code 008.61/A08.0]), AGE of undetermined etiology (presumed infectious [009/A09] and presumed noninfectious [558.4-558.9/K52.8-K52.9]) and noninfective neonatal AGE (P78.3). Hospitalizations for RVGE were identified in CIRESSS using laboratory data of positive stool analyses for rotavirus. Laboratory-confirmed RVGE hospitalizations represent a more specific and complete definition of severe RVGE than RVGE-coded hospitalizations, because some patients with rotavirus-positive test results are not assigned a rotavirus code, as has been documented in the US health care system.<sup>15</sup> Both primary and secondary diagnoses were considered, and two hospitalizations for the same infant occurring in less than 14 days were considered as one event. Hospitalizations rates were calculated by dividing the number of hospitalizations that occurred among children aged less than five years by the total number of children of the same age group in the birth cohort over a specified period.

LOGIVAC provided information about rotavirus vaccines, including name, date of administration and number of doses received. Coverage was first calculated at the age of three months to assess the coverage of  $\geq 1$  dose of rotavirus vaccine since the approval of the two vaccines in 2006 and 2007. Coverage of eligible infants in the funded vaccination program was also assessed at the end of the period study, on May 31, 2014. Coverage was defined as the receipt of  $\geq 1$  dose among children born between August 1, 2011 and February 28, 2014 (aged between 3 and 33 months).

## Individual Covariates

Several covariates were available in the CIRESSS database. Birth date allowed age to be calculated at the end of each "rotavirus" year (i.e., May 31), and this was then used to determine the denominators of age-specific hospitalization and vaccine coverage rates (<1, 1–2 and 3–4 years). Birth characteristics (all dichotomized) were sex, maternal age at birth (<25 vs.  $\geq$ 25 years), gestational age at birth (<37 weeks [preterm infant] vs.  $\geq$ 37 weeks [term infant]) and birth weight (<2500 g [low birth weight] vs.  $\geq$ 2500 g [normal birth weight]). Place of residence, defined as eastern, central (i.e., Sherbrooke city) and western territories, was determined by the municipality of residence at birth.

#### Ecological Covariates

The population density (i.e., number of people per square kilometre), the rate of low-income families (i.e., families having an annual income below the low-income cut-off), the unemployment rate among people  $\geq$ 25 years, the rate of single mothers (i.e., not living with a partner) and the proportion of mothers without a high school diploma (i.e., <11 school years

completed), derived from the National Census (2006) and the Live Births File (2002–2010), were measured at the dissemination area (DA) level. DA is the smallest geostatistical unit available from the census (approximately 400–700 persons by DA).<sup>16</sup> The six-digit residential postal codes at birth, provided by CIRESSS, were geocoded in order to assign a DA to each participant (total of 519 DAs), allowing pairing of the five ecological variables to respective children. These ecological variables were then categorized into tertiles (T1, T2, T3), T3 representing the highest rate or proportion of poor socio-economic indicators. In the absence of individual measures, these neighbourhood-level variables were used as proxy measures for the socio-economic status of participants, T1, T2 and T3 representing advantaged, middle and disadvantaged socioeconomic groups.

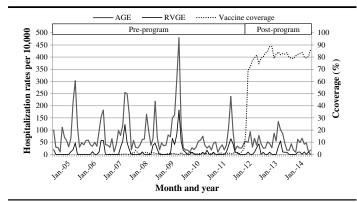
## **Statistical analyses**

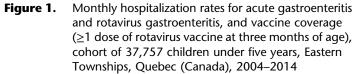
Monthly and annual AGE and RVGE hospitalization rates were examined to observe rotavirus seasonal patterns and long-term trends between June 2004 and May 2014. For further analyses, the focus was on AGE hospitalizations, which were considered to be more appropriate for assessing the overall trends in severe rotavirus infections, since laboratory-confirmed RVGE is less sensitive and may underestimate the rotavirus infections burden.<sup>17</sup> Focusing on AGE rather than RVGE also increased the statistical power to detect differences between subgroups. To compute the relative reduction in hospitalization rates between pre- and post-program periods, the mean annual AGE hospitalization rates were compared for years 2004/2005-2010/2011 versus years 2011/2012-2013/2014, using this formula: ([pre-program rate - post-program rate]/pre-program rate) x 100. Mean annual hospitalization and vaccine coverage rates were calculated overall and according to demographic and socio-economic characteristics measured at individual and ecological levels. Children with missing variables were excluded only in the specific analyses involving those variables. Statistical comparisons of rates within subgroups in each study period were made using the chi-square test with significance level set at 0.05 (two-sided). Data were analyzed using SPSS. The research project was approved by the CHUS Ethics Committee.

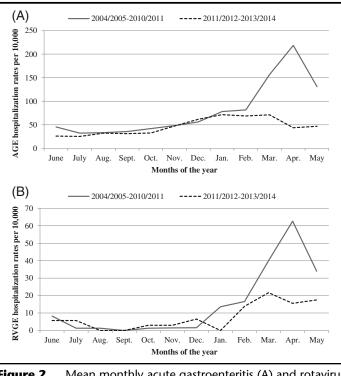
## RESULTS

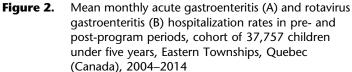
# Ten-year trends in hospitalization rates and vaccine coverage

In the cohort of 37,757 newborns, 882 hospitalizations for AGE were observed before the age of five years between June 2004 and May 2014. During the pre-program years, AGE hospitalization rates were characterized by a sharp increase between January and May (Figure 1). A similar seasonal pattern was observed for RVGE hospitalizations. In post-program years, AGE and RVGE hospitalization rates significantly decreased, particularly in the last year under investigation (2013/2014). The mean peaks of AGE and RVGE hospitalizations, observed in April for the pre-program period, were both dramatically flattened during the post-program period (Figures 2A and 2B). Furthermore, monthly vaccine coverage of  $\geq 1$  dose was very low before the arrival of the rotavirus vaccination program, ranging from 0% to 4%. Soon after the program implementation, vaccine uptake increased









markedly and was maintained during the following years to an average of 81% (Figure 1).

## Pre- and post-program AGE hospitalization trends

In the whole cohort of newborns, annual AGE hospitalization rates significantly decreased from 81/10,000 in the pre-program period to 46/10,000 in the post-program period, representing an overall relative reduction of 43% (95% confidence interval [CI]: 33–51)

Table 1.

I. Mean annual AGE hospitalization rates in pre- and post-program periods and vaccine coverage in the post-program period, according to individual-level characteristics, cohort of 37,757 children under five years, Eastern Townships, Quebec (Canada), 2004–2014

	2004/2005-2010/2011 AGE hospitalization		2011/2012-2013/2014				Rate reduction <sup>†</sup> (95% CI), %
			AGE hospitalization		Vaccine coverage*		( <b>33</b> % CI), %
	Mean rate <sup>‡</sup> (total <i>n</i> )	p§	Mean rate <sup>‡</sup> (total <i>n</i> )	p§	(%)	p§	
Total (<5 years)	80.5 (700)		46.0 (182)		80.6		43 (33–51)
Sex			. ,				. ,
Male	89.5 (404)	0.002	49.0 (100)	0.360	80.5	0.852	45 (32–56)
Female	70.8 (296)		42.7 (82)		80.7		40 (23–53)
Age at admission							. ,
<pre>~&lt;1 year</pre>	135.7 (244)	<0.001	87.8 (68)	<0.001	84.2	<0.001	35 (16–51)
1–2 years	101.3 (355)		49.6 (79)		79.1		51 (38–62)
3–4 years	29.7 (101)		22.0 (35)		NA		26 (-8–50)
Maternal age at bi	rth						
<25 years	89.5 (199)	0.086	72.3 (61)	<0.001	84.3	<0.001	19 (-8–39)
≥25 years	77.5 (501)		38.8 (121)		79.7		50 (39–59)
Gestational age at	birth						
<37 weeks	125.1 (92)	<0.001	92.1 (28)	<0.001	78.5	0.191	26 (-12–52)
≥37 weeks	76.4 (608)		42.1 (154)		80.8		45 (34–54)
Birth weight							
<2500 g	148.1 (81)	<0.001	75.8 (18)	0.027	76.4	0.022	49 (15–69)
≥2500 g	76.0 (619)		44.1 (164)		80.9		42 (31–51)
Place of residence	at birth		. ,				. ,
East	79.3 (151)	0.007	41.2 (35)	0.015	78.2	0.030	48 (25–64)
Central	87.4 (432)		53.4 (125)		81.4		39 (25–50)
West	63.2 (117)		28.7 (22)		80.7		55 (29–71)́

NOTE: Bold values are statistically significant (p < 0.05).

\* Vaccine coverage is defined as reception of  $\geq$ 1 rotavirus vaccine doses on May 31, 2014, among the children eligible for the vaccination program (children aged between 3 and 33 months).

<sup>†</sup> Rate reductions were calculated by comparing the pre-program rates and post-program rates.

<sup>‡</sup> Mean annual rates per 10,000 children <5 years of age.

 ${}^{\$}\chi^2$  test used to compare rates among subgroups for a respective study period. AGE, acute gastroenteritis; CI, confidence interval; NA, not applicable.

(Table 1). Less than 2% of children had missing information regarding sex, maternal age at birth or postal code. For all individual-level variables examined, each subgroup showed a decline in hospitalization rates during the post-program years in comparison with the pre-program years. However, lower relative and non-significant reductions were observed in specified subgroups, including children aged three and four years, children having a young mother and preterm children (26%, 19%, and 26% respectively). Regarding DA-level characteristics, all socioeconomic strata showed a significant relative reduction in the post-program period (Table 2). However, the lowest relative reductions were generally observed among the most urban and the most socio-economically disadvantaged areas (T3). Indeed, children from densest DAs (T3) had a 27% reduction in hospitalization rates, whereas those living in DAs with low (T1) and medium (T2) population density had a much greater reduction (47% and 53% respectively). In the same vein, hospitalization rates declined less sharply in DAs with higher unemployment rates, higher low-income family rates and higher single mother rates (relative reductions of 35%, 26% and 30% respectively) than more advantaged DAs. It is noteworthy that some of the observed differences in AGE hospitalization rates among subgroups in postprogram years were not present in pre-program years.

#### Post-program vaccine coverage

In post-program years, coverage of  $\geq 1$  dose for all infants eligible for free vaccination was 81% (Table 1). RV1 was the vaccine

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administered to 99.9% of these cases. Coverage in each socioeconomic subgroup ranged from 75% to 85%. Regarding individual characteristics, infants aged <1 year at admission, children having a young mother, normal birth weight children and those living in Sherbrooke were among the most frequently vaccinated. No significant differences were observed between DA-level subgroups.

# DISCUSSION

This longitudinal study based on a large birth cohort was the first to examine the simultaneous evolution over the last decade of gastroenteritis hospitalization and rotavirus vaccine coverage rates among young children, overall and according to various socioeconomic characteristics. The substantial decline in AGE and RVGE pediatric hospitalizations in post-program years is consistent with that observed in previous impact studies conducted in industrialized countries, where a sustained reduction has been observed since the beginning of the rotavirus vaccination program.<sup>18–21</sup> Reductions over three consecutive years simultaneously occurring with the rapid increase in vaccine coverage indicates that these changes are likely due to the new rotavirus vaccination program. However, an important reduction in hospitalizations for gastroenteritis was also observed in 2009-2010, before the implementation of the program. This unexpected decline could possibly be explained by the natural fluctuation in rotavirus activity related to different rotavirus strains<sup>22</sup> or by the increase in general hygiene measures following the 2009 H1N1 influenza pandemic. Indeed, the 2010 weak rotavirus season was

Table 2.Mean annual AGE hospitalization rates in pre- and post-program periods and vaccine coverage of post-program period,<br/>according to ecological-level\* characteristics, cohort of 37,757 children under five years, Eastern Townships, Quebec<br/>(Canada), 2004–2014

	2004/2005-2010/2011 AGE hospitalization		2011	Rate reduction <sup>‡</sup>			
			AGE hospitalization		Vaccine coverage <sup>†</sup>		(95% CI), %
	Mean rate <sup>§</sup> (total <i>n</i> )	P	Mean rate <sup>§</sup> (total <i>n</i> )	P	(%)	P	
Population den	sity						
Τ1 (low)	71.0 (205)	0.088	37.9 (50)	0.005	79.7	0.168	47 (27–61)
T2	83.6 (240)		39.2 (53)		80.1		53 (37–65)
T3 (high)	86.3 (253)		62.6 (79)		81.9		27 (7–44)
Unemployment	t rate						
T1 (low)	81.3 (229)	0.581	43.6 (62)	0.287	80.8	0.885	46 (29–59)
T2	76.4 (219)		41.7 (54)		80.2		45 (26–59)
T3 (high)	84.0 (251)		54.3 (66)		80.4		35 (15–51)
Low-income far	mily rate						
T1 (low)	72.2 (207)	0.136	41.4 (54)	0.003	81.0	0.625	43 (23–58)
T2	85.2 (243)		35.6 (49)		80.5		58 (43–69)
T3 (high)	85.0 (249)		63.1 (78)		79.8		26 (4–42)
Single mother r	rate						
T1 (low)	72.4 (205)	0.139	38.0 (52)	0.060	80.8	0.855	47 (29–61)
T2	87.1 (247)		43.9 (58)		80.1		50 (33–62)
T3 (high)	81.9 (248)		57.5 (72)		80.5		30 (9–46)
Proportion of m	nothers without high school dipl						
T1 (low)	81.6 (226)	0.327	40.5 (57)	0.151	81.2	0.567	50 (34–63)
T2	74.6 (218)		55.5 (72)		80.2		26 (3–43)
T3 (high)	85.4 (256)		42.8 (53)		80.0		50 (33–63)

NOTE: Bold values are statistically significant (p < 0.05).

\* Ecological variables were calculated according to the dissemination area of residence at the birth of the child. They are presented in tertiles, T1 representing the lowest rate. † Vaccine coverage is defined as reception of ≥1 rotavirus vaccine doses on May 31, 2014, among children eligible for the vaccination program (children aged between 3 and 33 months).

<sup>‡</sup> Rate reductions were calculated by comparing the pre-program rates and post-program rates.

<sup>§</sup> Mean annual rates per 10,000 children <5 years of age.

AGE, acute gastroenteritis; CI, confidence interval.

preceded by a strong rotavirus season in 2009, reflecting the biennial seasonal pattern of rotavirus.<sup>23</sup>

The observed vaccine coverage of  $\geq 1$  dose in 81% of children aged 3–33 months during the post-program period is consistent with estimates from a recent survey conducted in children of one and two years old in Quebec (81%–88% for  $\geq 1$  dose) as well as with reported coverage among children aged 0–2 years in the Eastern Townships on the basis of LOGIVAC data (75% for 2 doses).<sup>24,25</sup> The estimated coverage in the present study is slightly higher because coverage of  $\geq 1$  dose was assessed instead of a full series and possibly because our birth cohort did not include children born in birthing centres or at home. Indeed, a previous study found an association between assisted delivery by a midwife and incomplete immunization status (i.e., not all the recommended vaccines received).<sup>26</sup>

Among children younger than five years, AGE hospitalization rates were significantly reduced in the post-program period (43%). This reduction corresponds to that observed in many studies in industrialized countries, ranging from 30% to 60%.<sup>9–11,18–21</sup> However, our study went further than previous studies by examining these trends according to several individual- and neighbourhood-level characteristics. As expected, children less than three years, who were eligible to receive the funded rotavirus vaccine, had the highest reductions, suggesting that the observed decline in gastroenteritis hospitalizations was due to rotavirus vaccine. Interestingly, children aged three and four years, too old to receive the rotavirus vaccine, still had a relative reduction of 26%. Although it did not reach statistical

significance, this observation suggests a herd immunity effect of the vaccine, also observed in many other studies.<sup>18–21</sup> Children living in Sherbrooke, which is the most central and most populous city, as well as those living in the densest DAs, had the lowest reductions in AGE hospitalization rates in comparison with children living in more rural areas. Urban clusters with high population density could increase the potential for transmission of rotavirus or other gastrointestinal pathogens, explaining the lower reduction in AGE hospitalizations in urban areas despite high vaccine coverage.

For socio-economic ecological-level variables, the most disadvantaged subgroups generally showed the lowest rate reductions in post-program years. This may have been caused by factors other than vaccination itself as no significant difference in vaccine coverage according to socio-economic subgroups was observed in the present study. Indeed, people with low socioeconomic status generally differ from more well-off ones according to their living conditions (e.g., household crowding), their physical health (e.g., weaker immune status, smoking habits), their nutritional status and their health seeking behaviour.<sup>27</sup> A study from southern Israel showed similar results to ours in two distinct populations, and the authors suggested that the differential reduction could be partially explained by socio-economic conditions.<sup>28</sup> Moreover, because disadvantaged parents generally have fewer resources and may be less knowledgeable about the causes and cures of symptoms,<sup>27</sup> doctors tend to hospitalize these children more in order to achieve recovery. In Quebec, this practice was previously observed among asthmatic children, as those whose

 $<sup>\| \</sup>chi^2$  test used to compare rates among subgroups for a respective study period.

fathers held economically disadvantaged occupations were more likely to be hospitalized.<sup>29</sup> This differential management from doctors may be a complementary hypothesis for the lower reduction in AGE hospitalizations observed in disadvantaged subgroups.

This study had some limitations. Temporal trends could have been influenced by factors other than vaccination, such as natural variation in rotavirus activity and testing practices. However, the observed rate reductions were sustained over three consecutive years, suggesting that declines were most likely attributable to the vaccination program. For trends in RVGE hospitalizations, laboratory testing practices were probably similar over the study period, as the proportion of requests among hospitalized children was equivalent in pre- and post-program periods (data not shown). Concerning CIRESSS and LOGIVAC, both databases had no information about whether a child had moved out of the Eastern Townships after birth. This had the potential effect of underestimating gastroenteritis hospitalizations and vaccine coverage. However, this bias was presumably non-differential according to the birth and family characteristics or the outcomes examined, and did not preclude comparison of rates between preand post-program periods. Finally, the socio-economic status of parents was not available in both databases, but several proxies, measured at the finest ecological level available, were used to obtain the socio-economic level of the child's neighbourhood.

# CONCLUSIONS

This impact study strongly suggests that the publicly funded rotavirus vaccination program significantly reduced gastroenteritis hospitalizations in young children. Moreover, Quebec's universal vaccination program demonstrated equitable access to rotavirus vaccine among different socio-economic subgroups. However, disadvantaged subgroups experienced a less pronounced AGE reduction, suggesting that factors other than vaccination may influence part of the reduction in hospitalization for gastroenteritis among young children. Based on the present study, a forthcoming study will assess vaccine effectiveness directly among children eligible for the rotavirus vaccination program, overall and according to socio-economic characteristics, to further explore the present findings.

## REFERENCES

- Parashar UD, Gibson CJ, Bresse JS, Glass RI. Rotavirus and severe childhood diarrhea. *Emerg Infect Dis* 2006;12(2):304–06. PMID: 16494759. doi: 10.3201/ eid1202.050006.
- Kilgore A, Donauer S, Edwards KM, Weinberg GA, Payne DC, Szilagyi PG, et al. Rotavirus-associated hospitalization and emergency department costs and rotavirus vaccine program impact. *Vaccine* 2013;31(38):4164–71. PMID: 23845802. doi: 10.1016/j.vaccine.2013.06.085.
- Morton VK, Thomas MK, McEWEN SA. Estimated hospitalizations attributed to norovirus and rotavirus infection in Canada, 2006–2010. *Epidemiol Infect* 2015:143(16):3528–37. PMID: 25991407. doi: 10.1017/S0950268815000734.
- 4. Bernard S, Valiquette L, De Wals P, Nault V, Babakissa C, Cyr C, et al. Burden of rotavirus disease: A population-based study in Eastern Townships, Quebec. *Can J Infect Dis Med Microbiol* 2013;24(3):138–42. PMID: 24421824.
- Rivest P, Proulx M, Lonergan G, Lebel MH, Bédard L. Hospitalisations for gastroenteritis: The role of rotavirus. *Vaccine* 2004;22(15–16):2013–17. PMID: 15121314. doi: 10.1016/j.vaccine.2003.10.029.
- National Advisory Committee on Immunization. Updated statement on the use of rotavirus vaccines. *Can Commun Dis Rep* 2010;36(ACS-4):1–37.
- Vesikari T, Matson DO, Dennehy P, Van Damme P, Santosham M, Rodriguez Z, et al. Safety and efficacy of a pentavalent human-bovine (WC3) reassortant rotavirus vaccine. N Engl J Med 2006;354(1):23–33. PMID: 16394299. doi: 10. 1056/NEJMoa052664.

- Ruiz-Palacios GM, Pérez-Schael I, Velázquez FR, Abate H, Breuer T, Clemens SC, et al. Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. *N Engl J Med* 2006;354(1):11–22. PMID: 16394298. doi: 10. 1056/NEJMoa052434.
- Karafillakis E, Hassounah S, Atchison C. Effectiveness and impact of rotavirus vaccines in Europe, 2006–2014. *Vaccine* 2015;33(18):2097–107. PMID: 25795258. doi: 10.1016/j.vaccine.2015.03.016.
- Rha B, Tate JE, Payne DC, Cortese MM, Lopman BA, Curns AT, et al. Effectiveness and impact of rotavirus vaccines in the United States – 2006–2012. *Expert Rev Vaccines* 2014;13(3):365–76. PMID: 24392657. doi: 10.1586/14760584.2014.877846.
- Giaquinto C, Dominiak-Felden G, Van Damme P, Htar Myint TT, Maldonado YA, Spoulou V, et al. Summary of effectiveness and impact of rotavirus vaccination with the oral pentavalent rotavirus vaccine: A systematic review of the experience in industrialized countries. *Hum Vaccin* 2011; 7(7):734–48. PMID: 21734466. doi: 10.4161/hv.7.7.15511.
- Esparza-Aguilar M, Gastañaduy PA, Sánchez-Uribe E, Desai R, Parashar UD, Richardson V, et al. Diarrhoea-related hospitalizations in children before and after implementation of monovalent rotavirus vaccination in Mexico. *Bull World Health Organ* 2014;92(2):117–25. PMID: 24623905. doi: 10.2471/BLT. 13.125286.
- Gastañaduy PA, Sánchez-Uribe E, Esparza-Aguilar M, Desai R, Parashar UD, Patel M, et al. Effect of rotavirus vaccine on diarrhea mortality in different socioeconomic regions of Mexico. *Pediatrics* 2013;131(4):e1115–20. PMID: 23460689. doi: 10.1542/peds.2012-2797.
- 14. Roy M, Généreux M, Laverdière É, Vanasse A. Surveillance of social and geographic inequalities in housing-related issues: The case of the Eastern Townships, Quebec (Canada). *Int J Environ Res Public Health* 2014;11(5): 4825–44. PMID: 24806192. doi: 10.3390/ijerph110504825.
- Hsu VP, Staat MA, Roberts N, Thieman C, Bernstein DI, Bresee J, et al. Use of active surveillance to validate international classification of diseases code estimates of rotavirus hospitalizations in children. *Pediatrics*, 2005;115(1): 78–82. PMID: 15629984.
- Statistics Canada. Dissemination Area (DA). 2011 Census Dictionary. Ottawa, ON: Statistics Canada, 2012. Available at: http://www12.statcan.gc.ca/censusrecensement/2011/ref/dict/geo021-eng.cfm (Accessed November 24, 2015).
- Bettinger JA, Wills K, Le Saux N, Scheifele DW, Halperin SA, Vaudry W. Heterogeneity of rotavirus testing and admitting practices for gastroenteritis among 12 tertiary care pediatric hospitals: Implications for surveillance. *Can J Infect Dis Med Microbiol* 2011;22(1):15–8. PMID: 22379483.
- Desai R, Curns AT, Steiner CA, Tate JE, Patel MM, Parashar UD. All-cause gastroenteritis and rotavirus-coded hospitalizations among US children, 2000–2009. *Clin Infect Dis* 2012;55(4):e28–34. PMID: 22543022. doi: 10. 1093/cid/cis443.
- Yen C, Tate JE, Wenk JD, Harris JM, Parashar UD. Diarrhea-associated hospitalizations among US children over 2 rotavirus seasons after vaccine introduction. *Pediatrics* 2011;127(1):e9–15. PMID: 21172995. doi: 10.1542/ peds.2010-1393.
- Dey A, Wang H, Menzies R, Macartney K. Changes in hospitalisations for acute gastroenteritis in Australia after the national rotavirus vaccination program. *Med J Aust* 2012;197(8):453–57. PMID: 23072242. doi: 10.5694/ mja12.10062.
- Clarke MF, Davidson GP, Gold MS, Marshall HS. Direct and indirect impact on rotavirus positive and all-cause gastroenteritis hospitalisations in South Australian children following the introduction of rotavirus vaccination. *Vaccine* 2011;29(29–30):4663–67. 21575665. doi: 10.1016/j. vaccine.2011.04.109.
- 22. Payne DC, Szilagyi PG, Staat MA, Edwards KM, Gentsch JR, Weinberg GA, et al. Secular variation in United States rotavirus disease rates and serotypes: Implications for assessing the rotavirus vaccination program. *Pediatr Infect Dis* J 2009;28(11):948–53. PMID: 19859013. doi: 10.1097/INF.0b013e3181a6ad6e.
- 23. Aliabadi N, Tate JE, Haynes AK, Parashar UD. Centers for Disease Control and Prevention (CDC). Sustained decrease in laboratory detection of rotavirus after implementation of routine vaccination—United States, 2000–2014. *MMWR Morb Mortal Wkly Rep* 2015;64(13):337–42. PMID: 25856253.
- 24. Boulianne N, Audet D, Ouakki M. Enquête sur la couverture vaccinale des enfants de 1 an et 2 ans au Québec en 2014. Québec : Institut national de santé publique, 2015. Available at: http://www.inspq.qc.ca/pdf/publications/1973\_Enquete\_Couverture\_Vaccinale\_Enfants.pdf (Accessed August 19, 2015).
- 25. Poirier B. Rapport de la couverture vaccinale des 0-2 ans en Estrie. Sherbrooke, QC : Direction de santé publique de l'Estrie, 2015. Available at: http:// www.santeestrie.qc.ca/sante\_publique/protection\_maladies\_infectieuses/ vaccination/documents/RapportCV2014\_Estrie\_VFACCWeb.pdf (Accessed August 19, 2015).
- 26. Guay M, Gallagher F, Petit G, Ménard S, Clément P, Boyer G. Pourquoi les couvertures vaccinales chez les nourrissons de l'estrie sont-elles sous-optimales? Québec : CSSS-IUGS, 2009. Available at: http://www.santeestrie.qc.ca/publication\_documentation/documents/etude\_couvertures\_vaccinales\_chez\_les\_nourrissons\_sous-optimales.pdf (Accessed August 19, 2015).

- Bradley RH, Corwyn RF. Socioeconomic status and child development. *Annu Rev Psychol* 2002;53:371–99. PMID: 11752490. doi: 10.1146/annurev.psych. 53.100901.135233.
- Givon-Lavi N, Ben-Shimol S, Cohen R, Greenberg D, Dagan R. Rapid impact of rotavirus vaccine introduction to the National Immunization Plan in Southern Israel: Comparison between 2 distinct populations. *Vaccine* 2015; 33(16):1934–40. PMID: 25744226. doi: 10.1016/j.vaccine.2015.02.062.
- Amre DK, Infante-Rivard C, Gautrin D, Malo J-L. Socioeconomic status and utilization of health care services among asthmatic children. J Asthma 2002; 39(7):625–31. PMID: 12442952. doi:10.1081/JAS-120014927.

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## RÉSUMÉ

**OBJECTIFS :** Suite à l'implantation d'un programme de vaccination contre le rotavirus financé publiquement au Québec en 2011, son impact sur les taux d'hospitalisation pour gastro-entérite, un proxy pour les gastro-entérites sévères, a été évalué.

**MÉTHODES :** Grâce à l'utilisation d'une base de données hospitalières et d'un registre de vaccination régional, les tendances temporelles des taux

d'hospitalisation pour gastro-entérite aiguë (GEA) et gastro-entérite à rotavirus (GERV) survenues avant l'âge de cinq ans ainsi que la couverture vaccinale ont été examinées de juin 2004 à mai 2014 parmi une large cohorte rétrospective d'enfants nés dans la région de l'Estrie. Le taux annuel moyen d'hospitalisation pour GEA des années post-programme (2011/2012–2013/2014) a été

comparé à celui des années pré-programme (2004/2005–2010/2011), globalement et selon plusieurs caractéristiques de l'enfant, de sa famille et de son guartier résidentiel à la naissance.

**RÉSULTATS :** Le taux d'hospitalisation pour GEA a diminué de 81/10 000 dans la période pré-programme à 46/10 000 dans la période post-programme (réduction relative = 43 %). Suite à l'implantation du programme, la couverture vaccinale a rapidement augmenté et a atteint 81 %. Toutes les catégories socioéconomiques ont démontré un taux d'hospitalisation réduit dans la période postprogramme, néanmoins les plus faibles réductions relatives ont été observées chez les enfants vivant dans des quartiers ayant des taux élevés d'inemploi, de familles à faible revenu et de mères vivant seules. Cependant, ces sous-groupes défavorisés ne présentaient pas une couverture vaccinale plus faible.

**CONCLUSIONS :** Trois ans après son introduction dans un programme de vaccination universel, le vaccin contre le rotavirus a significativement réduit les gastro-entérites sévères chez les jeunes enfants. Malgré une couverture vaccinale similaire parmi tous les enfants, les groupes socioéconomiquement défavorisés semblent avoir connu une réduction moins prononcée des GEA, suggérant que des facteurs autre que la vaccination peuvent partiellement influencer la réduction de la morbidité reliée à la gastro-entérite chez les jeunes enfants.

**MOTS CLÉS :** infections à rotavirus; vaccins contre le rotavirus; programmes d'immunisation; gastro-entérite; enfant; socioéconomique