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Pre-birth cohort study of atopic dermatitis and severe bronchiolitis during infancy

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Abstract

Background: Infants hospitalized for bronchiolitis (i.e. severe bronchiolitis) are at increased risk of childhood asthma. There are many known risk factors for severe bronchiolitis, including cardiac and pulmonary diseases. Less is known about the association between atopic diseases and risk of severe bronchiolitis. We sought to further examine risk factors for severe bronchiolitis, focusing on atopic dermatitis (AD).

Methods: We conducted a nested cohort study within the Massachusetts General Hospital Obstetric Maternal Study (MOMS), a prospective cohort of pregnant women enrolled during

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Conflict of interest

Dr. Perlis has served on scientific advisory boards for, or received consulting fees from, Genomind, Healthrageous, Perfect Health, Pfizer, Proteus Biomedical, Psybrain, and RID Ventures. He receives royalties from Concordant Rater Systems (now UBC/Medco).

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1998–2006. Children of mothers enrolled in MOMS were included in the analysis if they received care within our health system (n = 5407). Potential risk factors for bronchiolitis and hospitalization data were extracted from the children's electronic health records; we also examined pregnancy and perinatal risk factors collected from the underlying MOMS data.

Results: During the first year of life, 125 infants (2.3%) had severe bronchiolitis. Eighteen of these patients had AD; 11 (61%) were diagnosed with AD prior to bronchiolitis hospitalization. In unadjusted analyses, AD was associated with severe bronchiolitis (χ^2 14.6;$p < 0.001$). In multivariable analyses adjusting for nine known risk factors for severe bronchiolitis, including demographics, birth season, disposition at birth, cardiac disease, maternal parity, and delivery mode, AD was associated with increased odds of severe bronchiolitis (odds ratio 2.72, 95% confidence interval 1.60–4.63).

Conclusions: Atopic dermatitis is significantly associated with severe bronchiolitis in infancy. The mechanism of the AD–bronchiolitis association is unclear and merits further study; this research may shed light on the pathogenesis of asthma.

Keywords

asthma; atopic dermatitis; birth season; bronchiolitis; congenital heart disease; eczema; respiratory syncytial virus; risk factors

Viral bronchiolitis is the most common cause of lower respiratory infection (LRI) in infancy, accounting for 18% of hospital admissions for infants <12 months old (1). While most infants have a mild course, approximately 2–3% (2, 3) of all infants require hospitalization for their bronchiolitis (hereafter referred to as severe bronchiolitis), making it a leading cause of hospitalization among infants (1, 2). Although bronchiolitis is a self-limiting disease, 30–50% of children with severe bronchiolitis will develop asthma by age 5 years (4).

There are several well-established risk factors for severe bronchiolitis, including young age (5–7), prematurity (5, 7), low birth weight (8), congenital heart disease (CHD) (5, 7), lung disease (7, 9), immunodeficiency (10), and birth during respiratory syncytial virus (RSV) season (11). Other risk factors for severe bronchiolitis, such as atopic dermatitis (AD) (12, 13), have been less established. Atopic diseases are common, with 10.7% of all United States children reporting a diagnosis of AD in the last 12 months (14). AD is a known risk factor for childhood asthma (15), but only two small studies have identified it as a risk factor for severe bronchiolitis (12, 13). We sought to confirm the association between AD and severe bronchiolitis in a large infant cohort.

Methods

Study design

We analyzed electronic health record (EHR) data collected on children born to mothers enrolled in a large prospective pre-birth cohort study of pregnant women, the Massachusetts General Hospital Obstetric Maternal Study (MOMS), which has been described in detail previously (16). Briefly, all women receiving prenatal care at Massachusetts General

Hospital or an affiliated health center between 1998 and 2006 were eligible for enrollment. Seventy percent of women approached consented to participate and were enrolled at their first prenatal visit (n = 9930); participants were similar to non-participants (16). Clinical data entered into the EHR at prenatal visits and delivery were subsequently used to populate the MOMS database (17).

We used the Partners HealthCare EHR to obtain clinical data on the children of the MOMS participants, generating a data mart using i2b2 server software (i2b2 v1.6.04, Boston, MA, USA). The Partners Human Research Committee approved the original study protocol as well as the present analysis.

For this study, children who were offspring of MOMS participants and who received health care at our institution comprised the analytic cohort. Inclusion criteria were having at least one healthcare encounter after birth but before age 1 year, and one healthcare encounter after age 1 year but before age 7 years in our EHR. A total of 5407 children met these inclusion criteria. We also examined all children of MOMS participants who delivered a live infant and for whom we could identify any medical record in our EHR (n = 8826). In a sensitivity analysis using the larger cohort, the main results were similar to those using the analytic cohort (Tables S1 and S2).

Exposure definition

We examined 21 exposures selected *a priori* as potentially related to the outcome of severe bronchiolitis. Sex, race/ethnicity, and insurance status at birth were obtained from the child's EHR. Diagnoses of relevant childhood health outcomes at age <1 year were also extracted from the children's EHR; these include any diagnosis of transient tachypnea of the newborn (ICD-9 770.6), AD (ICD-9 691.8), dermatitis due to food taken internally (ICD-9 693.1), or allergy to food (ICD-9 V15.01 – V15.05). A diagnosis of AD was made if a child had ≥2 billing codes for AD or dermatitis due to food taken internally, with the first code billed during the first year of life.

We also examined diagnoses of CHD (ICD-9 745.xx, 746.xx, or 747.xx), cystic fibrosis (ICD-9 277.0x), congenital anomalies of the respiratory system (ICD-9 748.xx), and immunodeficiency (ICD-9 279.0x, 279.1x, 279.2x, or 279.3x) that a child received at any time. A diagnosis of CHD was made if a child had ≥3 billing codes for CHD to exclude the possibility that the child received an initial (rule-out) evaluation. Gestational age, birth weight, multiple gestation, neonatal intensive care unit (NICU) admission after birth, maternal parity, years of maternal education, median maternal age at first prenatal visit, maternal smoking during pregnancy, and mode of delivery were obtained from the mothers' charts as part of the original MOMS data collection, or by chart review. Maternal history of asthma was diagnosed if the mother received ≥3 billing codes (ICD-9 493.xx) for asthma ever. In cases where information was available in both the child's chart and the MOMS database, information was reviewed for concordance, with clarification by chart review by one of the authors, Dr. Balekian, as needed.

Outcome definition

Given the known variability in diagnostic labeling for bronchiolitis hospitalizations (18), severe bronchiolitis was defined as hospital admission at age <1 year for a non-bacterial acute LRI and was extracted from the children's EHR. Children billed for bronchiolitis (ICD-9 466.xx), RSV (ICD-9 079.6), viral pneumonia (ICD-9 480.x), asthma (ICD-9 493.xx), or wheezing (ICD-9 786.07) from an inpatient location at age <1 year were considered to have severe bronchiolitis.

Statistical analyses

All statistical analyses were performed using StataSE 14 (Stata Corp, College Station, TX, USA). Data are presented as proportions with 95% confidence intervals (95% CIs) and medians with interquartile ranges (IQR). Unadjusted analyses of the potential risk factors for severe bronchiolitis were conducted using chi-square test, Fisher's exact test, or Mann–Whitney *U*-test, as appropriate. All p-values were two-tailed, with $p < 0.05$ considered statistically significant.

Next, we performed multivariable logistic regression to investigate independent risk factors of bronchiolitis, with generalized estimating equations to account for multiple births per mother. We did not differentiate between twin births and other births from the same mother. Variables were tested for inclusion in the model if they were found to be associated with the outcome in unadjusted analyses ($p < 0.20$) or were considered clinically relevant to the authors. In sensitivity analyses, we examined the potential impact of including additional covariates. In the final regression model, results are reported as odds ratios (ORs) with 95% CIs.

Results

Of the children of mothers enrolled in MOMS, 5407 children born to 4660 mothers met inclusion criteria. Children included in the analytic cohort were more likely to be older at admission, non-white, and have public insurance. Their mothers were more likely to be younger, less educated, and have asthma (see Tables S3 and S4). During the first year of life, 125 were admitted to the hospital for bronchiolitis (2.3%). Overall, 52% of the children in our cohort were male; 55% were white, and 63% had private insurance. The median age at severe bronchiolitis was 3.9 months old (IQR 1.9–7.9 months old). The cohort included 338 children with AD (6.3%). Eighteen patients with AD had severe bronchiolitis; 11 (61%) were diagnosed with AD prior to bronchiolitis hospitalization.

Table 1 shows unadjusted associations between patient characteristics and severe bronchiolitis. Compared to children who were not admitted for bronchiolitis, children with severe bronchiolitis were more likely to be male, non-white, and publicly insured. Children with severe bronchiolitis were more likely to be very premature (<32 weeks of gestation), to have low (<2000 g) or high (≥4000 g) birth weight, to be born in the fall or winter, or to have required NICU admission after birth. Children with severe bronchiolitis were also more likely to have been diagnosed with AD during infancy, to have CHD, cystic fibrosis, or immunodeficiency. The number of patients with a diagnosis of food allergy was too small

for meaningful analysis (n = 5 in the analytic cohort). Table 2 shows unadjusted associations between maternal characteristics and severe bronchiolitis.

In the multivariable logistic regression model of severe bronchiolitis (nine variables with 15 terms), the statistically significant risk factors were male sex, fall or winter birth, NICU admission after birth, AD, CHD, and multiparity (Table 3). AD was associated with almost threefold increased odds of severe bronchiolitis (OR 2.72, 95% CI 1.60–4.63). In sensitivity analysis, we substituted birth weight and gestational age for two other factors in the model, and the AD finding did not significantly change (data not shown).

Discussion

In this analysis of 5407 children born to mothers in the MOMS cohort (16), we found that 2.3% were admitted to our institution for bronchiolitis during infancy. This proportion matches the reported 2–3% admission rate for bronchiolitis during infancy (2, 3). This pre-birth cohort provided a unique data set, because it included prospectively collected maternal pregnancy data, along with EHR data from >5000 offspring. Accordingly, we were able to confirm many known risk factors for severe bronchiolitis, and also to investigate the role of less well-studied factors, such as AD, which was significantly related to the severe bronchiolitis outcome.

The diagnostic labeling of non-bacterial LRI varies greatly. In a multicenter study of young children who presented to an emergency department with LRI symptoms, the assigned diagnoses included bronchiolitis, RSV, viral pneumonia, asthma, and wheezing (18). Although all children had likely bronchiolitis (per attending physician of record), only 67% of children received an initial primary diagnosis of bronchiolitis from the emergency department. Thus, identification of severe bronchiolitis using diagnostic codes improves when including these alternate diagnoses.

Established risk factors for severe bronchiolitis include premature birth and comorbid medical conditions, such as CHD, lung disease, and immunodeficiency (5, 7, 9, 10). In both unadjusted and multivariable analyses, we also found a significant association between the diagnosis of CHD and bronchiolitis. Interestingly, we found that this association was of greater magnitude when the patient had multiple billing diagnoses for CHD. We believe that infants may have received one or two diagnoses of CHD for a less significant cardiac issue; they may have received a diagnostic code when being ‘ruled-out’ for CHD; or they may have been miscoded. Indeed, there are limitations in the ICD-9 coding of CHD, with misclassification of defects common (19). In unadjusted analyses, we confirmed the expected elevation in odds of severe bronchiolitis among those with cystic fibrosis or immunodeficiency; however, the small numbers (n < 10) precluded further analysis.

By contrast, we found that AD, which affected 6.3% of infants, was significantly associated with severe bronchiolitis in both unadjusted and multivariable analyses. Among the 18 patients with AD and severe bronchiolitis, 11 (61%) received a diagnosis of AD prior to the index hospitalization. While AD is a known risk factor for childhood asthma (15), only two small studies have identified it as a risk factor for severe bronchiolitis (12, 13). The earliest

description of an association between AD and severe bronchiolitis comes from Laing et al. in 1982 (13). They compared 31 hospitalized bronchiolitis cases to 32 hospitalized controls and found that 32% of cases had a history of eczema compared to only 9% of controls ($p < 0.05$). More recently, Al-Shehri et al. (12) compared AD in severe bronchiolitis (n = 51) vs. outpatient bronchiolitis (n = 115) in children under 5 years old and found an adjusted OR of 4.75.

One possible mechanism for the association of AD and severe bronchiolitis is through vitamin D status. Vitamin D deficiency has been associated with increased prevalence and severity of AD (20, 21). Additionally, studies have found that lower serum 25(OH)D levels are associated with more severe LRI (22, 23). Higher cord blood levels of 25(OH)D have been identified in mothers who gave birth in the summer months (22), which may also explain the seasonal association that we found between birth month and severe bronchiolitis. Blood was not collected from infants, so we were unable to examine vitamin D status.

Another possible mechanism of the AD–bronchiolitis association is through an altered epithelial barrier. Cadherins are cell surface proteins that participate in calcium-dependent cell adhesion. Variants in protocadherin-1 (PCDH1), a member of the cadherin superfamily of proteins, have been found to be associated with eczema, bronchial hyper-responsiveness, and asthma (24, 25). Cadherin-related family member 3 (CDHR3) was recently found to be the binding site for rhinovirus C (26), a viral cause of bronchiolitis, as well as a frequent cause of wheezing and asthma exacerbation. It remains unclear whether infants with a history of AD and severe bronchiolitis are more likely to develop persistent wheezing or asthma in the future.

Although maternal smoking during pregnancy and maternal asthma are previously reported risk factors for severe bronchiolitis (27), we did not find these associations in our cohort. One explanation is that maternal asthma status was obtained through diagnostic codes, possibly leading to misclassification. Maternal smoking status, however, was obtained directly from the EHR, although there may have been reporting bias. While a modest association (incidence rate ratio 1.11) between elective cesarean delivery and severe bronchiolitis was found in a large (n > 200,000) Australian cohort (28), we did not find this association in our Boston cohort. While the Australian cohort had excellent statistical power for the available variables, the study lacked data on many possible risk factors for severe bronchiolitis, including CHD and AD; the latter was the primary focus of our analysis.

Our study has some possible limitations. One limitation is the potential for missing cases of bronchiolitis (e.g. a child may have been admitted for bronchiolitis at another institution). We attempted to minimize this bias by only including children in the cohort who had one or more visits to our institution before and after 1 year of age, and thus, would have been more likely to be admitted to our hospital. Moreover, we were reassured by the 2.3% prevalence of admission, which is concordant with the published prevalence of 2–3% admission in the first year of life (2, 3). Another limitation is that many risk factors were obtained from the EHR. In many instances, ICD-9 codes were used to make diagnoses, which may lead to over- or underreporting of certain conditions. To account for potential overreporting of certain diagnoses, such as CHD, a child was only considered to have the disease if he/she had more

than two billing diagnoses in the past. Third, not all primary care providers in our hospital's catchment area share our EHR or billing system, and it is possible that some infants had exposures that were not captured by billing codes at our institution. However, we are confident in the associations observed, as missing diagnosis codes should bias associations toward the null. Finally, we cannot yet infer causality for the AD–bronchiolitis association given the observational nature of the data and because the exposure (AD) did not always precede the outcome (bronchiolitis). However, AD has a relapsing and remitting course, and infants can have varying stages of disease when presenting for medical evaluation.

In summary, we identified several risk factors for severe bronchiolitis during infancy. While some risk factors, such as CHD, are well established, we also identified less established risk factors for disease, such as AD. Further research will be helpful in elucidating the mechanism of this association – whether vitamin D, the epithelial barrier, or another factor – and could point the way toward helpful interventions. Likewise, future research might also examine the clinical impact of having both conditions – e.g. are children with both AD and severe bronchiolitis at even higher risk of developing childhood asthma? If yes, such findings would shed important light on the pathogenesis of asthma.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

AD	atopic dermatitis
CI	confidence interval
CHD	congenital heart disease
EHR	electronic health record
IQR	interquartile range
LRI	lower respiratory infection
MOMS	Massachusetts General Hospital Obstetric Maternal Study
NICU	neonatal intensive care unit
OR	odds ratio
RSV	respiratory syncytial virus

References

1. Hasegawa K, Tsugawa Y, Brown DF, Mansbach JM, Camargo CA Jr. Trends in bronchiolitis hospitalizations in the United States, 2000–2009. Pediatrics 2013: 132: 28–36. [PubMed: 23733801]
2. Shay DK, Holman RC, Newman RD, Liu LL, Stout JW, Anderson LJ. Bronchiolitis-associated hospitalizations among US children, 1980–1996. JAMA 1999: 282: 1440–6. [PubMed: 10535434]
3. Boyce TG, Mellen BG, Mitchel EF Jr, Wright PF, Griffin MR. Rates of hospitalization for respiratory syncytial virus infection among children in medicaid. J Pediatr 2000: 137: 865–70. [PubMed: 11113845]
4. Singh AM, Moore PE, Gern JE, Lemanske RF Jr, Hartert TV. Bronchiolitis to asthma: a review and call for studies of gene-virus interactions in asthma causation. Am J Respir Crit Care Med 2007: 175: 108–19. [PubMed: 17053206]
5. Purcell K, Fergie J. Driscoll Children's Hospital respiratory syncytial virus database: risk factors, treatment and hospital course in 3308 infants and young children, 1991 to 2002. Pediatr Infect Dis J 2004: 23: 418–23. [PubMed: 15131464]
6. Mansbach JM, Piedra PA, Stevenson MD, et al. Prospective multicenter study of children with bronchiolitis requiring mechanical ventilation. Pediatrics 2012: 130: e492–500. [PubMed: 22869823]
7. Wang EE, Law BJ, Stephens D. Pediatric Investigators Collaborative Network on Infections in Canada (PICNIC) prospective study of risk factors and outcomes in patients hospitalized with respiratory syncytial viral lower respiratory tract infection. J Pediatr 1995: 126: 212–9. [PubMed: 7844667]
8. Hasegawa K, Pate BM, Mansbach JM, et al. Risk factors for requiring intensive care among children admitted to ward with bronchiolitis. Acad Pediatr 2015: 15: 77–81. [PubMed: 25528126]
9. Groothuis JR, Gutierrez KM, Lauer BA. Respiratory syncytial virus infection in children with bronchopulmonary dysplasia. Pediatrics 1988: 82: 199–203. [PubMed: 3399292]
10. Hall CB, Powell KR, MacDonald NE, et al. Respiratory syncytial viral infection in children with compromised immune function. N Engl J Med 1986: 315: 77–81. [PubMed: 3724802]
11. Lanari M, Prinelli F, Adorni F, et al. Risk factors for bronchiolitis hospitalization during the first year of life in a multicenter Italian birth cohort. Ital J Pediatr 2015: 41: 40. [PubMed: 26006025]
12. Al-Shehri MA, Sadeq A, Quli K. Bronchiolitis in Abha, Southwest Saudi Arabia: viral etiology and predictors for hospital admission. West Afr J Med 2005: 24: 299–304. [PubMed: 16483044]
13. Laing I, Reidel F, Yap PL, Simpson H. Atopy predisposing to acute bronchiolitis during an epidemic of respiratory syncytial virus. Br Med J (Clin Res Ed) 1982: 284: 1070–2.
14. Shaw TE, Currie GP, Koudelka CW, Simpson EL. Eczema prevalence in the United States: data from the 2003 National Survey of Children's Health. J Invest Dermatol 2011: 131: 67–73. [PubMed: 20739951]
15. Neuman A, Bergstrom A, Gustafsson P, et al. Infant wheeze, comorbidities and school age asthma. Pediatr Allergy Immunol 2014: 25: 380–6. [PubMed: 24720853]
16. Wolf M, Kettyle E, Sandler L, Ecker JL, Roberts J, Thadhani R. Obesity and preeclampsia: the potential role of inflammation. Obstet Gynecol 2001: 98: 757–62. [PubMed: 11704165]
17. Faupel-Badger JM, Staff AC, Thadhani R, et al. Maternal angiogenic profile in pregnancies that remain normotensive. Eur J Obstet Gynecol Reprod Biol 2011: 158: 189–93. [PubMed: 21641103]
18. Mansbach JM, Espinola JA, Macias CG, Ruhlen ME, Sullivan AF, Camargo CA Jr. Variability in the diagnostic labeling of nonbacterial lower respiratory tract infections: a multicenter study of children who presented to the emergency department. Pediatrics 2009: 123: e573–81. [PubMed: 19273503]
19. Strickland MJ, Riehle-Colarusso TJ, Jacobs JP, et al. The importance of nomenclature for congenital cardiac disease: implications for research and evaluation. Cardiol Young 2008: 18(Suppl. 2): 92–100. [PubMed: 19063779]
20. Camargo CA Jr, Ganmaa D, Sidbury R, Erdenedelger K, Radnaakhand N, Khandsuren B. Randomized trial of vitamin D supplementation for winter-related atopic dermatitis in children. J Allergy Clin Immunol 2014: 134: 831–5.e1. [PubMed: 25282565]

21. Oren E, Banerji A, Camargo CA Jr. Vitamin D and atopic disorders in an obese population screened for vitamin D deficiency. J Allergy Clin Immunol 2008: 121: 533–4. [PubMed: 18177693]

22. Belderbos ME, Houben ML, Wilbrink B, et al. Cord blood vitamin D deficiency is associated with respiratory syncytial virus bronchiolitis. Pediatrics 2011: 127: e1513–20. [PubMed: 21555499]

23. McNally JD, Leis K, Matheson LA, Karuananyake C, Sankaran K, Rosenberg AM. Vitamin D deficiency in young children with severe acute lower respiratory infection. Pediatr Pulmonol 2009: 44: 981–8. [PubMed: 19746437]

24. Faura Tellez G, Nawijn MC, Koppelman GH. Protocadherin-1: epithelial barrier dysfunction in asthma and eczema. Eur Respir J 2014: 43: 671–4. [PubMed: 24585862]

25. Koning H, Postma DS, Brunekreef B, et al. Protocadherin-1 polymorphisms are associated with eczema in two Dutch birth cohorts. Pediatr Allergy Immunol 2012: 23: 270–7. [PubMed: 21929597]

26. Bochkov YA, Watters K, Ashraf S, et al. Cadherin-related family member 3, a childhood asthma susceptibility gene product, mediates rhinovirus C binding and replication. Proc Natl Acad Sci U S A 2015: 112: 5485–90. [PubMed: 25848009]

27. Carroll KN, Gebretsadik T, Griffin MR, et al. Maternal asthma and maternal smoking are associated with increased risk of bronchiolitis during infancy. Pediatrics 2007: 119: 1104–12. [PubMed: 17545377]

28. Moore HC, de Klerk N, Holt P, RichmondPC, Lehmann D. Hospitalisation for bronchiolitis in infants is more common after elective caesarean delivery. Arch Dis Child 2012: 97: 410–4. [PubMed: 22039179]

Table 1

Child characteristics of the child cohort, by bronchiolitis outcome (n = 5407)

Child characteristics	Inpatient bronchiolitis (n = 125) n (%)	No inpatient bronchiolitis (n = 5282) n (%)	p-value
Median age (months) at diagnosis of bronchiolitis (IQR)	3.9 (1.9–7.9)	–	–
Male sex	82 (65.6)	2737 (51.8)	0.002
Race/Ethnicity			0.050
White	56 (44.8)	2928 (55.4)	
Black	11 (8.8)	274 (5.2)	
Hispanic	20 (16.0)	614 (11.6)	
Other	38 (30.4)	1466 (27.8)	
Insurance status *			0.007
Private	63 (50.4)	3330 (63.0)	
Public	59 (47.2)	1770 (33.5)	
Other	3 (2.4)	182 (3.5)	
Gestational age, weeks			0.002
<32	7 (5.6)	58 (1.1)	
32–36	8 (6.4)	388 (7.4)	
≥37	110 (88.0)	4836 (91.6)	
Birth weight, g			0.04
<2000	7 (5.6)	119 (2.3)	
2000–3999	100 (80)	4522 (85.6)	
≥4000	18 (14.4)	641 (12.1)	
Multiple gestation	5 (4)	233 (4.4)	1.00
Season of birth			<0.001
Fall	43 (34.4)	1215 (23.0)	
Winter	39 (31.2)	1216 (23.0)	
Spring	26 (20.8)	1501 (28.4)	
Summer	17 (13.6)	1350 (25.6)	
Infant disposition at birth			<0.001
NICU	18 (14.4)	251 (4.8)	
Nursery/NICU triage	72 (57.6)	3642 (69.0)	
Unknown	35 (28)	1389 (26.3)	
Transient tachypnea of the newborn	9 (7.2)	244 (4.6)	0.18
Atopic dermatitis before age 1 year †	18 (14.4)	319 (6.0)	<0.001
Congenital heart disease	21 (16.8)	133 (2.5)	<0.001
Cystic fibrosis	5 (4)	65 (1.2)	0.02
Congenital anomaly of the respiratory system	3 (2.4)	33 (0.6)	0.050
Immunodeficiency	3 (2.4)	32 (0.6)	0.046

IQR, interquartile range; NICU, neonatal intensive care unit.

*At birth.

†n = 5406.

Table 2

Maternal characteristics of the child cohort, by bronchiolitis outcome (n = 5407)

Maternal characteristics	Inpatient bronchiolitis (n = 125) n (%)	No inpatient bronchiolitis (n = 5282) n (%)	p-value
Multiparity	85 (68)	2595 (49.1)	<0.001
Education < 12 years	42 (33.6)	1263 (23.9)	0.01
Median age at first prenatal visit (IQR)	29.4 (23.2–34.1)	30.6 (25.6–34.5)	0.045
Smoking during pregnancy			
Never smoked or quit smoking	112 (89.6)	4923 (93.2)	0.12
Current smoker	13 (10.4)	359 (6.8)	
Mode of delivery			
Vaginal	89 (71.2)	3787 (71.7)	0.90
Cesarean section	36 (28.8)	1495 (28.3)	
Asthma*	18 (14.4)	581 (11.0)	0.23

IQR, interquartile range.

* n = 5402.

Table 3

Multivariable logistic regression model of risk factors for severe bronchiolitis (n = 125 cases in cohort of 5406 infants)

Variable	Odds ratio (95% CI)	p-value
Male	1.85 (1.24–2.76)	0.002
Race/Ethnicity		
White	Reference	
Black	1.46 (0.71–3.03)	0.31
Hispanic	1.18 (0.62–2.24)	0.61
Other	0.95 (0.56–1.51)	0.82
Insurance status*		
Private	Reference	
Public	1.50 (0.97–2.34)	0.07
Other	0.78 (0.23–2.67)	0.69
Season of birth		
Summer	Reference	
Fall	2.78 (1.51–5.10)	0.001
Winter	2.65 (1.43–4.91)	0.002
Spring	1.36 (0.71–2.59)	0.35
Infant disposition at birth		
Nursery/NICU triage	Reference	
NICU	2.45 (1.26–4.77)	0.008
Unknown	1.20 (0.79–1.82)	0.39
Atopic dermatitis before age 1 year	2.72 (1.60–4.63)	<0.001
Congenital heart disease	7.25 (3.92–13.39)	<0.001
Parity		
Primiparous	Reference	
Multiparous	2.30 (1.55–3.41)	<0.001
Delivery mode		
Vaginal	Reference	
Cesarean section	0.87 (0.56–1.33)	0.52

NICU, neonatal intensive care unit.

*At birth.