Family and Child Risk Factors for Early-Life RSV Illness

Tiffany Fitzpatrick, MPH,[a,b,c] J. Dayre McNally, MD, PhD,[d] Thérèse A. Stukel, PhD,[a,b,e] Hong Lu, PhD,[a] David Fisman, MD, MPH,[b] Jeffrey C. Kwong, MD, MSc,[a,b,e,f,g,h,i,*] Astrid Guttmann, MDCM, MSc[a,b,c,e,j,k,*]

abstract

BACKGROUND AND OBJECTIVES: Most infants hospitalized with respiratory syncytial virus (RSV) do not meet common "high-risk" criteria and are otherwise healthy. The objective of this study was to quantify the risks and relative importance of socioeconomic factors for severe, early-life RSV-related illness. We hypothesized several of these factors, particularly those indicating severe social vulnerability, would have statistically significant associations with increased RSV hospitalization rates and may offer impactful targets for population-based RSV prevention strategies, such as prophylaxis programs.

METHODS: We used linked health, laboratory, and sociodemographic administrative data for all children born in Ontario (2012–2018) to identify all RSV-related hospitalizations occurring before the third birthday or end of follow-up (March 31, 2019). We estimated rate ratios and population attributable fractions using a fully adjusted model.

RESULTS: A total of 11 782 RSV-related hospitalizations were identified among 789 484 children. Multiple socioeconomic factors were independently associated with increased RSV-related admissions, including young maternal age, maternal criminal involvement, and maternal history of serious mental health and/or addiction concerns. For example, an estimated 4.1% (95% confidence interval: 2.2 to 5.9) of RSV-related admissions could be prevented by eliminating the increased admissions risks among children whose mothers used welfare-based drug insurance. Notably, 41.6% (95% confidence interval: 39.6 to 43.5) of admissions may be prevented by targeting older siblings (eg, through vaccination).

CONCLUSIONS: Many social factors were independently associated with early-life RSV-related hospitalization. Existing RSV prophylaxis and emerging vaccination programs should consider the importance of both clinical and social risk factors when determining eligibility and promoting compliance.

[a]*ICES, Toronto, Ontario, Canada;* [g]*Department of Family and Community Medicine,* [b]*Dalla Lana School of Public Health,* [e]*Institute for Health Policy, Management and Evaluation,* [h]*Centre for Vaccine Preventable Diseases, and* [k]*Edwin S.H. Leong Centre for Healthy Children, University of Toronto, Toronto, Ontario, Canada;* [j]*Division of Pediatric Medicine and* [c]*Child Health Evaluative Sciences, Hospital for Sick Children, Toronto, Ontario, Canada;* [d]*Children's Hospital of Eastern Ontario, Ottawa, Ontario, Canada;* [f]*Public Health Ontario, Toronto, Ontario, Canada; and* [i]*University Health Network, Toronto, Ontario, Canada*

[*]*Contributed equally as co-senior authors*

Dr Fitzpatrick conceptualized the study, analyzed the data, interpreted the findings, and drafted the manuscript; Dr McNally contributed critically to the study design, methods, interpretation, and final manuscript; Dr Stukel provided statistical guidance, assisted with statistical interpretation of the results, and critically contributed to the final manuscript; Dr Lu created the data set for analysis and critically contributed to the final manuscript; Drs Kwong and Guttmann supervised the study design, provided clinical context for study methods and findings and critically contributed to the final manuscript; and all authors approve the final manuscript as submitted and agree to be accountable for all aspects of the work.

WHAT'S KNOWN ON THIS SUBJECT: Only a small proportion of infants hospitalized with respiratory syncytial virus (RSV) are considered "high risk" according to common criteria (ie, prophylaxis guidelines based on prematurity and comorbidities). Socioeconomic factors play important roles in the transmission, severity, and prevention of many childhood respiratory viruses.

WHAT THIS STUDY ADDS: RSV admission rates are greater among infants with family histories suggestive of social vulnerability, such as maternal use of social welfare programs and involvement with the criminal system. In the prevaccine era, these factors offer feasible targets for RSV prophylaxis.

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Respiratory syncytial virus (RSV) is the most common cause of pediatric hospitalization worldwide.[1,2] RSV is a ubiquitous infection, and early-life RSV infection has been shown to increase asthma risk.[3] No RSV vaccines have yet been approved, although several candidates are currently in phase III trials.[4–6] In the current absence of vaccination, the severity of RSV-related illness can be reduced through prophylaxis with palivizumab.[7,8] Given its high costs and administrative burden, palivizumab is currently only recommended for infants considered high risk for RSV-related complications.[7,9,10] Most palivizumab programs are restricted to young infants who were born very preterm and/or have been diagnosed with serious underlying heart or lung diseases.[7,9,11]

However, >80% of infants hospitalized with RSV do not have any underlying conditions and are otherwise healthy.[12,13] In recent years, several organizations have adopted risk scoring tools to identify other children who may benefit from palivizumab, typically, children born preterm with other risk factors.[14] Many of these tools consider nonclinical factors related to transmission and disease severity, such as day care attendance, presence of school-aged siblings, and exposure to household tobacco smoke.[14] Given the geographic landscape of Canada, many provinces also recommend palivizumab for young children living in isolated communities where care is not readily accessible.[15] In recent years, there have also been calls for the inclusion of Indigenous infants in palivizumab recommendations given the disproportionate RSV-related hospitalization rates within these populations, particularly in Canada, the United States, and Australia.[16,17] Relatively little attention has been given to other social risk factors for RSV-related illness (despite their importance for the transmission and severity of other respiratory infections, such as influenza).[13,18–21]

The objective of the current study was to comprehensively investigate the independent associations between multiple social and sociodemographic characteristics and severe, early-life RSV-related illness, adjusting for known clinical and transmission risk factors. We uniquely leveraged linked sociodemographic and health administrative data for all children born in Ontario, Canada's most populous province, to investigate novel characteristics related to maternal social vulnerability, which have previously not been studied in the context of RSV. To better inform the relative public health importance of these factors, we further estimated population attributable fractions (PAFs).

METHODS

Study Population and Follow-up

We created a birth cohort of all children born in Ontario hospitals, April 1, 2012, through March 31, 2018. Health outcomes were identified until the earliest of death, third birthday, moving out of province, or March 31, 2019 (the end of follow-up). We excluded infants not successfully linked to maternal records, with gestational ages of <22 or >44 weeks (ie, coding errors), and stillbirths.

Data Sources

We used several linked population-based administrative health and demographic databases. Births were identified by using a provincial birth registry (MOMBABY), covering all in-hospital births in Ontario since 1988.[22] RSV-related admissions were identified from the Canadian Institute for Health Information's Discharge Abstract Database (DAD) and National Ambulatory Care Reporting System (NACRS). Demographic characteristics were determined from MOMBABY, census, Ontario Drug Benefit (ODB) program, and Immigration, Refugees and Citizenship Canada (IRCC) permanent resident databases. These data sets were linked by using unique encoded identifiers and analyzed at ICES, formerly the Institute for Clinical Evaluative Sciences.

Outcomes

RSV-related hospitalizations were those with an RSV-related diagnostic code identified anywhere on the discharge record, on the basis of a highly specific (99.6%) and sensitive (97.9%) algorithm previously validated within this population,[23] and admissions with a concurrent laboratory confirmation for RSV.[24] Specifically, the following *International Classification of Diseases, 10th Revision* (ICD-10) diagnostic codes were considered: RSV pneumonia (J12.1); acute bronchiolitis due to RSV (J21.0); acute bronchitis due to RSV (J22.0); or RSV as the cause of disease classified elsewhere (B97.4). *ICD-10* classification was used in Ontario throughout the entire study period.

Laboratory testing data, available from April 1, 2012, through June 30, 2016, included all specimens submitted to provincial laboratories (Public Health Ontario Laboratories), both of Ontario's major pediatric hospitals (Hospital for Sick Children and Children's Hospital of Eastern Ontario), and 7 major community and teaching hospitals and/or networks: London Health Sciences Centre (including the Children's Hospital at London Health Sciences Centre), William Osler Health System, North York General Hospital, the University Health Network, St. Joseph's Healthcare Hamilton (including the McMaster Children's Hospital), Mount Sinai Hospital, and Sunnybrook Hospital.[24]

The primary outcome of interest was community-acquired RSV infections requiring admission; thus, possible

nosocomial infections were excluded, defined as any postadmission diagnosis of RSV and admissions for which laboratory confirmation of RSV was sought >7 days after admission.[25] In Supplemental Fig 1, we provide further details.

To capture a broader spectrum of illness and investigate potential testing biases, our secondary outcome was a composite measure including all community-acquired RSV-related hospitalizations and emergency department (ED) visits with laboratory confirmation of RSV. We restricted the analysis to include only the years captured by the laboratory data (ie, births until June 30, 2015, and outcomes until June 30, 2016).

Covariates

We selected measures that were credible and supported by previous literature. Current and previous teenage motherhood is a long-recognized risk factor for poor childhood health outcomes due, in part, to the association between teenage motherhood and lower socioeconomic status (SES).[13,16,26] Several studies have revealed differences in RSV admission rates on the basis of geography, race and ethnicity, neighborhood deprivation and income, and other measures of SES.[18,27] Given Canada's expansive geography, geographic remoteness is a known factor influencing health care availability.[15] Race and ethnicity data are not routinely collected in Canada; however, individual-level immigration status is identifiable through the Immigration, Refugees and Citizenship Canada database, and neighborhood-level ethnic diversity is identifiable through the census-based Ontario Marginalization ethnic concentration index (ie, the proportion of new immigrants and those who identify in the census as visible minorities); notably, Indigenous status is not considered in this index.[22,28] Other area-level measures of social deprivation can also be determined at a neighborhood-level, including income and 3 other Ontario Marginalization indices: residential instability, a measure of family and/or housing instability; material deprivation, a composite measure of poverty (ie, receipt of government transfer payments, unemployment, and households earning less than the low-income cutoff), the ability of individuals and communities to access basic material needs (ie, quality housing), family composition (ie, lone parent households), and educational attainment (ie, high school completion); and dependency, the proportion of the population not participating in the labor force.[28]

We leveraged the linked health data infrastructure of ICES to investigate several indicators of maternal SES, particularly those indicative of extreme social vulnerability: recent experiences with the criminal system, namely imprisonment or other circumstances resulting in medical referral from police or legal counsel; homelessness; abuse and/or violence (eg, woman abuse); serious mental health and/or addiction(s) concerns (eg, resulting in hospital admission); and use of public low-income drug benefits (ie, insurance claims to submitted to the ODB program for residents receiving provincial financial social assistance [welfare]).

Unless otherwise stated, covariates were determined at delivery. Neighborhood-level measures were ascertained from the census and measured at the dissemination area, Canada's smallest census area consisting of 400 to 700 persons.[28] Maternal age at first birth and parity were determined on the basis of all preceding births captured in MOMBABY; other maternal covariates were specific to the 2 years preceding birth and determined on the basis of previous encounters with Ontario's publicly funded health care system. Detailed descriptions of all covariates are provided in Supplemental Table 8.

Statistical Analysis

Poisson regression, with an offset term for log person-time, was used to calculate rate ratios (RRs) with corresponding 95% confidence intervals (CIs). In addition to crude RRs, we adjusted for known factors related to medical complexity and transmission risk, determined a priori: gestational age; birth weight; diagnosis of hemodynamically significant congenital heart disease (hs-CHD), bronchopulmonary dysplasia (BPD), and/or trisomy 21; sex; multiparous births; parity; and young chronological age (<6 months) during RSV season. We, additionally, present a model adjusted for all included covariates. Collinearity was examined from the parameter estimate Hessian correlation matrix, in which correlation coefficients between 0.7 and 0.9 are considered highly correlated.[29] In the case of highly correlated variables, only 1 variable was included in the final model, determined on the basis of strength of association and clinical relevance.

PAFs were calculated for all characteristics included in the fully adjusted final model, by using the approach of Bruzzi et al[30]:in which S indicates the exposure levels and p_i indicates the prevalence of exposure among cases.

To better inform potential policy revisions, which have, historically, been focused on preterm births,[14,31,32] a subgroup analysis was performed specific to children born 33 to 35 weeks' gestational age (wGA).

Missing data were minimal (<5%), and complete case analyses were performed.

$$PAF = 1 - \sum_{i=1}^{S} \frac{p_i}{aRR_i}$$

Analyses were performed in SAS version 9.4 (SAS Institute, Inc, Cary, NC).

Ethics

The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require research ethics board review.

RESULTS

Our cohort included 789 484 children and 11 782 RSV-related admissions. A total of 10 749 (1.4%) children had at least 1 RSV-related admission; 9716 (90.4%) children had exactly 1, 711 (6.6%) had 2, and 120 (1.2%) had 3 to 5 RSV-related admissions before their third birthday. A total of 57.4% of RSV-related admissions occurred among children <6 months old, 16.4% occurred among those 6 to 11 months old, 18.5% occurred among those 12 to 23 months old, and 7.7% occurred among those 2 to 3 years old. A total of 90.6% of admissions occurred among children who were <6 months old during their first RSV season, and only 4.1% of admitted children were considered palivizumab-eligible in Ontario (Table 1). A total of 1.9% of children experienced at least 1 RSV admission or laboratory-confirmed ED visit; only 3.6% of these children were palivizumab-eligible (Supplemental Table 5).

After adjusting for factors known to increase the risk of RSV transmission and illness severity, many of the crude RRs for the examined social factors were attenuated (Table 2). In the fully adjusted model, many social characteristics remained associated with independent and statistically significant increased rates of RSV-related hospitalization, including several suggestive of maternal social vulnerability: teenage motherhood (RR: 1.50 [95% CI: 1.33 to 1.70] relative to 25 to 29 years), recent involvement with the criminal system (RR: 1.31 [95% CI: 1.13 to 1.53]), recent mental health and/or addictions concerns (RR: 1.14 [95% CI: 1.02 to 1.27]), and recent use of low-income drug insurance (RR: 1.05–1.25, depending on the program). The following sociodemographic factors had protective associations: rural residence (RR: 0.83 [95% CI: 0.77 to 0.89]), geographic isolation (RR: 0.44 [95% CI: 0.31 to 0.60]), and having a mother born outside Canada, for example, recent immigrant versus Canadian born (RR: 0.76 [95% CI: 0.70 to 0.83]).

If all children had RSV admissions risks comparable with children born to mothers aged ≥40 years, 35.5% (95% CI: 28.0 to 42.1) fewer admissions would be expected (Table 3). Reductions of 3% to 7% might occur if all children had RSV admission risks similar to children living in the highest income neighborhoods (7%), with short birth stays (6%), with spontaneous vaginal delivery (4%), with no recent maternal use of low-income drug benefits (4%), or without congenital anomalies (3%). If the protective effects observed among children born to immigrant and refugee mothers were removed, 4% more RSV-related admissions may occur. Given their low prevalence, the following factors could have minimal, albeit statistically significant, impacts on reducing RSV-related admissions: maternal criminal system involvement (0.4%), maternal mental health and/or addictions concerns (0.4%), and diagnosis of trisomy 21 (0.4%) or BPD (0.2%). In contrast, an estimated 45.5% (95% CI: 42.4 to 48.4) of RSV-related admissions might be prevented in the presence of interventions that effectively eliminate the excess risk experienced by young infants (<6 months). Targeting children with siblings could prevent 41.6% (95% CI: 39.6 to 43.5) of admissions. Eliminating the excess risks associated with living in urban or low ethnic diversity neighborhoods could reduce admissions by 16% each.

These findings did not appreciably differ in our secondary analysis of RSV-related admissions and laboratory-confirmed ED visits (Table 3; Supplemental Table 6).

Our primary findings were also qualitatively comparable to our subgroup analysis of children born 33 to 35 wGA (Table 4; Supplemental Table 7). However, the preventive impacts possible through eliminating the admissions risk associated with singleton births, prolonged birth stays, and neighborhood income were enhanced and that of young chronological age and male sex were slightly reduced. Statistically significant attributable proportions were noted for only 8 characteristics: siblings (38.2% fewer RSV admissions could be achieved if all children had admission risks comparable with those without any siblings at birth); young age (33.3% fewer, if comparable with those ≥6 months old during their first RSV season); prolonged birth stays (21.8% fewer, if comparable with those with birth stays ≤4 days); low neighborhood ethnic diversity (18.6% fewer, if comparable with those living in more diverse neighborhoods); diagnosis of any major congenital anomaly (6.6% fewer, if comparable with those without any congenital anomalies); diagnosis of trisomy 21 (0.7% fewer, if comparable with those without trisomy 21); singleton births (10.7% more admissions would be expected if all children had RSV admission risks comparable with multiparous births); and birth weight (44.3% more, if comparable with those born 3000–3499 g).

DISCUSSION

In this population-based study, we identified multiple social characteristics independently associated with RSV hospitalization,

TABLE 1 Characteristics of All Children Born in Ontario Hospitals, April 1, 2012, to March 31, 2018; Stratified According to Ever Being Admitted to Hospital With RSV-Related Illness Before 3 Years of Age

Characteristic	Cohort (N = 789 484), n (%)	No RSV Admission (n = 778 735), %	≥1 RSV Admission (n = 10 749), %
Birth characteristics			
High-risk birth month (November to January)	189 315 (24.0)	23.8	37.7
<6 mo old during first RSV season	657 594 (83.3)	83.2	90.6
Birth sex			
Female	384 838 (48.8)	48.8	42.9
Male	404 615 (51.3)	51.2	57.1
Missing	31 (0)	0	0
Multiparous birth set	6348 (3.3)	3.3	5.4
Gestational age, wk			
<28	3082 (0.4)	0.4	1.3
28–32	8209 (1.0)	1.0	2.5
33–35	24 870 (3.1)	3.1	5.9
36–38	241 614 (30.6)	30.5	36.7
39–40	419 041 (53.1)	53.2	45.7
≥41	92 668 (11.7)	11.8	7.9
Median (SD)	39 (1.9)	39 (1.9)	39 (2.6)
Range, minimum to maximum	22–44	22–44	23–43
Birth wt, g			
<1500	7099 (0.9)	0.9	2.8
1500–1999	10 055 (1.3)	1.3	2.5
2000–2499	33 994 (4.3)	4.3	6.4
2500–2999	134 349 (17.0)	17.0	17.8
3000–3499	295 738 (37.5)	37.5	33.7
3500–3999	226 483 (28.7)	28.7	26.5
4000–4499	69 033 (8.7)	8.7	8.6
≥4500	12 293 (1.6)	1.6	1.6
Missing	440 (0.1)	0.1	0.1
Median (SD)	3360 (574.4)	3360 (571.2)	3310 (690.0)
Range, minimum to maximum	500–5984	500–5984	500–5720
Prolonged birth stay (>90th percentile)	58 965 (7.5)	7.4	15.4
Small for GA (<10th percentile)	106 248 (13.5)	13.5	13.6
Type of labor			
Spontaneous vaginal	350 256 (44.4)	44.4	43.8
Induced vaginal	138 614 (17.6)	17.5	18.6
Uninduced cesarean delivery	185 933 (23.6)	23.5	27.2
Induced cesarean delivery	42 691 (5.4)	5.4	4.0
Induced and assisted, any mode	23 497 (3.0)	3.0	2.0
Other assisted, any mode	47 523 (6.0)	6.0	4.3
Missing	970 (0.1)	0.1	0.2
No. siblings (at birth)			
None	338 092 (42.8)	43.1	26.2
1	284 709 (36.1)	36.0	41.7
2	110 920 (14.1)	14.0	19.7
3	35 401 (4.5)	4.5	7.6
≥4	20 361 (2.6)	2.6	4.7
Median (SD)	1 (1.1)	1 (1.1)	1 (1.2)
Range, minimum to maximum	0–16	0–16	0–14
Demographics (at birth)			
Rural residence			
Urban	698 984 (88.5)	88.5	88.8
Rural	76 334 (9.7)	9.7	10.5
Missing	14 166 (1.8)	1.8	0.7
Geographic isolation (RIO >74)	5761 (0.7)	0.7	0.4
Mother's immigration status			
Canadian born	564 614 (71.5)	71.4	76.9
Long-term immigrant	140 603 (17.8)	17.8	15.6
Recent immigrant	74 859 (9.5)	9.5	6.3
Recent refugee	9408 (1.2)	1.2	1.2

TABLE 1 Continued

Characteristic	Cohort (N = 789 484), n (%)	No RSV Admission (n = 778 735), %	≥1 RSV Admission (n = 10 749), %
Health status			
Major congenital anomalies			
Any major congenital anomaly	47 270 (6.0)	5.9	10.1
BPD	803 (0.1)	0.1	0.7
CHD	8024 (1.0)	0.9	2.7
hs-CHD	1492 (0.2)	0.2	0.3
Trisomy 21	745 (0.1)	0.1	0.5
Palivizumab eligibility			
Clearly eligible: meets ≥1 of the above	11 864 (1.5)	1.4	4.1
Possibly eligible: 33–35 wGA with other CHD or CLD	18 288 (2.3)	0.9	2.7
Maternal social vulnerabilities[a]			
Child apprehended at birth	3146 (0.4)	0.4	0.8
Maternal age at birth, y[a]			
<20	17 858 (2.3)	2.3	3.0
20–24	84 742 (10.7)	10.7	13.7
25–29	212 699 (26.9)	26.9	27.2
30–34	289 038 (36.6)	36.6	35.2
35–39	151 347 (19.2)	19.2	17.6
≥40	33 569 (4.3)	4.3	3.3
Missing	231 (0)	0	0
Median (SD)	31 (5.3)	31 (5.3)	30 (5.4)
Range, minimum to maximum	12–49	12–49	13–49
Maternal age at first birth, y[a]			
<20	60 891 (7.7)	7.6	12.8
20–24	145 151 (18.4)	18.3	23.7
25–29	255 303 (32.3)	32.4	31.4
30–34	233 625 (29.6)	29.7	23.6
35–39	79 172 (10.0)	10.1	7.3
≥40	15 193 (1.9)	1.9	1.2
Missing	149 (0)	0	0
Median (SD)	28 (5.6)	29 (5.6)	27 (5.7)
Range, minimum to maximum	12–49	12–49	13–47
Maternal history of social vulnerabilities[b]			
Involvement with criminal justice system	9691 (1.2)	1.2	1.7
Experienced homelessness	545 (0.1)	0.1	0.1
Mental health and/or addiction concerns	19 309 (2.5)	2.4	3.7
Victim of violence and/or woman abuse	4975 (0.6)	0.6	1.0
Use of low-income drug benefits			
Welfare	67 526 (8.6)	8.5	14.4
Disability support	19 469 (2.5)	2.4	4.2
High prescription costs	8265 (1.1)	1.0	1.3
Other program(s)	71 031 (9.0)	9.0	8.2
No claims	623 193 (78.9)	79.0	71.8
Area-level SES measures[c]			
Dependency quintile			
Q1 (least dependent)	262 562 (33.3)	33.3	30.3
Q2	162 832 (20.6)	20.6	20.7
Q3	129 639 (16.4)	16.4	17.1
Q4	114 814 (14.5)	14.5	16.1
Q5 (most dependent)	98 587 (12.5)	12.5	13.8
Missing	21 050 (2.7)	2.7	1.9
Material deprivation quintile			
Q1 (least deprived)	151 421 (19.2)	19.2	17.8
Q2	150 514 (19.1)	19.1	17.3
Q3	145 132 (18.4)	18.4	18.2
Q4	146 640 (18.6)	18.6	19.7
Q5 (most deprived)	174 727 (22.1)	22.1	25.1
Missing	21 050 (2.7)	2.7	1.9
Residential instability quintile			
Q1 (most stable)	170 773 (21.6)	21.6	20.4

TABLE 1 Continued

Characteristic	Cohort (N = 789 484), n (%)	No RSV Admission (n = 778 735), %	≥1 RSV Admission (n = 10 749), %
Q2	142 321 (18.0)	18.0	18.7
Q3	138 026 (17.5)	17.5	18.0
Q4	143 218 (18.1)	18.1	20.1
Q5 (least stable)	174 096 (22.1)	22.1	20.8
Missing	21 050 (2.7)	2.7	1.9
Ethnic diversity quintile			
Q1 (mostly white)	100 257 (12.7)	12.7	14.6
Q2	113 301 (14.4)	14.3	17.0
Q3	129 207 (16.4)	16.3	18.0
Q4	161 908 (20.5)	20.5	20.0
Q5 (most ethnically diverse)	263 761 (33.4)	33.5	28.4
Missing	21 050 (2.7)	2.7	1.9
Income quintile			
Q1 (lowest income)	170 157 (21.6)	21.5	23.9
Q2	155 288 (19.7)	19.7	20.8
Q3	159 577 (20.2)	20.2	19.7
Q4	160 976 (20.4)	20.4	19.6
Q5 (highest income)	127 913 (16.2)	16.2	14.9
Missing	15 573 (2.0)	2.0	0.9

$P < .0001$ for the comparison between characteristics of children with ≥1 RSV admission versus those with none, except for small for gestational age (P = .9224), delivery type (P = .3387), diagnosis of trisomy 21 (P = .0457), and mental health and additions concerns (P = .0051), by using likelihood ratio χ^2 for categorical variables and t test for continuous variables. CHD, congenital heart disease; CLD, chronic lung disease; RIO, rurality index for Ontario.

[a] Ages <10 and ≥50 y were assumed to be coding errors and are reported as missing.

[b] Specific to the 2 y before birth, unless otherwise noted.

[c] Dependency, material deprivation, residential instability, and ethnic concentration are based on the Ontario Marginalization Index; missing values are the same across measures.

even after adjusting for factors known to influence transmission, disease severity, and palivizumab eligibility. With this, we highlight the presence of social inequities in early-life RSV outcomes, suggesting these children experience additional risks associated with RSV transmission, disease severity, or reduced access and/or adherence to preventive interventions. Critically, these findings are in the context of a publicly funded health care system, which freely provides palivizumab to children considered high risk for severe RSV illness. Although only a few of these social factors were prevalent enough to translate into large population impacts, the same was true for a number of medical conditions currently targeted for prophylaxis (eg, RSV-related hospitalization is more common among children with certain medical conditions [namely, trisomy 21 and BPD], yet they represent a small proportion of admissions). Our subgroup analysis of children born 33 to 35 wGA further suggests substantial reductions in early-life RSV illness may be achieved through ensuring all palivizumab-eligible children receive palivizumab and adhere to the monthly dosing schedule or by expanding the eligibility criteria.

This is the first population-based study to comprehensively explore the medical and social risk factors for early-life RSV-related hospitalizations in Canada and one of few of its kind internationally. In a recent study, researchers using comparable data for Scottish children reached similar conclusions.[13] The authors reported the majority of RSV-related admissions occurred among children <6 months (48.6%), and, although those with underlying health conditions or born preterm were at greater risk of RSV-related admissions, they constituted only a small proportion of admissions (11.1% and 11.7%, respectively).[13] They also estimated that 31.4% of admissions could be prevented if all children had risks similar to those born to mothers aged ≥40; with the exception of area-level deprivation, which had no significant independent effect, no other SES characteristics were reported.[13] However, several studies have revealed children with various factors related to lower SES experience higher RSV-related admission rates.[18,27]

These findings have critical implications for emerging RSV vaccination strategies.[4,6] We estimate that >46% of early-life RSV-related admissions could be prevented if the risk among young infants was eliminated. RSV-vaccination programs could effectively target this group (eg, immunizing mothers or older siblings).[4,33] Widespread recommendation of palivizumab is not feasible, and, although children meeting common palivizumab eligibility criteria experience a substantially greater risk of severe RSV-related outcomes, they represent a minor proportion of admissions.[12,13] A recent clinical trial of a less administratively burdensome prophylactic alternative (nirsevimab) revealed promising results; if

TABLE 2 Unadjusted, Adjusted (Adjusted for Traditional Risk Factors), and Fully Adjusted (Adjusted for All Listed Covariates) RRs of Ever Being Admitted to a Hospital With RSV-Related Illness Among Ontario Children <3 Years of Age: April 1, 2012, to March 31, 2019

Characteristic	Unadjusted, RR (95% CI)	Adjusted,[a] RR (95% CI)	Fully Adjusted,[b] RR (95% CI)
Demographics (at birth)			
Rural residence	1.08 (1.01 to 1.14)	1.03 (0.97 to 1.10)	0.83 (0.77 to 0.89)
Geographic isolation	0.68 (0.54 to 0.86)	0.53 (0.39 to 0.72)	0.44 (0.31 to 0.60)
Mother's immigration status			
Canadian born	1.00 (reference)	1.00 (reference)	1.00 (reference)
Long-term immigrant	0.82 (0.78 to 0.86)	0.73 (0.70 to 0.77)	0.88 (0.83 to 0.93)
Recent immigrant	0.61 (0.56 to 0.66)	0.64 (0.59 to 0.70)	0.76 (0.70 to 0.83)
Recent refugee	0.94 (0.79 to 1.12)	0.79 (0.66 to 0.94)	0.83 (0.70 to 1.00[c])
Maternal social vulnerabilities[d]			
Child apprehended at birth	2.00 (1.61 to 2.49)	1.52 (1.22 to 1.89)	0.98 (0.78 to 1.26)
Maternal age at birth, y[e]			
<20	1.37 (1.22 to 1.53)	1.75 (1.56 to 1.97)	1.50 (1.33 to 1.70)
20–24	1.32 (1.24 to 1.40)	1.36 (1.28 to 1.45)	1.23 (1.15 to 1.32)
25–29	1.00 (reference)	1.00 (reference)	1.00 (reference)
30–34	1.05 (1.00[c] to 1.10)	0.86 (0.82 to 0.90)	0.89 (0.85 to 0.94)
35–39	0.96 (0.91 to 1.02)	0.72 (0.68 to 0.77)	0.76 (0.71 to 0.81)
≥40	0.83 (0.74 to 0.92)	0.56 (0.50 to 0.63)	0.59 (0.53 to 0.67)
Criminal justice system involvement	1.43 (1.23 to 1.65)	1.33 (1.15 to 1.54)	1.31 (1.13 to 1.53)
Experienced homelessness	2.10 (1.26 to 3.48)	1.83 (1.10 to 3.04)	1.15 (0.67 to 1.96)
Mental health or addiction concerns	1.53 (1.38 to 1.69)	1.51 (1.36 to 1.67)	1.14 (1.02 to 1.27)
Violence/woman abuse	1.56 (1.28 to 1.89)	1.43 (1.18 to 1.74)	1.01 (0.82 to 1.24)
Use of low-income drug benefits			
Welfare	1.85 (1.75 to 1.95)	1.53 (1.44 to 1.62)	1.22 (1.15 to 1.30)
Disability support	1.91 (1.73 to 2.10)	1.67 (1.52 to 1.84)	1.25 (1.13 to 1.39)
High prescription costs	1.40 (1.18 to 1.65)	1.21 (1.03 to 1.43)	1.22 (1.03 to 1.44)
Other program(s)	1.02 (0.95 to 1.09)	1.04 (0.97 to 1.11)	1.05 (0.98 to 1.13)
No claims	1.00 (reference)	1.00 (reference)	1.00 (reference)
Area-level SES measures, quintiles			
Dependency (reference: Q1)			
Q2	1.11 (1.05 to 1.17)	1.10 (1.05 to 1.16)	1.00 (0.95 to 1.06)
Q3	1.15 (1.08 to 1.21)	1.14 (1.08 to 1.21)	0.98 (0.92 to 1.04)
Q4	1.22 (1.15 to 1.30)	1.23 (1.16 to 1.30)	1.04 (0.97 to 1.11)
Q5 (most dependent)	1.21 (1.14 to 1.29)	1.23 (1.16 to 1.31)	1.02 (0.95 to 1.10)
Material deprivation (reference: Q1)			
Q2	0.98 (0.92 to 1.04)	0.97 (0.91 to 1.03)	0.95 (0.89 to 1.02)
Q3	1.07 (1.00 to 1.14)	1.05 (0.98 to 1.12)	1.02 (0.95 to 1.10)
Q4	1.14 (1.07 to 1.21)	1.11 (1.04 to 1.18)	1.07 (0.99 to 1.16)
Q5 (most deprived)	1.22 (1.15 to 1.29)	1.12 (1.05 to 1.18)	1.03 (0.94 to 1.12)
Residential instability (reference: Q1)			
Q2	1.10 (1.04 to 1.17)	1.14 (1.07 to 1.21)	1.03 (0.96 to 1.09)
Q3	1.10 (1.03 to 1.17)	1.14 (1.07 to 1.21)	0.97 (0.91 to 1.04)
Q4	1.18 (1.11 to 1.25)	1.21 (1.14 to 1.28)	0.97 (0.90 to 1.03)
Q5 (least stable)	1.00 (0.94 to 1.06)	1.07 (1.01 to 1.13)	0.88 (0.82 to 0.95)
Ethnic diversity (reference: Q5)			
Q1 (mostly white)	1.36 (1.28 to 1.44)	1.42 (1.33 to 1.51)	1.29 (1.19 to 1.40)
Q2	1.41 (1.33 to 1.49)	1.47 (1.38 to 1.56)	1.33 (1.24 to 1.43)
Q3	1.31 (1.23 to 1.38)	1.37 (1.29 to 1.45)	1.28 (1.20 to 1.37)
Q4	1.15 (1.09 to 1.22)	1.20 (1.14 to 1.27)	1.17 (1.10 to 1.24)
Income (reference: Q5)			
Q1 (lowest income)	1.21 (1.13 to 1.29)	1.14 (1.07 to 1.21)	1.12 (1.01 to 1.24)
Q2	1.15 (1.08 to 1.23)	1.14 (1.07 to 1.22)	1.10 (1.01 to 1.19)
Q3	1.07 (1.00[c] to 1.14)	1.06 (0.99 to 1.13)	1.03 (0.96 to 1.11)
Q4	1.05 (0.98 to 1.12)	1.05 (0.98 to 1.12)	1.06 (0.99 to 1.14)
Birth characteristics			
<6 mo old during RSV season	1.99 (1.87 to 2.12)	2.00 (1.87 to 2.14)	2.01 (1.88 to 2.14)
Male sex	1.27 (1.22 to 1.32)	1.26 (1.21 to 1.31)	1.24 (1.20 to 1.29)
Multiple birth set	1.66 (1.52 to 1.80)	0.74 (0.68 to 0.82)	0.72 (0.65 to 0.79)
Gestational age[f]			
<28 wGA	5.52 (4.67 to 6.53)	2.59 (1.92 to 3.51)	1.89 (1.39 to 2.57)
28–32 wGA	2.90 (2.57 to 3.28)	1.83 (1.50 to 2.24)	1.32 (1.08 to 1.62)

TABLE 2 Continued

Characteristic	Unadjusted, RR (95% CI)	Adjusted,[a] RR (95% CI)	Fully Adjusted,[b] RR (95% CI)
33–35 wGA	2.22 (2.04 to 2.41)	1.81 (1.63 to 2.02)	1.35 (1.20 to 1.51)
36–38 wGA	1.41 (1.35 to 1.47)	1.30 (1.25 to 1.37)	1.26 (1.21 to 1.32)
39–40 wGA	1.00 (reference)	1.00 (reference)	1.00 (reference)
≥41 wGA	0.78 (0.72 to 0.84)	0.86 (0.79 to 0.92)	0.83 (0.77 to 0.90)
Birth wt, g[f]			
<1500	3.92 (3.48 to 4.41)	1.92 (1.52 to 2.43)	1.57 (1.24 to 1.99)
1500–1999	2.26 (1.99 to 2.55)	1.45 (1.23 to 1.71)	1.15 (0.97 to 1.36)
2000–2499	1.69 (1.56 to 1.84)	1.30 (1.18 to 1.43)	1.15 (1.04 to 1.27)
2500–2999	1.17 (1.11 to 1.24)	1.09 (1.03 to 1.15)	1.06 (1.00 to 1.13)
3000–3499	1.00 (reference)	1.00 (reference)	1.00 (reference)
3500–3999	1.03 (0.98 to 1.08)	1.04 (0.99 to 1.10)	1.03 (0.98 to 1.08)
4000–4499	1.09 (1.02 to 1.18)	1.09 (1.02 to 1.18)	1.04 (0.96 to 1.12)
≥4500	1.13 (0.97 to 1.32)	1.09 (0.93 to 1.27)	1.01 (0.86 to 1.18)
Prolonged birth stay (>4 d)	2.32 (2.20 to 2.44)	1.79 (1.66 to 1.93)	1.58 (1.46 to 1.71)
Type of labor			
Spontaneous vaginal	1.00 (reference)	1.00 (reference)	1.00 (reference)
Induced vaginal	1.08 (1.02 to 1.14)	1.11 (1.05 to 1.17)	1.10 (1.04 to 1.16)
Uninduced cesarean delivery	1.18 (1.13 to 1.24)	1.03 (0.99 to 1.08)	1.09 (1.04 to 1.15)
Induced cesarean delivery	0.75 (0.68 to 0.83)	1.05 (0.95 to 1.16)	1.08 (0.97 to 1.20)
Induced and assisted to any mode	0.66 (0.57 to 0.76)	0.93 (0.80 to 1.07)	0.96 (0.83 to 1.11)
Other assisted, any mode	0.72 (0.66 to 0.79)	0.97 (0.88 to 1.06)	1.03 (0.93 to 1.13)
No. siblings (at birth)			
None	1.00 (reference)	1.00 (reference)	1.00 (reference)
1	1.91 (1.82 to 2.00)	1.89 (1.80 to 1.98)	2.07 (1.96 to 2.18)
2	2.32 (2.19 to 2.45)	2.24 (2.12 to 2.37)	2.49 (2.34 to 2.65)
3	2.81 (2.60 to 3.04)	2.67 (2.47 to 2.89)	2.94 (2.70 to 3.21)
≥4	3.03 (2.75 to 3.33)	2.83 (2.57 to 3.12)	3.20 (2.88 to 3.56)
Health status factors[g]			
Any major congenital anomaly	1.82 (1.71 to 1.94)	1.46 (1.36 to 1.56)	1.35 (1.26 to 1.45)
BPD	5.61 (4.47 to 7.04)	1.53 (1.15 to 2.02)	1.28 (0.96 to 1.70)
hs-CHD	2.22 (1.58 to 3.11)	1.56 (1.11 to 2.18)	1.13 (0.80 to 1.59)
Trisomy 21	5.07 (3.89 to 6.61)	3.82 (2.92 to 4.98)	2.67 (2.03 to 3.53)

[a] Adjusted for age (<6 mo) during RSV season, gestational age, birth wt, hs-CHD, BPD, trisomy 21, sex, birth set, and sibling count.

[b] Adjusted for all factors in this table.

[c] Rounded up.

[d] Specific to the 2 y before birth, unless otherwise noted.

[e] Maternal age at first and current birth were highly correlated; age at first birth was excluded from the fully adjusted model, given its weaker association with RSV outcomes.

[f] The 28 to 32 wGA category had a low correlation with birth weights of 1500 to 2000 g (correlation coefficient = −0.49), and the 33 to 35 wGA group had a low correlation with birth weights of 1500 to 2000 g (−0.31) and 2000 to 2500 g (−0.35); thus, both variables were included in the final adjusted model.

[g] Palivizumab eligibility was highly correlated with multiple variables and, thus, excluded from the fully adjusted model in favor of more specific characteristics. The crude RR for palivizumab-eligible children was 3.20 (95% CI: 2.91 to 3.52) and 0.68 (95% CI: 0.52 to 0.90) in the adjusted model.

approved, nirsevimab may support greater prophylaxis compliance, adherence, and coverage, particularly if offered at a lower cost than palivizumab.[34] With our results, we highlight several feasible candidates for the enhanced targeting of, and revisions to, RSV prophylaxis programs. For several of these, the number of "exposed" children is small, highlighting feasible targets for prophylaxis, if determined cost-effective. For example, we observed that children born to teenage mothers were more likely to be admitted with RSV[13]; only 2.3% of children in our cohort were born to teenage mothers, a manageable target, particularly in combination with other criteria, such as prematurity. We reached comparable conclusions in our subgroup analysis of children born 33 to 35 wGA, for whom a risk scoring tool is currently used to determine palivizumab eligibility in Ontario; new risk factors could readily be added to such a tool. Regardless, these results suggest a child's living situation may pose unique barriers. Clinicians should pay special attention to educating parents and promoting the availability of palivizumab, especially in jurisdictions where offered free of charge.[27]

Given the unique, linked population-based data infrastructure in Ontario, we were able to investigate all RSV-related hospitalizations occurring among all children born in Ontario over a multiyear period, thereby reducing concerns regarding selection bias and loss to follow-up, while providing

TABLE 3 Adjusted PAF of RSV-Related Hospital Admissions and Laboratory-Confirmed ED Visits Occurring Before 3 Years of Age That Could be Prevented Among Ontario Infants

Characteristic	PAF	
	Hospital Admissions,[a] % (95% CI)	Hospital Admissions and Laboratory-Confirmed ED Visits,[a] % (95% CI)
Demographic factors		
Rural residence	15.8 (10.1 to 21.2)	−0.6 (−8.2 to 6.2)
Not geographically isolated	−0.5 (−0.8 to −0.3)	−0.4 (−0.8 to −0.2)
Mother's immigration status: Canadian born	−4.4 (−6.5 to −2.5)	−3.5 (−5.8 to −1.4)
Maternal history of social vulnerabilities[b]		
Child not apprehended at birth	0 (−0.2 to 0.2)	0 (−0.3 to 0.2)
Maternal age at birth: ≥40 y	35.5 (28.0 to 42.1)	35.0 (26.3 to 42.7)
No involvement with the criminal justice system	0.4 (0.2 to 0.6)	0.4 (0.2 to 0.6)
No history of experiencing homelessness	0 (−0.1 to 0.1)	0 (−0.1 to 0)
No mental health or addiction concerns	0.4 (0.1 to 0.8)	0.4 (0 to 0.8)
No history of violence and/or woman abuse	0 (−0.2 to 0.2)	0 (−0.2 to 0.2)
No use of low-income drug benefit programs	4.1 (2.2 to 5.9)	5.1 (3.0 to 6.9)
Area-level SES measures		
Material deprivation quintile: least deprived	3.4 (−3.0 to 9.3)	−4.0 (−12.2 to 3.5)
Dependency quintile: least dependent	2.5 (−1.8 to 6.6)	0.9 (−4.2 to 5.6)
Residential instability quintile: most stable	−1.5 (−7.2 to 3.8)	4.9 (−1.0 to 10.4)
Ethnic diversity quintile: most diverse	16.4 (12.5 to 20.1)	15.3 (10.6 to 19.6)
Income quintile: highest income	7.1 (0.3 to 13.3)	5.7 (−1.8 to 12.6)
Birth characteristics		
≥6 mo old during RSV season	45.5 (42.4 to 48.4)	38.3 (35.0 to 41.5)
Female sex	11.2 (9.4 to 13.0)	13.6 (11.5 to 15.5)
Singleton birth	−2.1 (−2.9 to −1.4)	−2.2 (−3.1 to −1.4)
Gestational age: 39–40 wGA	9.1 (5.4 to 12.4)	6.3 (1.8 to 10.2)
Birth wt: 3000–3499 g	4.3 (−0.4 to 8.6)	4.7 (−0.7 to 9.5)
Birth stay ≤4 d	5.7 (4.9 to 6.4)	5.4 (4.4 to 6.2)
Type of labor: spontaneous vaginal	4.4 (0.9 to 7.5)	4.9 (1.0 to 8.5)
No. siblings (at birth): none	41.6 (39.6 to 43.5)	37.7 (35.2 to 39.9)
Health status factors		
No diagnosis of a major congenital anomaly	2.6 (2.1 to 3.1)	2.4 (1.8 to 3.0)
No diagnosis of BPD	0.2 (0 to 0.3)	0.2 (0 to 0.3)
No diagnosis of hs-CHD	0 (−0.1 to 0.1)	0.1 (−0.1 to 0.1)
No diagnosis of trisomy 21	0.4 (0.4 to 0.5)	0.3 (0.2 to 0.3)

Adjusted for all factors in the table. The percentage of RSV-related admissions (or ED visits) prevented if the excess risk was eliminated (ie, if a given risk factor was set to the specified category for all children and all other variables were kept the same). Negative values indicate a percentage increase in admissions.

[a] Not mutually exclusive.

[b] Specific to the 2 y before birth unless otherwise noted.

sufficient sample size to investigate rare characteristics, such as maternal experiences with homelessness.[13] These data further allowed for a uniquely comprehensive investigation into novel social factors, which have received little attention in the RSV literature and, when studied, have largely been limited to maternal age and area-level income.[18,27] SES is a multifaceted concept extending beyond these 2 factors, and area-level measures are prone to ecological fallacy.[35] Critically, we were also able to uniquely investigate the impact of siblings, immigration, comorbidities, and delivery type.

Despite these strengths, there are some limitations to consider. Foremost, there are no provincial guidelines for RSV laboratory testing, and there are known biases in testing practices. In our primary analysis, we identified RSV-related admissions on the premise of both laboratory confirmation and a validated diagnostic algorithm.[23] Our secondary analysis was limited to the time period in which laboratory data were available, and we investigated a broader range of RSV outcomes (ie, RSV-related hospitalizations and laboratory-confirmed ED visits). These results were quantitatively comparable, suggesting robustness to testing biases. In contrast, previous studies have been limited to studying laboratory-confirmed RSV or, more broadly, bronchiolitis admissions.[12,36] A second limitation was the lack of available information regarding other important factors, such as tobacco smoke exposure, breastfeeding, and day care attendance. In addition, we could not identify children of Indigenous backgrounds, for whom the risk of RSV admissions is known to be substantially greater than the general population, particularly in remote communities.[16,26] Similarly, receipt of palivizumab cannot currently be ascertained through

TABLE 4 Adjusted PAF of RSV-Related Hospital Admissions and Laboratory-Confirmed ED Visits Occurring Before 3 y of Age That Could be Prevented Among Ontario Infants; Subgroup Analysis Among 24 870 Children Born 33–35 wGA

Characteristic	PAF Among Children Born 33–35 wGA[a]	
	Hospital Admissions,[b] % (95% CI)	Hospital Admissions and Laboratory-Confirmed ED Visits,[b] % (95% CI)
Demographic factors		
Rural residence	17.4 (−9.6 to 37.1)	−6.4 (−45.9 to 21.4)
Not geographically isolated	−0 (−1.0 to 0.4)	−0.2 (−2.2 to 0.4)
Mother's immigration status: Canadian born	−2.9 (−11.9 to 3.3)	−0.5 (−10.8 to 6.2)
Maternal history of social vulnerabilities[c]		
Child not apprehended at birth	−1.5 (−7.7 to 1.2)	−0.1 (−2.2 to 0.7)
Maternal age at birth: ≥40 y	25.2 (−10.0 to 48.6)	17.1 (−29.6 to 46.2)
No involvement with the criminal justice system	−0.3 (−1.8 to 0.5)	−0.1 (−2.2 to 0.7)
No history of experiencing homelessness	N/A	N/A
No mental health or addiction concerns	0.8 (−0.6 to 1.8)	0.8 (−0.7 to 1.9)
No history of violence/woman abuse	N/A	N/A
No use of low-income drug benefit programs	1.1 (−6.6 to 7.2)	1.2 (−10.0 to 9.3)
Area-level SES measures		
Material deprivation quintile: least deprived	0.6 (−30.9 to 23.3)	−7.0 (−46.9 to 20.4)
Dependency quintile: least dependent	−0.4 (−20.7 to 15.3)	−0.7 (−24.3 to 16.7)
Residential instability quintile: most stable	−11.4 (−40.2 to 10.3)	9.1 (−17.1 to 28.2)
Ethnic diversity quintile: most diverse	18.6 (1.1 to 31.8)	13.1 (−10.2 to 29.7)
Income quintile: highest income	11.3 (−19.6 to 33.0)	−10.7 (−53.4 to 18.4)
Birth characteristics		
≥6 mo old during RSV season	33.3 (17.9 to 45.4)	18.0 (0[d] to 32.2)
Female sex	6.8 (−2.2 to 14.5)	1.3 (−9.8 to 10.5)
Singleton birth	−10.7 (−18.9 to −4.0)	−10.0 (−19.9 to −2.2)
Birth wt: 3000–3499 g	−44.3 (−101.9 to −5.9)	−18.2 (−76.3 to 18.6)
Birth stay ≤4 d	21.8 (7.7 to 33.2)	18.0 (0.5 to 31.7)
Type of labor: spontaneous vaginal	−3.6 (−21.6 to 9.9)	0.3 (−19.4 to 14.5)
No. siblings (at birth): none	38.2 (27.8 to 46.2)	32.7 (18.5 to 43.0)
Clinical factors		
No diagnosis of a major congenital anomaly	6.6 (3.7 to 9.1)	4.3 (0.5 to 7.2)
No diagnosis of BPD	0.2 (0[d] to 0.3)	0.4 (0.3 to 0.4)
No diagnosis of hs-CHD	0.5 (−0.5 to 0.9)	0.7 (−0.2 to 1.1)
No diagnosis of trisomy 21	0.7 (0.2 to 0.9)	0.6 (−0.1 to 0.9)

[a] Including 632 children with ≥1 RSV-related hospital admissions and 472 with an RSV-related admission or laboratory-confirmed RSV ED visit (of 13 831 included children). Estimates are reported as N/A when the number of outcomes within a binary variable was <5. Adjusted for all factors in the table. Percentage of RSV-related admissions (or ED visits) prevented if the excess risk was eliminated (ie, if a given risk factor was set to the specified category for all children and all other variables were kept the same). Negative values indicate a percentage increase in admissions. N/A, not applicable.

[b] Not mutually exclusive.

[c] Specific to the 2 y before birth unless otherwise noted.

[d] Rounded up.

provincial health administrative data.[15] The children we have classified as palivizumab-eligible are those clearly meeting provincial criteria on the basis of prematurity and chronic health conditions, which are well-captured.[37] In addition, our ability to identify social vulnerability is limited to interactions with Ontario's publicly funded health care system and relies on maternal or institutional reports, resulting in under ascertainment; however, the increased health care use of expectant mothers and delivering mothers supports greater ascertainment of these characteristics through health administrative data.

As noted by others, we observed increased RSV admission rates among children living in lower-income and more economically deprived neighborhoods[20]; these effects were almost entirely diminished after controlling for factors related to transmission and disease severity, with the exception of children living in the lowest-income and least ethnically diverse neighborhoods. The latter result is surprising, given known social inequities affecting racialized populations.[19] These results may point to a healthy immigrant effect or relate to Canada's entry criteria, which favor skilled and highly educated immigrants.[38] This is further suggested by the lower admission rates observed among children born to immigrant and refugee mothers. Considering many of Ontario's most ethnically diverse neighborhoods are in metropolitan regions, this observation may be confounded by variables we were unable to adjust for or subject to biases in health care seeking behaviors and/or admission

practices. Albeit, given Canada's universal health care system, the latter may be less relevant.[19,20] A detailed investigation is required to determine the potential mechanisms underlying these protective effects and their generalizability.

CONCLUSIONS

With this study, we suggest preventive measures targeting young children and siblings could drastically reduce early-life hospitalizations for RSV. Although widespread recommendation of palivizumab is not feasible, vaccination strategies may effectively target these children. With these results, we highlight feasible targets for the improved delivering of, or future additions to, RSV prophylaxis programs and eligibility criteria. Factors related to a child's living situation could be realistically added to existing palivizumab recommendations, either independently, particularly for rare "exposures," or in combination with other criteria, such as prematurity. Critically, these results highlight the existence of social inequities in the transmission, severity, and/or uptake of RSV preventive measures, even within the context of Ontario's publicly funded health care system. Clinicians caring for young children should be mindful of these factors to ensure that parents of both medically and socially at-risk children are adequately educated regarding the severity of RSV illness and preventive measures, such as palivizumab.

ABBREVIATIONS

BPD: bronchopulmonary dysplasia
CI: confidence interval
DAD: Discharge Abstract Database
ED: emergency department
hs-CHD: hemodynamically significant congenital heart disease
ICD-10: *International Classification of Diseases, 10th Revision*
NACRS: National Ambulatory Care Reporting System
ODB: Ontario Drug Benefit
PAF: population attributable fraction
RR: rate ratio
RSV: respiratory syncytial virus
SES: socioeconomic status
wGA: weeks' gestational age

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Address correspondence to Astrid Guttmann, MDCM, MSc, ICES, G1 06, 2075 Bayview Ave, Toronto, ON Canada M4N 3M5. E-mail: astrid.guttmann@ices.on.ca

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