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MECHANISMS



Association between early childhood lower respiratory tract infections and subsequent asthma

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ABSTRACT

Objective: We examined the relationship between recurrent lower respiratory tract infections (LRTI) in young children and subsequent childhood asthma outcomes.

Methods: Retrospective cohort study using 2009–2017 Colorado All Payer Claims Database to assess 0- to 2-year-old children with visits due to LRTI and acute gastroenteritis (AGE). The primary exposure was number of LRTI visits prior to 2 years of age. Children with AGE served as the no LRTI comparator group. The primary outcome was incident asthma, defined by ICD-9 (490.XX) or ICD-10 (J45.9XX) codes, in the same children between 3 and 9 years of age. Multivariable accelerated failure time (AFT) models were used to estimate the effect of LRTI visits on median time to asthma diagnosis. Sensitivity analyses were performed using more conservative asthma diagnostic criteria and with hospitalized children only.

Results: Of 38,441 eligible subjects, 32,729 had ≥ 1 LRTI and 5,712 had AGE (no LRTI) between 0 and 2 years of age. Children with ≥ 3 LRTI visits had an 80% decrease in median time to asthma diagnosis relative to those with AGE visits only (time ratio [TR] 0.2; 95% CI 0.16, 0.24). Children with ≥ 3 LRTI hospitalizations had a 98% reduction in median time to asthma diagnosis relative to those with AGE hospitalizations only (TR 0.02; 95% CI 0.01, 0.07). History of atopy, wheezing, and family history of asthma documented prior to 2 years of age were also associated with earlier asthma diagnosis.

Conclusions: Recurrent LRTIs, especially LRTI hospitalizations, before 2 years of age are associated with earlier diagnosis of pediatric asthma.

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Introduction

In the USA, asthma is the most common chronic childhood condition affecting more than 6 million children and leading to 200 000 hospitalizations per year (1). The annual cost of treating pediatric asthma is approximately 6 billion dollars and cost of care is substantially higher in patients with poorly controlled asthma (2,3). Timely identification of young children at risk for developing asthma can reduce asthma-related morbidity and health care expenditures (4,5).

Lower respiratory tract infections (LRTI) in children under 2 years of age account for many pediatric healthcare visits (6–9) and are associated with elevated risk of subsequent childhood asthma (10–14). However, these studies primarily assess subsequent asthma risk

based on the presence or absence of the LRTI exposure, rather than the cumulative number of exposures. One exception is a German birth cohort study that examined the impact of multiple early childhood infectious diseases, including LRTIs, on the development of asthma up to school age (15). In this study, children under 3 years of age with multiple LRTIs were significantly more likely to be diagnosed with asthma by 7 years of age than children with ≤ 1 LRTI. The study did not distinguish risk for children with LRTI hospitalizations from those with less severe clinical events.

In the present study, we used the Colorado All Payer Claims Database (CO APCD) to further assess the impact of repeated LRTI visits under 2 years of

age on time to asthma diagnosis after 3 years of age. We hypothesized that an increasing number of LRTI episodes in early childhood would be associated with earlier time to initial asthma diagnosis. We separately tested this hypothesis in children with LRTI-associated hospitalizations to provide evidence on patients with more clinically severe diseases. The results of this study may more comprehensively inform clinical care and future research to prevent or delay the onset of pediatric asthma.

Methods

This was a retrospective cohort study using 2009–2017 administrative claims from the CO APCD, administered by the Center for Improving Value in Health Care (CIVHC). The CO APCD is a comprehensive source of health care insurance claims information representing most insured Coloradans (approximately 70%) across commercial health insurance plans, Medicare and Health First Colorado (Colorado's Medicaid program) (16). The CO APCD includes administrative claims from over 40 payers for approximately 4.5 million unique patients of whom approximately 25% are children 0–18 years of age. The University of Colorado Institutional Review Board exempted this study from human subjects review.

Study population

From the CO APCD Database, we selected children with any LRTI or acute gastroenteritis (AGE) claims before 2 years of age. Children with AGE were included to provide a comparator group of children with no LRTI claims for all analyses. AGE was selected for this purpose as it is a common cause of early childhood illness with no known association with subsequent asthma (15).

LRTI was defined using the *International Classification of Diseases, Ninth and Tenth Revision, Clinical Modification* (ICD-9-CM; ICD-10-CM) diagnosis codes previously derived by Nakamura et al. (see accompanying data supplement for relevant diagnosis codes) (9,17). LRTI claims include those for viral bronchiolitis and bacterial pneumonia, both of which have known associations with childhood asthma (18,19) and are often conflated in young children with respiratory illness (20). The AGE group comprised ICD-9 and ICD-10 codes for acute infectious gastroenteritis (21).

We excluded children with underlying complex chronic conditions (CCCs) using Feudtner's algorithm

(22), children with an asthma diagnosis prior to 3 years of age, and those with no administrative claims after 3 years of age. CCCs include conditions expected to last at least 12 months and to involve multiple organ systems or 1 organ system severely enough to require specialty pediatric care and/or hospitalization in a tertiary care center. Examples of respiratory CCCs include cystic fibrosis and chronic lung disease. Children with an asthma diagnosis prior to 3 years of age were excluded to eliminate overlap between exposure and outcome and to provide a 1-year washout period to minimize misclassification (i.e. misclassifying children with preschool wheezing as having asthma). Those with no claims after age 3 years were excluded as it would be impossible to assess their outcomes.

Exposures and outcomes

The primary exposure was number of LRTI visits in any clinical setting in children prior to 2 years of age, categorized as 0, 1, 2, or ≥ 3 LRTI visits. The latter category (≥ 3 LRTI) was included as enough children ($N=2,041$) with ≥ 3 LRTI visits claims were identified in the primary cohort to make this a clinically relevant group to evaluate. LRTI claims were required to be at least 7 days apart to avoid counting a single illness twice. Children with AGE and without LRTI claims served as the comparator group. Children with both LRTI and AGE claims were included in the LRTI group.

The primary outcome was incident asthma in children after age 3 years, defined by an ICD-9 (490.XX) or ICD-10 (J45.9XX) diagnosis code. The upper age of 9 years was imposed by the limited longitudinal duration of the dataset. As an additional means to reduce the likelihood of misclassification biases, we performed a sensitivity analysis using more conservative diagnostic criteria for asthma based on previous administrative claims studies (23–25). For this sensitivity analysis, we defined asthma as the occurrence of either (1) persistent asthma or (2) asthma exacerbation using Healthcare Effectiveness Data and Information (HEDIS) criteria, with some overlap between the definitions. Per HEDIS, persistent asthma was defined as the occurrence within any 12-month period of at least one of the following: one or more inpatient or emergency department (ED) visits with asthma as the primary diagnosis; four or more prescription claims for any asthma medication (inhaled beta-agonist, controller medication, oral corticosteroids); or four or more outpatient visits with asthma listed as one of the diagnoses, and 2 or more asthma

prescription claims. Asthma exacerbation was defined as one or more inpatient or ED visits with asthma as the primary diagnosis; a cluster of two visits within 14 days, one of which is an outpatient visit with primary diagnosis of asthma and one is a visit in any setting with diagnosis of asthma (primary diagnosis or otherwise); a diagnosis code for asthma exacerbation using the ICD-9 or 10 code; or prescription claim for systemic corticosteroid within 3 days of any visit with an asthma diagnosis (primary diagnosis or otherwise). Prescription claims categories were derived from HEDIS National Drug Codes (26). Only prescriptions filled after 3 years of age were used for this purpose, and the date of persistent asthma or asthma exacerbation was taken as the date the last criteria was met for a subject.

Covariates

Covariates included variables with known or potential association with asthma, including gender, race, ethnicity, history of prematurity, family history of asthma, history of wheezing, and presence of atopy (11). Asthma family history, wheezing and prematurity were defined by available ICD-9 and -10 codes within the dataset (Appendix A). Atopy was characterized through ICD-9 and -10 diagnosis codes into separate categories of food allergy, atopic dermatitis, allergic rhinitis, or allergic reaction/anaphylaxis (Appendix A). We examined exposure to 0, 1, 2, or ≥ 3 atopic categories before 2 years of age. While wheezing can be associated clinically with both LRTI and asthma, it is a distinct diagnostic code found in the dataset exclusive of the asthma and LRTI diagnostic codes. As recurrent early childhood wheeze is predictive of asthma, we included this covariate in the analysis.

Claims informing clinical covariates were derived only from the 0- to 2-year-old cohort to mimic the availability of such data for risk assessment through 2 years of age.

Analysis

Bivariate associations were assessed using chi-square tests. Multivariable accelerated failure time (AFT) and Cox proportional hazards (PH) regression models were used to examine the effect of number of LRTI visits prior to 2 years of age on time to asthma diagnosis after 3 years of age, with children with AGE but without LRTI claims serving as the reference group. AFT models can be used to analyze time to event data to estimate the effects of covariates on

acceleration or deceleration of the survival time, and do not require the PH assumption to hold. From a clinical perspective, the AFT model has the advantage of being easier to interpret than comparable Cox PH models (27). The group estimated (adjusted) ratio of geometric means, or time ratio (TR) (28), is interpreted as the ratio of the median survival time between exposed and unexposed groups.

For the AFT model, distributional assumptions (exponential, lognormal, gamma, Weibull, and log-logistic) were assessed with goodness-of-fit plots based on cumulative hazard and Cox-Snell residual plots. For the Cox model, the PH assumption was assessed using Schoenfeld residuals and interactions with time.

Covariates chosen *a priori* included gender, race, ethnicity, presence of atopic category, and wheezing claims 0–2 years of age. Covariates effects were presented as TRs. Sensitivity analyses included (1) use of more conservative criteria for asthma (presence of persistent asthma or asthma exacerbation), (2) restricting to hospitalized visits for LRTI or AGE, and (3) combination of hospitalized with LRTI or AGE and conservative criteria for asthma.

Data were analyzed using SAS version 9.4 software. All statistical tests were two-sided with a level of significance of 0.05.

Results

During the study period, claims were recorded for 71 090 unique children <2 years of age. After exclusions, the final cohort included 38 441 patients with either LRTI or AGE claims, of whom 32 729 (85%) had ≥ 1 LRTI claim and 5,712 (15%) had an AGE claim without any LRTI claims (Figure 1). Patients were predominantly male (54%) and insured by Medicaid (77%).

Of children with LRTI, 25 176 (65.5%) had 1 claim, 5,512 (14.3%) had 2 claims, and 2,041 (5.3%) had ≥ 3 claims. In the hospitalized cohort, 3,631 (90%) had 1 claim, 186 (4.6%) had 2 claims, and 21 (0.5%) had ≥ 3 claims (for hospital admissions). For both the primary cohort and hospitalized cohort, children with ≥ 1 LRTI visits prior to 2 years of age were more likely to have a family history of asthma, wheezing prior to 2 years of age, and asthma between 3 and 9 years of age, than children with AGE and no LRTI visits (Tables 1 and 2).

The primary cohort prevalence of asthma between 3 and 9 years of age was 18.2% (outcome defined as any asthma ICD-9 or -10 code) and 12.9% (outcome defined as persistent asthma or asthma exacerbation).

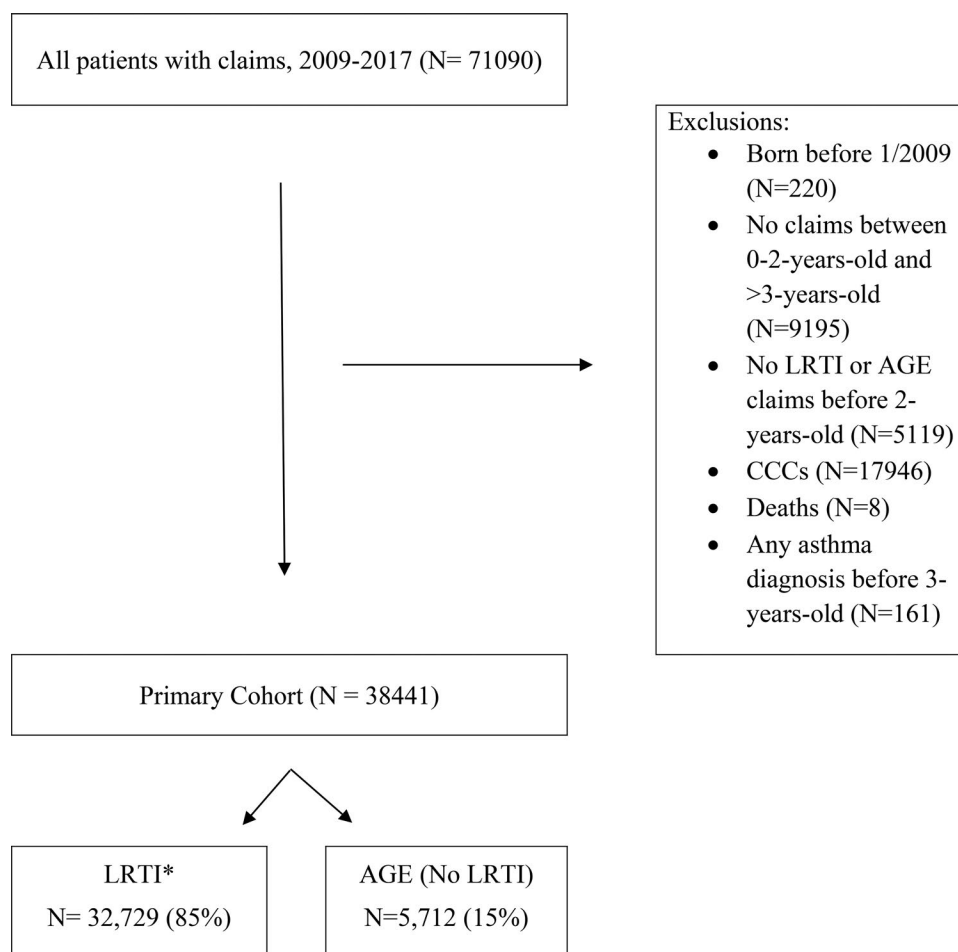


Figure 1. Patient cohort.*Patients with both LRTI and AGE claims were included in the LRTI group. CCCs, complex, chronic conditions; LRTI, lower respiratory tract infection; AGE, acute gastroenteritis.

Cox PH regression models were fit to the data initially but showed significant violations of the PH assumption, so results are not presented here. In multivariable AFT regression analysis, transformation of the hazard function had a linear relationship with log time and Cox-Snell residuals followed the referent line, both features indicating a good fit of the log-normal AFT model to the data. After adjusting for other covariates, increasing number of LRTI exposures before 2 years of age was associated with decreased median time to asthma diagnosis after 3 years of age (Table 3). In the primary cohort, children with 2 LRTI visits had a 66% reduction in median time to asthma diagnosis relative to those with AGE visits only (TR 0.34; 95% CI 0.30, 0.40); those with ≥ 3 LRTI visits had an 80% reduction in median time to asthma diagnosis relative to those with AGE visits only (TR 0.20; 95% CI 0.16, 0.24). Children with 2 LRTI hospitalizations had a 90% reduction in median time to asthma diagnosis relative to those with AGE hospitalizations only (TR 0.10; 95% CI 0.05, 0.21); those with ≥ 3 LRTI hospitalizations had a 98% reduction

in median time to asthma diagnosis relative to those with AGE hospitalizations only (TR 0.02; 95% CI 0.01, 0.07).

In the primary cohort, 78.6% of children with AGE, 50.4% of children with 2 LRTI, and 46.4% of children with ≥ 3 LRTI remained asthma-free by 9 years of age (Figure 2). In the hospitalized cohort, 90.5% of children with AGE, 49.8% of children with 2 LRTI, and 9.5% of children with ≥ 3 LRTI remained asthma-free by 5 years of age (Figure 2).

Children with atopic exposures, history of wheezing, and documented family history of asthma were also found to have an earlier diagnosis of asthma (Table 3). As with LRTI, increasing atopic exposures were associated with decreased median time to asthma diagnosis after 3 years of age. Additional variables associated with earlier asthma diagnosis included male vs. female gender (TR 0.64; 95% CI 0.59, 0.69) and black vs. white race (TR 0.57; 95% CI 0.36, 0.91). Use of more conservative diagnostic criteria for asthma yielded similar results across covariates (Table 3; sensitivity analyses 1, 3).

Table 1. Primary cohort demographic and clinical characteristics.

Variable	Total N (%) N=38,441	LRTI N=32,729 (85%)	AGE N=5,712 (15%)	P-value
Gender				
F	17,404 (45)	14,548 (44)	2,856 (50)	<.01
M	20,756 (54)	17,942 (55)	2,814 (49)	
U	281 (1)	239 (1)	42 (1)	
Hispanic				
N	21,672 (56)	18,504 (57)	3,168 (55)	<.01
Y	3,866 (10)	3,219 (10)	647 (11)	
U	12,903 (34)	11,006 (34)	1,897 (33)	
Race				
American Indian/Alaska Native	286 (1)	251 (1)	35 (1)	<.01
Asian	542 (1)	442 (1)	100 (2)	
Black/African American	276 (1)	226 (1)	50 (1)	
Other race	10,756 (28)	9,307 (28)	1,449 (25)	
Unknown/not specified	23,247 (60)	19,560 (60)	3,687 (65)	
White	3,334 (9)	2,943 (9)	391 (7)	
Insurance				
Commercial	7,942 (21)	6,674 (20)	1,268 (22)	<.01
Medicaid	29,727 (77)	25,353 (77)	4,374 (77)	
Missing	772 (2)	702 (2)	70 (1)	
Asthma ICD 9/10 code				
Y	6,986 (18)	6,323 (19)	663 (12)	<.01
Persistent asthma or exacerbation				
Y	4,940 (13)	4,493 (14)	447 (8)	<.01
Atopy categories (0–2 years old)				
0	31,266 (81)	26,509 (81)	4,757 (83)	<.01
1	6,023 (16)	5,207 (16)	816 (14)	
2	916 (2)	802 (2)	114 (2)	
≥3	236 (1)	211 (1)	25 (0)	
Wheezing ICD-9/10 code (0–2 years old)				
Y	5,196 (14)	4,998 (15)	198 (3)	<.01
History of prematurity				
Y	1,627 (4)	1,416 (4)	211 (4)	.03
Family history of asthma				
Y	1,223 (3)	1,144 (3)	79 (1)	<.01

Table 2. Hospital cohort demographic and clinical characteristics.

Variable	Total N (%) N=4,033	LRTI N=3,838 (95%)	AGE N=195 (5%)	P-value
Gender				
F	**	1,668 (43)	**	.64
M	2,240 (56)	2,138 (56)	102 (52)	
U	**	32 (1)	**	
Hispanic				
N	2,354 (58)	2,241 (58)	113 (58)	.98
Y	444 (11)	423 (11)	21 (11)	
U	1,235 (31)	1,174 (31)	61 (31)	
Race				
Other race	1,234 (31)	1,175 (31)	59 (30)	
Unknown/not specified	2,477 (61)	2,356 (61)	121 (62)	
White	322 (8)	307 (8)	15 (8)	
Insurance				
Commercial	564 (14)	540 (14)	24 (13)	.50
Medicaid	3,396 (86)	3,229 (86)	167 (87)	
Asthma ICD 9/10 code				
Y	1,079 (27)	1,054 (27)	25 (13)	<.01
Persistent asthma or exacerbation				
Y	768 (19)	751 (20)	17 (9)	<.01
Atopy categories (0–2 years old)				
0	3,238 (80)	3,082 (80)	156 (80)	.68
1	667 (17)	637 (17)	30 (15)	
2	**	94 (2)	**	
≥3	**	25 (1)	**	
Wheezing ICD-9/10 code (0–2 years old)				
Y	932 (23)	919 (24)	13 (7)	<.01
History of prematurity				
Y	258 (6)	246 (6)	12 (6)	.89
Family history of asthma				
Y	**	461 (12)	**	<.01

**Data suppressed per CMS cell size suppression policy to avoid displaying a cell frequency of <11. Due to small cell frequencies, data for American Indian/Alaska Native, Asian, Black/African American, and Native Hawaiian or other Pacific Islander Race were included in the Other Race category.

Table 3. Risk of asthma in children with and without clinical risk factors between 0 and 2 years old.

Variables ^a	Primary analysis ^b	SA1	SA2	SA3
	Adjusted TR (95% CI)	Adjusted TR (95% CI)	Adjusted TR (95% CI)	Adjusted TR (95% CI)
1 LRTI visit	0.63 (0.56, 0.71)	0.37 (0.32, 0.42)	0.36 (0.19, 0.65)	0.20 (0.10, 0.40)
2 visits	0.34 (0.30, 0.40)	0.20 (0.17, 0.23)	0.10 (0.05, 0.21)	0.05 (0.02, 0.12)
≥3 visits	0.20 (0.16, 0.24)	0.11 (0.09, 0.14)	0.02 (0.01, 0.07)	0.01 (0.00, 0.04)
1 atopic category	0.47 (0.43, 0.52)	0.46 (0.42, 0.51)	0.45 (0.34, 0.60)	0.46 (0.35, 0.60)
2 categories	0.18 (0.14, 0.22)	0.17 (0.14, 0.21)	0.13 (0.07, 0.23)	0.12 (0.07, 0.22)
≥3 categories	0.08 (0.05, 0.11)	0.07 (0.05, 0.11)	0.13 (0.04, 0.37)	0.12 (0.04, 0.36)
≥1 wheeze	0.23 (0.21, 0.25)	0.23 (0.21, 0.25)	0.17 (0.13, 0.21)	0.17 (0.13, 0.21)
FH of asthma	0.20 (0.17, 0.24)	0.20 (0.17, 0.24)	0.32 (0.24, 0.44)	0.32 (0.24, 0.44)

SA, sensitivity analysis; TR, time ratio.

^aOther covariates in the model included race, ethnicity, gender, and history of prematurity.

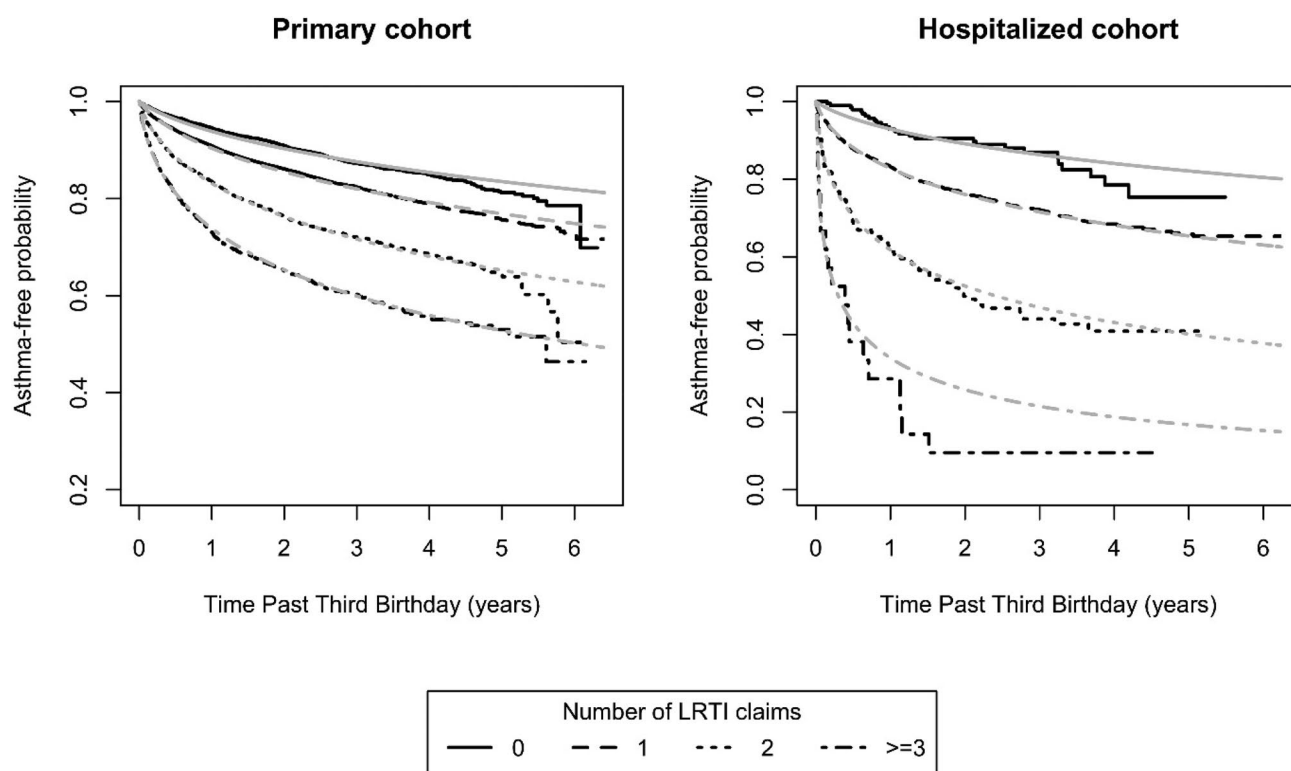
^bPrimary analysis: all claims cohort with outcome defined as any asthma ICD-9 or -10 code.

SA 1: All claims cohort with outcome defined as persistent asthma or asthma exacerbation.

SA 2: Hospital claims cohort with outcome defined as any asthma ICD-9 or -10 codes.

SA 3: Hospital claims cohort with outcome defined as persistent asthma or asthma exacerbation.

Reference variables are no LRTI visits, no atopic categories, no wheeze, and no FH of asthma.

**Figure 2.** Asthma-free survival probabilities for primary and hospitalized cohorts. Black lines represent the Kaplan–Meier curves and the gray lines are the model fitted (log-normal) curves.

Discussion

For children with multiple LRTIs prior to 2 years of age, we found a reduced time to asthma diagnosis after 3 years of age relative to children with AGE but without LRTI. Although decreased time to asthma diagnosis is not synonymous with increased risk of asthma, the differences in proportions of children who are asthma-free at a given age, stratified by prior infectious exposures, suggest that there is an increased risk of developing asthma associated with recurrent

early childhood LRTIs. This difference is particularly notable in children with more clinically severe illness (i.e. hospitalization for LRTI). While the underlying reason is not clearly understood, two pathophysiologic mechanisms may be at play. LRTIs may injure the developing airway, predisposing to subsequent airway dysfunction and asthma; or preexisting airway dysfunction manifests as increased susceptibility to both early LRTIs and later asthma (19).

Prior studies have demonstrated increased risk of subsequent childhood asthma in infants with more

clinically severe bronchiolitis (14,29) and in those with recurrent early childhood LRTIs (15). The latter study, a longitudinal birth cohort study of 1314 children, found that children with repeated LRTIs (including diagnoses of pneumonia, bronchitis, pertussis, tracheobronchitis, flu, croup, and bronchiolitis) in the first 3 years of life were significantly more likely to have physician-diagnosed asthma and bronchial hyperreactivity by age 7 than those with one or fewer LRTIs (15). Our retrospective cohort study reaffirmed these findings but differed by including a larger sample size, confining the LRTI definition to pneumonia and bronchiolitis, and using different age cutoffs for the exposure and outcome periods. We also separately modeled outcomes for children hospitalized with LRTI and explored the temporal relationship between LRTI recurrence and asthma onset.

Other studies have shown an association between wheezing in infancy due to specific viral pathogens and increased risk of subsequent childhood asthma (30–32). Wheezing and LRTI may or may not describe the same clinical condition or pathophysiology (33,34). The variability in clinical definitions of both predictor and outcome variables between studies continues to be a significant limitation in this field of research (35). Nonetheless, our study indicates that clinicians can rely on LRTI counts, among other factors, to estimate future asthma risk in their patients. Since the American Academy of Pediatrics advises against routine use of respiratory viral testing in patients with bronchiolitis (36), pathogen-specific data may not be available to figure into the risk calculus.

While not the primary focus on this study, we found a dose-dependent reduction in time to asthma diagnosis with cumulative atopic exposures prior to 2 years of age. This may be of interest for future research in asthma predictive modeling. We also verified the importance of previously reported demographic and clinical risk factors for pediatric asthma, including family history of asthma, male gender, black race, and prior wheezing. We did not find an association between prematurity and timing of asthma onset, most likely because our exclusion criteria eliminated premature children with more severe comorbidities from the dataset.

This study has several limitations. Insurance claims are prone to inaccuracies and missing data (37), which can lead to misclassification. We were also unable to validate diagnoses or verify specific LRTI viral or bacterial pathogens (33). There were substantial rates of missing data in race and ethnicity variables, which undermines health disparities

research and should be the focus of future data quality improvement efforts. There may be uncaptured data (i.e. clinical presence but no claim) for atopy, wheeze, and family history of asthma which may lead to an underestimate of the strength of association between these variables and future asthma. We were not able to estimate the proportion of missing data for these variables. Less than 1% of the total sample was found to have diagnosis codes for secondhand tobacco smoke exposure, a likely unreliable estimate. Therefore, this variable was not included in the analysis. Clinical practice behaviors may skew results away from the null. For example, recurrent preschool wheeze may be misdiagnosed as asthma (34). Selection bias can result from increased subspecialty referral and asthma diagnosis among young children with more severe respiratory problems. We attempted to mitigate these impacts by treating the period between 2 and 3 years of age as a washout, and by using a more conservative asthma definition in the sensitivity analysis.

Our comparison population was not the general population, but specifically children with AGE, and may not truly represent a “control” group. However, our asthma prevalence estimate of 9% for the AGE group (using the more conservative asthma definition) is similar to pediatric asthma prevalence reported in the general population by the Centers for Disease Control and Prevention (38), which increases our confidence about its validity as a proxy.

Conclusions

Children with multiple LRTIs, especially LRTI hospitalizations, before 2 years of age warrant careful monitoring for asthma onset during their preschool years. This information may guide patient care, clinical prediction models, and clinical trial design to reduce pediatric asthma morbidity.

Declaration of interest

Dr. Brittan served on an advisory board for Sanofi Pasteur but has not received any research funding from the company. Dr. Dempsey participated in this work while at the University of Colorado Denver. She is now employed by Merck and Co. This company played no role in the research.

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Appendix A. Supplemental table ICD code categories

Diagnosis group	ICD code	Description	ICD code set
Food allergy	V1501	Allergy to peanuts	9
	V1502	Allergy to milk products	9
	V1503	Allergy to eggs	9
	V1504	Allergy to seafood	9
	V1505	Allergy to other foods	9
	Z91010	Allergy to peanuts	10
	Z91011	Allergy to milk products	10
	Z91012	Allergy to eggs	10
	Z91013	Allergy to seafood	10
	Z91018	Allergy to other foods	10
Atopic dermatitis	T780.X	Anaphylactic reaction due to food	10
	691	Atopic dermatitis and related conditions	9
	6918	Other atopic dermatitis	9
	L2084	Intrinsic (allergic) eczema	10
	L2081	Atopic neurodermatitis	10
	L2082	Flexural Eczema	10
	L2083	Infantile (acute) (chronic) eczema	10
	L2084	Intrinsic Allergic eczema	10
	L2089	Other atopic dermatitis	10
	L209	Atopic dermatitis unspecified	10
Allergic rhinitis	477	Allergic rhinitis	9
	4770	Allergic rhinitis due to pollen	9
	4771	Allergic rhinitis due to food	9
	4772	Allergic rhinitis due to animal (cat) (dog) hair and dander	9
	4778	Allergic rhinitis due to other allergen	9
	4779	Allergic rhinitis, cause unspecified	9
	J301	Allergic rhinitis due to pollen	10
	J305	Allergic rhinitis due to food	10
	J3081	Allergic rhinitis due to animal (cat) (dog) hair and dander	10
	J302	Other seasonal allergic rhinitis	10
Unspecified allergic reaction/ anaphylaxis	J3089	Other allergic rhinitis	10
	J309	Allergic rhinitis, unspecified	10
	9950	Other anaphylactic reaction	9
	9951	Angioneurotic edema, not elsewhere classified	9
	9953	Allergy, unspecified, not elsewhere classified	9
	T782	Anaphylactic shock, unspecified	10
	T783	Angioneurotic edema	10
	T7840	Allergy, unspecified	10
Asthma family history	V175	Family history of asthma	9
	Z825	Family history of asthma and other chronic lower respiratory diseases	10

(Continued)

(Continued)

Diagnosis group	ICD code	Description	ICD code set
Prematurity	76500	Extreme immaturity, unspecified [weight]	9
	76501	Extreme immaturity, less than 500 grams	9
	76502	Extreme immaturity, 500–749 grams	9
	76503	Extreme immaturity, 750–999 grams	9
	75504	Extreme immaturity, 1,000–1,249 grams	9
	76505	Extreme immaturity, 1,250–1,499 grams	9
	76506	Extreme immaturity, 1,500–1,749 grams	9
	76507	Extreme immaturity, 1,749–1,999 grams	9
	76508	Extreme immaturity, 2,000–2,499 grams	9
	76509	Extreme immaturity, 2,500 grams and over	9
	76510	Other preterm infants, unspecified [weight]	9
	76511	Other preterm infants, less than 500 grams	9
	76512	Other preterm infants, 500–749 grams	9
	76513	Other preterm infants, 750–999 grams	9
	76514	Other preterm infants, 1,000–1,249 grams	9
	76515	Other preterm infants, 1,250–1,499 grams	9
	76516	Other preterm infants, 1,500–1,749 grams	9
	76517	Other preterm infants, 1,750–1,999 grams	9
	76518	Other preterm infants, 2,000–2,499 grams	9
	76519	Other preterm infants, 2,500 grams and over	9
	76520	Unspecified weeks of gestation	9
	76521	Less than 24 completed weeks of gestation	9
	76522	24 completed weeks of gestation	9
	76523	25–26 completed weeks of gestation	9
	76524	27–28 completed weeks of gestation	9
	76525	29–30 completed weeks of gestation	9
	76526	31–32 completed weeks of gestation	9
	76527	33–34 completed weeks of gestation	9
	76528	35–36 completed weeks of gestation	9
	P070	Extremely low birth weight newborn	10
	P071	Other low birth weight newborn	10
	P0700	Extremely low birth weight newborn, unspecified weight	10
	P0701	Extremely low birth weight newborn, less than 500 grams	10
	P0702	Extremely low birth weight newborn, 500–749 grams	10
	P0703	Extremely low birth weight newborn, 750–999 grams	10
	P0710	Other low birth weight newborn, unspecified weight	10
	P0714	Other low birth weight newborn, 1000–1249 grams	10
	P0715	Other low birth weight newborn, 1250–1499 grams	10
	P0716	Other low birth weight newborn, 1500–1749 grams	10
	P0717	Other low birth weight newborn, 1750–1999 grams	10
	P0718	Other low birth weight newborn, 2000–2499 grams	10
	P0730	Preterm newborn, unspecified weeks of gestation	10
	P0720	Extreme immaturity of newborn	10
	P0721	Extreme immaturity of newborn, gestational age less than 23 completed weeks	10
	P0722	Extreme immaturity of newborn, gestational age 23 completed weeks	10
	P0723	Extreme immaturity of newborn, gestational age 24 completed weeks	10
	P0724	Extreme immaturity of newborn, gestational age 25 completed weeks	10
	P0725	Extreme immaturity of newborn, gestational age 26 completed weeks	10
	P0726	Extreme immaturity of newborn, gestational age 27 completed weeks	10
	P0731	Preterm newborn, gestational age 28 completed weeks	10
	P0732	Preterm newborn, gestational age 29 completed weeks	10
	P0733	Preterm newborn, gestational age 30 completed weeks	10
	P0734	Preterm newborn, gestational age 31 completed weeks	10
	P0735	Preterm newborn, gestational age 32 completed weeks	10
	P0736	Preterm newborn, gestational age 33 completed weeks	10
	P0737	Preterm newborn, gestational age 34 completed weeks	10
	P0738	Preterm newborn, gestational age 35 completed weeks	10
	P0739	Preterm newborn, gestational age 36 completed weeks	10
Wheezing	78607	Wheezing	9
	R062	Wheezing	10