Being Overweight or Obese and the Development of Asthma

Jason E. Lang, MD, MPH,[a,b,c] H. Timothy Bunnell, PhD,[d] Md Jobayer Hossain, PhD,[d] Tim Wysocki, PhD,[e] John J. Lima, PharmD,[f] Terri H. Finkel, MD, PhD,[a] Leonard Bacharier, MD,[g] Amanda Dempsey, MD, PhD, MPH,[h] Lisa Sarzynski, MD,[i] Matthew Test, MD,[j] Christopher B. Forrest, MD, PhD[k]

abstract

OBJECTIVES: Adult obesity is linked to asthma cases and is estimated to lead to 250 000 new cases yearly. Similar incidence and attributable risk (AR) estimates have not been developed for children. We sought to describe the relationship between overweight and obesity and incident asthma in childhood and quantify AR statistics in the United States for overweight and obesity on pediatric asthma.

METHODS: The PEDSnet clinical data research network was used to conduct a retrospective cohort study (January 2009–December 2015) to compare asthma incidence among overweight and/or obese versus healthy weight 2- to 17-year-old children. Asthma incidence was defined as ≥2 encounters with a diagnosis of asthma and ≥1 asthma controller prescription. Stricter diagnostic criteria involved confirmation by spirometry. We used multivariable Poisson regression analyses to estimate incident asthma rates and risk ratios and accepted formulas for ARs.

RESULTS: Data from 507 496 children and 19 581 972 encounters were included. The mean participant observation period was 4 years. The adjusted risk for incident asthma was increased among children who were overweight (relative risk [RR]: 1.17; 95% confidence interval [CI]: 1.10–1.25) and obese (RR: 1.26; 95% CI: 1.18–1.34). The adjusted risk for spirometry-confirmed asthma was increased among children with obesity (RR: 1.29; 95% CI: 1.16–1.42). An estimated 23% to 27% of new asthma cases in children with obesity is directly attributable to obesity. In the absence of overweight and obesity, 10% of all cases of asthma would be avoided.

CONCLUSIONS: Obesity is a major preventable risk factor for pediatric asthma.

FREE

[a]Nemours Children's Hospital, Nemours Children's Health System, Orlando, Florida; Divisions of [b]Allergy and Immunology and [c]Pulmonary Medicine, School of Medicine, Duke University and Duke Children's Hospital and Health Center, Durham, North Carolina; [d]Department of Biomedical Research, Nemours Alfred I. DuPont Hospital for Children, Wilmington, Delaware; [e]Centers for Health Care Delivery Science and [f]Pharmacogenomics and Translational Research, Nemours Children's Health System, Jacksonville, Florida; [g]Department of Pediatrics, Washington University, St Louis, Missouri; [h]Department of Pediatrics, School of Medicine, Anschutz Medical Campus, University of Colorado, Aurora, Colorado; [i]Section of Pulmonary Medicine, Nationwide Children's Hospital and Department of Pediatrics, College of Medicine, The Ohio State University, Columbus, Ohio; [j]Department of Pediatrics, Seattle Children's Hospital, Seattle, Washington; and [k]Department of Pediatrics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

Drs Lang, Hossain, Bunnell, and Wysocki conceptualized and designed the study, assisted in data collection, contributed to data analysis, drafted the initial manuscript, and revised the manuscript; Dr Lima helped conceptualize and design the study, drafted the initial manuscript, and revised the manuscript; Dr Finkel helped conceptualize and design the study, assisted in data collection, drafted the initial manuscript, and revised the manuscript; Drs Bacharier, Dempsey, Sarzynski, and Test assisted in data collection and reviewed and revised the manuscript; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

WHAT'S KNOWN ON THIS SUBJECT: Obesity has been linked to new asthma cases in adults, but the nature of asthma risk in children is less clear. In previous research, attributable risk has not been measured across a large diverse population of US children.

WHAT THIS STUDY ADDS: An estimated 23% to 27% of new asthma cases in children with obesity is directly attributable to obesity. In the absence of overweight and obesity, 10% of all US cases of pediatric asthma could be avoided.

To cite: Lang JE, Bunnell HT, Hossain MJ, et al. Being Overweight or Obese and the Development of Asthma. *Pediatrics.* 2018;142(6):e20182119

Downloaded from www.aappublications.org/news by guest on December 1, 2018

Obesity and asthma both cause enormous suffering and cost for children in the United States and around the world.[1–3] Despite reports of progress in slowing pediatric obesity, the latest evidence suggests an increase in obesity, particularly in 2- to 5-year-old children.[4] Adult obesity is linked to adult-onset asthma[5,6] and is estimated to cause 250 000 new adult asthma cases each year.[7] Similar incidence and attributable risk (AR) estimates have not been developed for children.

Roughly, 18% of US children are obese, which impairs quality of life and increases the risk for chronic disease.[4,8,9] The link between obesity and new asthma cases in children has been debated and remains incompletely defined. Authors of more than a dozen longitudinal studies report on the risk of obesity and incident asthma.[10–27] Authors of several studies report that obesity increases incident asthma in a subset of the patients,[17–19,21,22,25,26] whereas other studies revealed no effect.[10–16,23,24,27] Among positive studies, the findings were remarkably inconsistent regarding the effects of race, sex, atopic status, and timing of obesity, although most studies were underpowered to assess the effects of these covariables. Previous authors have argued that strong effect differences across subgroups undermine the likelihood that obesity directly causes asthma because causality would be expected to work across demographic groups.[18]

Most cases of asthma are diagnosed clinically without confirmation by pulmonary function testing.[28,29] Numerous studies have demonstrated the imprecise nature of physician diagnosis of asthma,[30–35] and expert guidelines recommend the use of spirometry to assess for airflow obstruction defects or airway reversibility in the confirmation of asthma.[36–38] Thus, reliance solely on physician-diagnosed asthma in measuring the incidence rates and causative determinants of asthma is problematic. To date, authors of longitudinal pediatric studies in which overweight and obesity and asthma risk are assessed have not used pulmonary function testing.

The nature and degree of a possible association between obesity and asthma in children may benefit from novel approaches with improved power and feasibility.[39] Large prospective epidemiological studies are costly and time consuming and have been criticized for developing evidence too slowly.[40] Newly distributed data networks have been used to take advantage of advances in electronic health records (EHRs) and clinical informatics, such as common data models, allowing for consistent data standards across sites and improved quality control checks during data collection and entry as well as allowing for extracting, transforming, and loading EHRs into common data models to increase the validity, linkage, size, and diversity of pooled EHR data. The recent development of PEDSnet, a national pediatric network that is used to pool and standardize EHR data, offers a novel opportunity to define the obesity-asthma relationship in children.[41,42] PEDSnet includes data recorded during real-world clinical care across all clinical settings among 8 large pediatric health systems across the United States in a single common data model.[41,42] Our purpose for this study was to leverage data obtained by PEDSnet to conduct a longitudinal study in which we compare the risk of asthma among children with normal weight and obesity, taking into account important covariates and assessing the AR of excess body weight in pediatric asthma.

METHODS

This study, which involved only deidentified data, was evaluated by the Duke University Health System Institutional Review Board (No. Pro00077780) and determined to be exempt research. The requirement for informed consent was waived under 45 CFR 46.116 at all participating institutions.

Study Design

We used a retrospective cohort study design that included data from January 2009 to December 2015. We matched each individual case of overweight or obesity with children with a healthy weight using a 1:1 ratio. Routine clinical data were obtained from 6 PEDSnet institutions. The 3 groups were defined as follows: overweight, those with a BMI in the 85th to 94th percentile adjusted for sex and age; obesity, those with a BMI in the ≥95th percentile adjusted for sex and age; and a group of matched comparators whose BMI percentile ranged between the 25th to 64th percentile adjusted for sex and age (to reduce weight status misclassification). None of the participants had previous documentation of asthma at baseline. Rates of incident, study-defined asthma were compared over time for each group.

PEDSnet

PEDSnet (pedsnet.org) standardize EHR data to the observational health data sciences and informatics common data model.[42] PEDSnet currently comprises 8 US pediatric academic medical centers, 6 of which participated in this study: Nemours Children's Health System, Children's Hospital of Philadelphia, Seattle Children's Hospital, Children's Hospital Colorado, St Louis Children's Hospital, and Nationwide Children's Hospital. The primary market for PEDSnet institutions crosses 22 states; each institution also serves as a national and international referral base. All clinical settings are included in the data network, inclusive of primary, hospital, emergency, ambulatory, and subspecialty care

Downloaded from www.aappublications.org/news by guest on December 1, 2018

as well as laboratory and imaging settings.

Participant Selection

Patients aged 2 to 17 years seen within a PEDSnet site from January 1, 2009, to December 31, 2015, were eligible for inclusion if they had (1) an age- and sex-adjusted BMI value in the ≥85th percentile, (2) no health record diagnosis of asthma (all 493 codes) or wheezing (786.07) at or before the study-defined initial visit, and (3) at least 2 subsequent (total of 3) clinic visits spanning at least 12 months. The initial visit was defined as the first health care visit after January 1, 2009. Patients with any documented diagnosis of cystic fibrosis, ciliary dyskinesia, childhood cancer, inflammatory bowel disease, or bronchopulmonary dysplasia were excluded. For each subject who fit the criteria for the overweight or obesity risk groups, we randomly selected 1 control patient with normal weight who was identically matched for age at initial visit (±12 months), sex, race (white, African American, Asian American, or other), ethnicity (Hispanic versus non-Hispanic), insurance status (Medicaid, private, or other), and PEDSnet site. Subjects in the comparator group with a normal BMI adhered to the same comorbidity exclusions and requirements for follow-up visits. Matching occurred within each site to reduce confounding due to geographic factors and site-specific differences in care. To reduce the erroneous inclusion of children with occult (undiagnosed) asthma at baseline who had been prescribed an asthma controller, a more select cohort was created, which excluded patients who did not have asthma at baseline but were prescribed an asthma controller medication and patients who were diagnosed with asthma within 18 months of their initial visit.

Baseline Data and Outcome Measures

Baseline data for each subject were taken from the initial visit encounter or from encounters before the study-defined initial visit and included demographics, year and month of birth, age, race, sex, ethnicity, insurance status (Medicaid, private, or other), gestational age, BMI percentile, BMI *z*-score, past and current comorbid health conditions, and medications. Each participant had their own observation period, which was defined as the time from the initial visit to the patient's last recorded encounter and provided the following data: observation period duration, number and setting of encounters, encounter diagnoses, encounter medications, and spirometry values. Spirometry values included forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1), measured in liters and as a percentage of the age- and sex-adjusted predicted value.

Diagnosis of Asthma

The primary outcome was the incidence of asthma during the observation period, defined as ≥2 encounters with a diagnosis of asthma and ≥1 asthma medication prescription. Secondary outcomes included looser and stricter criteria for an asthma diagnosis, including ≥1 encounter with an asthma diagnosis, ≥2 encounters with an asthma diagnosis (without the requirement of an asthma drug prescription), and ≥2 encounters with an asthma diagnosis with an additional confirmation by spirometry. A spirometry confirmation required either a predicted percentage of forced expiratory volume in 1 minute of <80%, an FEV_1/FVC ratio of <0.85, or postbronchodilator improvement of ≥10% in either the FEV_1 or FVC.[43,44]

Analysis

Crude and adjusted incident asthma rates (per person time) and rate (risk) ratios were determined for each group (normal weight and overweight and obese) by using univariable and multivariable Poisson regressions. Because each participant had a different observation period duration, the asthma incidence in each risk group was adjusted for each group's observation period duration and expressed as an incidence rate (per person time). In addition to the rates and rate ratios, we estimated the following indices for participants who were overweight and obese using standard formulas: AR ([$\text{incidence}_{exposed}$] − [$\text{incidence}_{unexposed}$]), AR percent (AR/$\text{incidence}_{exposed}$), population attributable risk (PAR) ([$\text{incidence}_{population}$] − [$\text{incidence}_{unexposed}$]), and PAR percent (PAR/$\text{incidence}_{population}$) (see Supplemental Tables 6 and 7). Variables in the multivariable model included age at initial visit, sex, race, ethnicity, insurance status, observation period, and institution. A second model included adjustments for baseline allergic rhinitis, baseline food allergy, and baseline proton pump inhibitor medication use. The model was checked for over- and underdispersion of response variables. All tests were 2-sided, and *P* values <.05 were considered statistically significant. The statistical package SAS version 9.3 (SAS Institute, Inc, Cary, NC) was used for data analysis.

RESULTS

Baseline Characteristics

The baseline characteristics of 507 496 patients meeting criteria for inclusion are shown by BMI and body habitus category in Table 1. By the matching design, participants were evenly split between normal BMI (50%) and

Downloaded from www.aappublications.org/news by guest on December 1, 2018

overweight or obese BMI (50%). Baseline characteristics differed statistically by body habitus groups for age, sex, race, ethnicity, health insurance status, and institution. Health care use, including total observation period, total encounters, outpatient and inpatient encounters, and emergency department visits, were associated statistically with body habitus. Several comorbidities were associated with body habitus, including esophageal reflux, eczema, urticaria, anaphylaxis, food allergy, and allergic rhinitis. Prevalence of allergic rhinitis, food allergy, anaphylaxis, urticaria, and eczema was reduced among children with obesity. Nearly all medications collected at baseline were more common in the obesity group.

Risk Factors for Study-Defined Incident Asthma

Among the 507 496 total children meeting inclusion criteria for study entry, 41 330 (8.14%) and 27 461 (5.41%) were diagnosed with asthma by a pediatric health care provider at least 1 and 2 encounters, respectively. The overall incidence rate for new asthma cases in the population was 2.7 per 1000 patient years, ranging from 2.4 per 1000 patient years among children with normal weight to 3.2 per 1000 patient years among children with obesity. In univariate analyses, both overweight and obesity were associated with an increased risk for new asthma diagnosis (Table 2). Male sex, African-American race, multiple race, Medicaid insurance, no insurance or self-pay, and younger age grouping were associated with a higher asthma incidence. Baseline presence of allergic rhinitis, food allergy, anaphylaxis, and past use of various medications (any proton pump inhibitor or histamine-2 blocker) was significantly associated with a higher risk for incident asthma (Table 3).

Baseline Body Habitus and Risk for Incident Asthma

Multivariable models used to assess the independent risk of overweight and obesity on incident asthma are shown in Table 4. Obesity was significantly associated with a greater risk of incident asthma by using the primary definition and all other definitions, including confirmation by spirometry. The crude effect size range for obesity-related risk for new asthma was generally consistent and ranged from 1.30 to 1.38. For children who were overweight, the risk for incident asthma was significant for the primary incidence end point and looser definitions. The overweight-related crude risk ratio (normal weight referent) was modest, ranging from 1.08 to 1.17. However, when children were evaluated with spirometry testing, overweight was not associated with a significant increase in asthma incidence.

The risk of asthma confirmed by a repeat diagnosis and either asthma medication or spirometry was only modestly increased among children who were overweight. However, an increased risk of confirmed asthma in children with obesity ranged from 26% to 38% in crude and both multivariable models. In the selected cohort in which patients taking baseline asthma controllers and patients with an asthma diagnosis early in the observation period were excluded, the rate ratio for asthma among children who were overweight and obese was 1.14 (95% confidence interval [CI]: 1.10–1.18) and 1.28 (95% CI: 1.23–1.32), respectively.

ARs of Overweight and Obesity in Childhood Asthma

ARs and PARs of incident asthma related to overweight status and obesity status are shown in Table 5. The proportion of clinically diagnosed asthma incidence in children with obesity that is attributed specifically to obesity was 23% to 25%. When considering asthma confirmed by spirometry, the proportion of asthma attributable to obesity in children with obesity was 28%. The percentage of clinically diagnosed asthma among all children in the population attributable to obesity was 10%, whereas the percentage of incident asthma confirmed by spirometry among all children in the population attributable to obesity was 13%.

DISCUSSION

This study demonstrates that obesity in children increases the risk of new asthma diagnosis even when the asthma diagnosis is confirmed by rigorous diagnostic means (eg, by repeated asthma encounters, medication prescription, and spirometry evidence of airway obstruction, bronchodilator reversibility, or both). These results do not support evidence of an overdiagnosis of asthma in children who are overweight and obese. The effect of overweight status was only a modest risk factor and was not associated with a greater risk of spirometry-confirmed asthma. However, obesity status was a significant risk factor for confirmed asthma by all definitions and was a significant contributor to incident asthma. Roughly one-quarter of the incidences of new asthma were directly attributable to obesity. Currently, there are few known preventable risk factors that can be used to reduce childhood asthma. With these data, it is suggested that reducing the onset of obesity in childhood would significantly reduce the public health burden of asthma in children.

Because of the lack of a simple objective definition for asthma, attempts at measuring asthma prevalence and incidence have been challenging and have been called into question.[33] Prevalence data for

Downloaded from www.aappublications.org/news by guest on December 1, 2018

TABLE 1 Participant Characteristics by Body Habitus at Baseline

Variables	Total Participants	BMI Percentile Groupings			*P*
		Normal Weight (5th–84th)	Overweight (85th–94th)	Obesity (≥95th)	
N (%)	507 496	253 748 (50.0)	129 255 (25.5)	124 493 (24.5)	—
Age, y, mean (SD)	507 496	8.98 (4.64)	8.62 (4.73)	9.36 (4.52)	<.0001
Male sex, *n* (%)	257 438 (50.73)	128 719 (50.73)	64 210 (49.68)	64 509 (51.82)	<.0001
Race, *n* (%)	507 496				<.0001
White	281 394	140 697 (55.45)	74 943 (57.98)	65 754 (52.82)	—
African American	117 164	58 582 (23.09)	28 064 (21.71)	30 518 (24.51)	—
Asian American	12 108	6841 (2.7)	2960 (2.29)	2307 (1.85)	—
American Indian	1183	530 (0.21)	278 (0.22)	375 (0.3)	—
Hawaiian or Pacific Islander	1457	662 (0.26)	369 (0.29)	426 (0.34)	—
Multiple races	13 619	6507 (2.56)	3429 (2.65)	3683 (2.96)	—
Other or refused	80 571	39 929 (15.74)	19 212 (14.86)	21 430 (17.21)	—
Ethnicity, *n* (%)					
Hispanic	71 490	35 745 (14.09)	16 100 (12.46)	19 645 (15.78)	<.0001
Health insurance status, *n* (%)					<.0001
Medicaid or SCHIP	191 618	95 808 (37.76)	45 384 (35.11)	50 426 (40.51)	—
Medicare	58	30 (0.01)	17 (0.01)	11 (0.01)	—
Other public	2870	1486 (0.59)	768 (0.59)	616 (0.49)	—
Private or commercial	180 072	90 036 (35.48)	48 968 (37.88)	41 068 (32.99)	—
Self-pay	58 024	29 269 (11.53)	16 487 (12.76)	12 268 (9.85)	—
Undetermined	74 854	37 119 (14.63)	17 631 (13.64)	20 104 (16.15)	—
Clinical centers, *n* (%)					<.0001
Site 1	47 298	23 649 (9.32)	12 270 (9.49)	11 379 (9.14)	—
Site 2	103 476	51 738 (20.39)	24 490 (18.95)	27 248 (21.89)	—
Site 3	140 456	70 228 (27.68)	34 057 (26.35)	36 171 (29.05)	—
Site 4	44 334	22 167 (8.74)	11 274 (8.72)	10 893 (8.75)	—
Site 5	16 732	8366 (3.3)	3991 (3.09)	4375 (3.51)	—
Site 6	155 200	77 600 (30.58)	43 173 (33.4)	34 427 (27.65)	—
Observation period, y, mean (SD)	507 496	4.00 (1.88)	3.97 (1.87)	3.93 (1.87)	<.0001
Total encounters, mean (SD)	19 581 972	24.52 (33.46)	24.54 (33.18)	25.92 (34.24)	<.0001
Outpatient, mean (SD)	16 637 436	32.21 (0.097)	31.93 (0.1364)	34.85 (0.1465)	<.0001
Outpatient other, mean (SD)	2 338 964	4.55 (0.0285)	4.96 (0.0416)	4.37 (0.0411)	<.0001
Inpatient, mean (SD)	199 720	0.38 (0.0038)	0.37 (0.0047)	0.43 (0.0055)	<.0001
Emergency department, mean (SD)	376 049	0.72 (0.0037)	0.73 (0.0051)	0.8 (0.0058)	<.0001
Emergency to hospital, mean (SD)	7093	0.01 (0.0005)	0.01 (0.0006)	0.01 (0.0008)	.1647
Comorbidities at baseline, *n* (%)					
Esophageal reflux	18 547	9444 (3.72)	4467 (3.46)	4636 (3.72)	<.0001
Eczema or atopic dermatitis	8441	4115 (1.62)	2426 (1.88)	1900 (1.53)	<.0001
Hives or urticaria	7013	3552 (1.4)	1936 (1.5)	1525 (1.22)	<.0001
Anaphylaxis	633	353 (0.14)	166 (0.13)	114 (0.09)	.0005
Food allergy	5937	3135 (1.24)	1608 (1.24)	1194 (0.96)	<.0001
Allergic rhinitis	52 109	26 166 (10.31)	13 948 (10.79)	11 995 (9.64)	<.0001
Medications at baseline, *n* (%)					
Proton pump inhibitors	33 012	16 216 (6.39)	8088 (6.26)	8708 (6.99)	<.0001
Histamine-2 receptor blockers	32 542	15 820 (6.23)	8219 (6.36)	8503 (6.83)	<.0001
Albuterol	69 949	32 650 (12.87)	18 959 (14.67)	18 340 (14.73)	<.0001
Inhaled corticosteroids	33 601	15 457 (6.09)	9035 (6.99)	9109 (7.32)	<.0001
ICS/LABA	3495	1541 (0.61)	910 (0.7)	1044 (0.84)	<.0001
Prednisone or prednisolone	55 631	26 095 (10.28)	15 428 (11.94)	14 108 (11.33)	<.0001
Dexamethasone	25 772	12 200 (4.81)	6651 (5.15)	69 201 (5.56)	<.0001
Progesterone	32 916	15 845 (6.24)	9425 (7.29)	7646 (6.14)	<.0001
Metformin	5842	338 (0.13)	746 (0.58)	4758 (3.82)	<.0001
Sulfonylurea	80	21 (0.01)	12 (0.01)	47 (0.04)	<.0001
Leukotriene modifiers	18 508	8392 (3.31)	5037 (3.9)	5079 (4.08)	<.0001
ACE inhibitors	5805	2158 (0.85)	1257 (0.97)	2390 (1.92)	<.0001

ACE, angiotensin-converting enzyme; ICS, inhaled corticosteroid; LABA, long-acting β-2 agonist; SCHIP, State Children's Health Insurance Program; —, not applicable.

asthma typically have come from self-report and have been widely published.[1,45,46] Asthma is thought to affect roughly 8.4% of children in the United States, with the highest prevalence (10.2%) occurring among 15- to 19-year-old children.[1] Overall prevalence of a single asthma diagnosis in the current study was 8.1%, remarkably close to current US prevalence rates. Incidence rates are more difficult to determine and

Downloaded from www.aappublications.org/news by guest on December 1, 2018

TABLE 2 Crude Demographic Determinants of Incident Asthma

	Incidence Rate[a] (SE)	Rate Ratio	95% CI	*P*
Body habitus				
Lean (referent)	2.4 (0.05)	1.00	1.00–1.00	—
Overweight	2.8 (0.07)	1.17	1.10–1.25	<.0001
Obese	3.2 (0.08)	1.30	1.22–1.38	<.0001
Sex				
Female (referent)	2.3 (0.05)	1.00	1.00–1.00	—
Male	3.1 (0.06)	1.30	1.24–1.38	<.0001
Ethnicity				
Non-Hispanic (referent)	2.9 (0.04)	1.00	1.00–1.00	—
Hispanic	2.3 (0.09)	0.79	0.72–0.86	<.0001
Other or missing	1.2 (0.12)	0.41	0.34–0.51	<.0001
Race				
White (referent)	1.8 (0.04)	1.00	1.00–1.00	—
African American	5.1 (0.10)	2.74	2.58–2.90	<.0001
Asian American	1.4 (0.18)	0.76	0.59–0.97	.0303
American Indian or Alaskan native	0.9 (0.42)	0.51	0.21–1.22	.1290
Hawaiian or Pacific Islander	3.4 (0.89)	1.87	1.12–3.10	.0161
Multiple race	4.6 (0.29)	2.48	2.17–2.83	<.0001
Refused	1.9 (0.08)	1.01	0.92–1.11	.8768
Age groupings, y				
0–4 (referent)	4.4 (0.01)	1.00	1.00–1.00	—
5–11	2.2 (0.05)	0.50	0.47–0.53	<.0001
12–17	1.8 (0.06)	0.40	0.37–0.43	<.0001
Payer				
Private (referent)	1.3 (0.04)	1.00	1.00–1.00	—
Medicaid	2.5 (0.06)	1.95	1.80–2.11	<.0001
Medicare	0.0 (0.00)	0.00	0.00–0.00	.9979
Self-pay	1.6 (0.08)	1.21	1.08–1.37	.0014
Other public	0.8 (0.29)	0.59	0.28–1.24	.1644

Asthma was defined as ≥2 encounters with a diagnosis and prescription of ≥1 asthma drug. —, not applicable.
[a] Rate per 1000 patient years.

TABLE 3 Baseline Comorbidities and Medications and Incident Asthma

	Incidence Rate[a] (SE)	Rate Ratio	95% CI	*P*
Comorbidities present at baseline				
Allergic rhinitis	3.45 (0.12)	1.32	1.23–1.42	<.0001
Food allergy	3.91 (0.39)	1.45	1.20–1.77	.0002
Anaphylaxis	5.88 (2.22)	2.17	1.03–4.55	.0405
Atopic dermatitis	2.38 (0.25)	0.88	0.71–1.08	.2173
Urticaria	2.61 (0.31)	0.96	0.76–1.22	.7417
GERD	1.10 (0.10)	1.11	0.89–1.38	.3582
Medications present at baseline				
PPI	5.39 (0.19)	2.15	2.00–2.32	<.0001
Histamine-2 blockers	5.99 (0.20)	2.45	2.28–2.63	<.0001
ACE inhibitors	3.30 (0.35)	1.22	0.99–1.50	.0616
Metformin	2.35 (0.31)	0.87	0.67–1.12	.2769

The reference group for each row analysis are children without the specified baseline comorbidity or medication. Asthma was defined as ≥2 encounters with a diagnosis and prescription of ≥1 asthma drug. ACE, angiotensin-converting enzyme; PPI, proton pump inhibitor.
[a] Rate per 1000 patient years.

are less frequently reported. Using National Health Interview Survey self-reports, Rudd and Moorman[47] calculated an asthma incidence of 6.0 per 1000 patient years over 1980–1996. Similarly, Behavioral Risk Factor Surveillance System self-report data (asthma call-back survey) were used to estimate an overall pediatric asthma incidence of 12.5 per 1000 patient years from 2006 to 2008.[48] Incidence rates in the current study were influenced by how asthma was defined. When asthma required a single encounter with a physician diagnosis, the incidence ranged from 18.41 per 1000 patient years in children with normal weight to 24.53 per 1000 patient years in children with obesity. When an asthma diagnosis was defined as 2 encounters with a physician diagnosis and medication prescription, the incidence ranged from 2.4 (normal weight) to 3.2 (obesity) per 1000 patient years.

Previous studies have not had sufficient power to detect differences between racial and/or ethnic groups and other important modifiers. Significant risk determinants in our data included male sex, age <5 years, African-American race, and public or Medicaid insurance. Hispanic ethnicity was associated with a reduced incidence, likely reflecting the heterogeneity of the Hispanic population in the United States and the so-called "Hispanic Paradox."[49] The comorbidities allergic rhinitis, food allergy, and anaphylaxis were significantly associated with asthma risk. The role of gastroesophageal reflux disease (GERD) in promoting asthma has been debated, but we found no association between GERD-related conditions (heartburn, esophagitis, and esophageal reflux) and incident asthma. Interestingly, proton pump inhibitors and histamine-2 blockers, commonly used to treat GERD, were significantly associated with asthma risk and warrant further study.

Regardless of the diagnostic definition we used, the risk of incident asthma diagnosis among children with obesity was increased by 26% to 38% compared with that of children with a normal-range BMI percentile in our study. The risk of asthma among children who were overweight was modestly increased by 8% to 17%. Importantly, when an asthma diagnosis required a second asthma encounter and confirmation by spirometry, the association between obesity and asthma risk remained. After adjustments for site and demographic variables (and

Downloaded from www.aappublications.org/news by guest on December 1, 2018

TABLE 4 Incidence Rates and RRs for New Asthma by BMI Percentile at Baseline

	Normal Weight (5th–84th)	Overweight (85th–94th)	*P*	Obesity (≥95th)	*P*
Any asthma diagnosis					
N (%)	18 661 (7.35)	10 660 (8.5)	—	12 009 (9.65)	—
Incidence rate[a]	18.41	20.80	—	24.53	—
Crude RR (95% CI)	1.0 (reference)	1.13 (1.10–1.16)	<.0001	1.33 (1.30–1.36)	<.0001
Model 1 (95% CI)	1.0 (reference)	1.14 (1.11–1.17)	<.0001	1.32 (1.29–1.35)	<.0001
Model 2 (95% CI)	1.0 (reference)	1.14 (1.11–1.17)	<.0001	1.31 (1.28–1.34)	<.0001
2 asthma diagnoses and asthma medication					
N (%)	2462 (0.97)	1455 (1.13)	—	1545 (1.24)	—
Incidence rate[a]	2.43	2.84	—	3.16	—
Crude RR (95% CI)	1.0 (reference)	1.17 (1.10–1.25)	<.0001	1.30 (1.22–1.38)	<.0001
Model 1 (95% CI)	1.0 (reference)	1.17 (1.09–1.25)	.002	1.28 (1.20–1.36)	<.0001
Model 2 (95% CI)	1.0 (reference)	1.17 (1.09–1.24)	<.0001	1.26 (1.18–1.34)	<.0001
2 asthma diagnoses plus confirmation with spirometry					
N (%)	976 (0.38)	527 (0.41)	—	649 (0.52)	—
Incidence rate[a]	0.96	1.03	—	1.33	—
Crude RR (95% CI)	1.0 (reference)	1.08 (0.96–1.20)	.2231	1.38 (1.25–1.52)	<.0001
Model 1 (95% CI)	1.0 (reference)	1.08 (0.97–1.20)	.1411	1.31 (1.18–1.44)	<.0001
Model 2 (95% CI)	1.0 (reference)	1.09 (0.98–1.21)	.1255	1.29 (1.16–1.42)	<.0001

Multivariable model 1 was adjusted for age, race, ethnicity, sex, site, and insurance status. Multivariable model 2 was adjusted for age, race, ethnicity, sex, site, insurance status, baseline allergic rhinitis, baseline food allergy, and baseline proton pump inhibitor use. RR, risk ratio; —, not applicable.

[a] Per 1000 patient years.

TABLE 5 AR of Overweight and Obesity in Asthma Incidence

	BMI Percentile at Baseline		
	Overweight (85th–94th)	Obesity (≥95th)	Overweight and Obesity (≥85th)
Any asthma diagnosis			
AR incidence[a]	2.39 (2.26, 2.52)	6.12 (5.95, 6.29)	4.21 (4.18, 4.24)
AR%[b]	11.49 (11.08, 11.89)	24.95 (24.68, 25.21)	18.61 (18.50, 18.73)
PAR incidence[c]	0.80 (0.75, 0.85)	1.99 (1.95, 2.03)	2.09 (2.02, 2.16)
PAR%[d]	4.16 (3.88, 4.45)	9.75 (9.47, 10.05)	10.20 (9.78, 10.63)
2 asthma diagnoses and asthma medication			
AR incidence[a]	0.41 (0.36, 0.46)	0.73 (0.67, 0.79)	0.57 (0.55, 0.58)
AR%[b]	14.48 (13.44, 15.42)	23.07 (22.25, 23.81)	18.90 (18.63, 19.20)
PAR incidence[c]	0.14 (0.12, 0.15)	0.24 (0.23, 0.25)	0.28 (0.26, 0.31)
PAR%[d]	5.38 (4.67, 6.23)	8.90 (8.18, 9.75)	10.38 (9.27, 11.61)
2 asthma diagnoses plus confirmation with spirometry			
AR incidence[a]	0.07 (0.04, 0.09)	0.36 (0.32, 0.40)	0.21 (0.20, 0.22)
AR%[b]	6.32 (4.00, 8.28)	27.38 (26.29, 28.30)	17.90 (17.41, 18.45)
PAR incidence[c]	0.02 (0.01, 0.03)	0.12 (0.11, 0.13)	0.10 (0.09, 0.12)
PAR%[d]	2.20 (1.15, 3.62)	10.90 (9.78, 12.37)	9.78 (8.06, 11.83)

AR%, attributable risk percent; PAR%, population attributable risk percent.

[a] AR is expressed as an incidence rate per 1000 patient years.

[b] AR% is the percent of the incidence due to the exposure and the proportion of the incidence of a disease in the exposed population that would be eliminated if exposure were absent.

[c] The incidence of disease in the whole population due to the exposure; PAR = $\text{incidence}_{population} - \text{incidence}_{unexposed}$, expressed per 1000 patient years.

[d] PAR% is the percent of disease incidence for the whole population due to the exposure or the percent of disease incidence avoided if the study population were unexposed; $\text{PAR/incidence}_{population}$.

including the addition of influential atopic conditions and proton pump inhibitor use), obesity remained a strong risk factor for spirometry-confirmed asthma.

With our study, we provide a novel understanding for the extent to which childhood obesity worsens the pediatric asthma epidemic in the United States. On account of childhood obesity alone, the rate of new asthma diagnosis increases by >6 cases per 1000 patient years. By avoiding obesity, children would reduce their risk for new asthma by 26% to 38% compared with children with a normal BMI percentile. The World Health Organization and the 2014 Global Asthma Report show that as many as 334 million persons worldwide suffer from asthma, with a sizable portion being children. Assuming that current estimates of the US pediatric asthma prevalence (6–8 million cases) are correct, it is suggested in our data that up to 12.7% (or up to 1 million) of cases of childhood asthma are directly attributable to overweight and obesity. Currently, there are few known preventable factors that can be used to reduce childhood asthma. With these data, it is suggested that reducing the onset of obesity in childhood may significantly reduce the public health burden of asthma. Our data reveal that the effect of obesity makes a common high-morbidity condition significantly more common. In addition, because we and others have shown that obesity among children with asthma

Downloaded from www.aappublications.org/news by guest on December 1, 2018

appears to increase disease severity,[50–52] the findings of the current report are particularly compelling.

There are several limitations of this study, including retrospective electronic health data. Our study results depended on the accuracy of record-keeping that was collected for clinical care, not research. The documentation of asthma diagnosis and ordering of spirometry was made at the discretion of the treating clinician. Given the retrospective nature of the study, we are unable to draw absolute conclusions regarding the causal nature of the association between obesity and asthma. Selection bias and the inability to affect exposures are also limitations for retrospective studies. Our study reflects a fairly broad geographic distribution of the United States that involves local urban and suburban patient populations and likely many surrounding rural patients sent to these generally urban centers; the relative representativeness of urban versus rural populations is not known. Rural children may be relatively underrepresented. Considering that current rates of childhood overweight and obesity are greater in rural areas versus suburban and urban areas,[53] the finding that 10% to 13% of all US cases are directly due to overweight or obesity should be considered a conservative estimate.

Strengths of this study are its large sample size and matching design used to adjust for region, demographic effects, and variable observation periods. Additionally, this longitudinal data set spans over 7 years and includes multidimensional data (involving all clinical settings) from 6 large pediatric hospital systems across the United States, with locations in the Northeast, mid-Atlantic, Southeast, West, and Pacific Northwest. The health care data came from diverse settings, including primary, subspecialty, urgent, and hospital care, from urban and rural settings and has been curated for quality assurance.[41,42,54] Lastly, in this study, we reduced the potential for differential misdiagnostic bias between children with normal weight and obesity by excluding children with the highest likelihood for occult asthma at baseline and using both clinical features and spirometry (airflow obstruction or bronchodilator responsiveness) to confirm asthma.

CONCLUSIONS

Obesity in children significantly increases the risk for new physician-diagnosed asthma and asthma confirmed by pulmonary function testing. Pediatric obesity accounts for a substantial component of new asthma cases among children in the United States. Successful interventions which reduce pediatric obesity must be a major public health priority to improve the quality of life of children and reduce obesity's contribution to pediatric asthma.

ACKNOWLEDGMENTS

The research reported in this publication was conducted by using PEDSnet, a pediatric learning health system, and includes data from the following PEDSnet institutions: Children's Hospital Colorado, Children's Hospital of Philadelphia, Nemours Children's Health System, Nationwide Children's Hospital, Seattle Children's Hospital, and St Louis Children's Hospital. PEDSnet is a partner network and clinical data research network in PCORnet, the National Patient-Centered Clinical Research Network, an initiative funded by the Patient-Centered Outcomes Research Institute.

ABBREVIATIONS

AR: attributable risk
CI: confidence interval
EHR: electronic health record
FEV_1: forced expiratory volume in 1 second
FVC: forced vital capacity
GERD: gastroesophageal reflux disease
PAR: population attributable risk

DOI: https://doi.org/10.1542/peds.2018-2119

Accepted for publication Sep 19, 2018

Address correspondence to Jason E. Lang, MD, MPH, Divisions of Allergy and Immunology and Pulmonary Medicine, Duke Children's Hospital and Health Center, 203 Research Dr, MSRB-1 Room 127, Durham, NC 27710. E-mail: jason.lang@duke.org

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2018 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: Dr Dempsey serves on advisory boards for Merck, Sanofi Pasteur, and Pfizer and as a consultant for Pfizer; she does not receive any research funding from these entities; the other authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: Funded by Patient-Centered Outcomes Research Institute contract CDRN-1306-01556 and by institutional development funds from Nemours Children's Hospital and Nemours Children's Health System.

POTENTIAL CONFLICT OF INTEREST: Dr Dempsey received payment for serving on advisory boards for Merck, Sanofi Pasteur, and Pfizer and as a consultant for Pfizer; the other authors have indicated they have no potential conflicts of interest to disclose.

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2018-2979.

Downloaded from www.aappublications.org/news by guest on December 1, 2018

REFERENCES

1. Akinbami LJ, Moorman JE, Bailey C, et al. Trends in asthma prevalence, health care use, and mortality in the United States, 2001-2010. *NCHS Data Brief*. 2012;(94):1–8
2. Swallen KC, Reither EN, Haas SA, Meier AM. Overweight, obesity, and health-related quality of life among adolescents: the National Longitudinal Study of Adolescent Health. *Pediatrics*. 2005;115(2):340–347
3. Lang JE, Hossain MJ, Lima JJ. Overweight children report qualitatively distinct asthma symptoms: analysis of validated symptom measures. *J Allergy Clin Immunol*. 2015;135(4):886–893.e3
4. Skinner AC, Ravanbakht SN, Skelton JA, Perrin EM, Armstrong SC. Prevalence of obesity and severe obesity in US children, 1999-2016 [published correction appears in *Pediatrics*. 2018;142(3):e20181916]. *Pediatrics*. 2018;141(3):e20173459
5. Camargo CA Jr, Weiss ST, Zhang S, Willett WC, Speizer FE. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. *Arch Intern Med*. 1999;159(21):2582–2588
6. Nystad W, Meyer HE, Nafstad P, Tverdal A, Engeland A. Body mass index in relation to adult asthma among 135, 000 Norwegian men and women. *Am J Epidemiol*. 2004;160(10): 969–976
7. Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med*. 2007;175(7):661–666
8. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of childhood and adult obesity in the United States, 2011-2012. *JAMA*. 2014;311(8):806–814
9. Kumar S, Kelly AS. Review of childhood obesity: from epidemiology, etiology, and comorbidities to clinical assessment and treatment. *Mayo Clin Proc*. 2017;92(2):251–265
10. Zhang Z, Lai HJ, Roberg KA, et al. Early childhood weight status in relation to asthma development in high-risk children. *J Allergy Clin Immunol*. 2010;126(6):1157–1162
11. Burgess JA, Walters EH, Byrnes GB, et al. Childhood adiposity predicts adult-onset current asthma in females: a 25-yr prospective study. *Eur Respir J*. 2007;29(4):668–675
12. Jartti T, Saarikoski L, Jartti L, et al. Obesity, adipokines and asthma. *Allergy*. 2009;64(5):770–777
13. Mandhane PJ, Greene JM, Cowan JO, Taylor DR, Sears MR. Sex differences in factors associated with childhood- and adolescent-onset wheeze. *Am J Respir Crit Care Med*. 2005;172(1):45–54
14. Scholtens S, Wijga AH, Seidell JC, et al. Overweight and changes in weight status during childhood in relation to asthma symptoms at 8 years of age. *J Allergy Clin Immunol*. 2009;123(6):1312–1318.e2
15. Eneli IU, Karmaus WK, Davis S, Kuehr J. Airway hyperresponsiveness and body mass index: the Child Health and Environment Cohort Study in Hesse, Germany. *Pediatr Pulmonol*. 2006;41(6):530–537
16. Tollefsen E, Langhammer A, Romundstad P, Bjermer L, Johnsen R, Holmen TL. Female gender is associated with higher incidence and more stable respiratory symptoms during adolescence. *Respir Med*. 2007;101(5):896–902
17. Gilliland FD, Berhane K, Islam T, et al. Obesity and the risk of newly diagnosed asthma in school-age children. *Am J Epidemiol*. 2003;158(5):406–415
18. Castro-Rodríguez JA, Holberg CJ, Morgan WJ, Wright AL, Martinez FD. Increased incidence of asthmalike symptoms in girls who become overweight or obese during the school years. *Am J Respir Crit Care Med*. 2001;163(6):1344–1349
19. Gold DR, Damokosh AI, Dockery DW, Berkey CS. Body-mass index as a predictor of incident asthma in a prospective cohort of children. *Pediatr Pulmonol*. 2003;36(6):514–521
20. Chinn S, Rona RJ. Can the increase in body mass index explain the rising trend in asthma in children? *Thorax*. 2001;56(11):845–850
21. Mannino DM, Mott J, Ferdinands JM, et al. Boys with high body masses have an increased risk of developing asthma: findings from the National Longitudinal Survey of Youth (NLSY). *Int J Obes (Lond)*. 2006;30(1):6–13
22. Black MH, Zhou H, Takayanagi M, Jacobsen SJ, Koebnick C. Increased asthma risk and asthma-related health care complications associated with childhood obesity. *Am J Epidemiol*. 2013;178(7):1120–1128
23. Noal RB, Menezes AM, Macedo SE, et al. Is obesity a risk factor for wheezing among adolescents? A prospective study in southern Brazil. *J Adolesc Health*. 2012;51(suppl 6):S38–S45
24. Mamun AA, Lawlor DA, Alati R, O'Callaghan MJ, Williams GM, Najman JM. Increasing body mass index from age 5 to 14 years predicts asthma among adolescents: evidence from a birth cohort study. *Int J Obes (Lond)*. 2007;31(4):578–583
25. Murray CS, Canoy D, Buchan I, Woodcock A, Simpson A, Custovic A. Body mass index in young children and allergic disease: gender differences in a longitudinal study. *Clin Exp Allergy*. 2011;41(1):78–85
26. Taveras EM, Rifas-Shiman SL, Camargo CA Jr, et al. Higher adiposity in infancy associated with recurrent wheeze in a prospective cohort of children. *J Allergy Clin Immunol*. 2008;121(5):1161–1166.e3
27. Wake M, Canterford L, Patton GC, et al. Comorbidities of overweight/obesity experienced in adolescence: longitudinal study. *Arch Dis Child*. 2010;95(3):162–168
28. van Huisstede A, Castro Cabezas M, van de Geijn GJ, et al. Underdiagnosis and overdiagnosis of asthma in the morbidly obese. *Respir Med*. 2013;107(9):1356–1364
29. Ekström S, Magnusson J, Kull I, et al. Body mass index development and asthma throughout childhood. *Am J Epidemiol*. 2017;186(2):255–263
30. Abu-Hasan M, Tannous B, Weinberger M. Exercise-induced dyspnea in children and adolescents: if not asthma then what? *Ann Allergy Asthma Immunol*. 2005;94(3):366–371

Downloaded from www.aappublications.org/news by guest on December 1, 2018

31. Weinberger M, Abu-Hasan M. Pseudo-asthma: when cough, wheezing, and dyspnea are not asthma. *Pediatrics*. 2007;120(4):855–864

32. Weinberger M, Abu-Hasan M. Perceptions and pathophysiology of dyspnea and exercise intolerance. *Pediatr Clin North Am*. 2009;56(1): 33–48, ix

33. Chawla J, Seear M, Zhang T, Smith A, Carleton B. Fifty years of pediatric asthma in developed countries: how reliable are the basic data sources? *Pediatr Pulmonol*. 2012;47(3): 211–219

34. Seear M, Wensley D, West N. How accurate is the diagnosis of exercise induced asthma among Vancouver schoolchildren? *Arch Dis Child*. 2005;90(9):898–902

35. Lowe L, Murray CS, Martin L, et al. Reported versus confirmed wheeze and lung function in early life. *Arch Dis Child*. 2004;89(6):540–543

36. National Asthma Education and Prevention Program. *Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Full Report 2007*. Bethesda, MD: National Heart, Lung, and Blood Institute, National Institutes of Health, US Department of Health and Human Services; 2007

37. Global Initiative for Asthma. 2018 GINA report: Global strategy for asthma management and prevention. Available at: https://ginasthma.org/2018-gina-report-global-strategy-for-asthma-management-and-prevention/. Accessed October 5, 2018

38. British Thoracic Society; Scottish Intercollegiate Guidelines Network. British guideline on the management of asthma. *Thorax*. 2014;69(suppl 1): 1–192

39. Shore SA. Obesity and asthma: possible mechanisms. *J Allergy Clin Immunol*. 2008;121(5):1087–1093; quiz 1094–1095

40. Song JW, Chung KC. Observational studies: cohort and case-control studies. *Plast Reconstr Surg*. 2010;126(6):2234–2242

41. Forrest CB, Margolis P, Seid M, Colletti RB. PEDSnet: how a prototype pediatric learning health system is being expanded into a national network. *Health Aff (Millwood)*. 2014;33(7):1171–1177

42. Forrest CB, Margolis PA, Bailey LC, et al. PEDSnet: a national pediatric learning health system. *J Am Med Inform Assoc*. 2014;21(4):602–606

43. Dundas I, Chan EY, Bridge PD, McKenzie SA. Diagnostic accuracy of bronchodilator responsiveness in wheezy children. *Thorax*. 2005;60(1):13–16

44. Galant SP, Morphew T, Guijon O, Pham L. The bronchodilator response as a predictor of inhaled corticosteroid responsiveness in asthmatic children with normal baseline spirometry. *Pediatr Pulmonol*. 2014;49(12):1162–1169

45. Akinbami LJ, Moorman JE, Garbe PL, Sondik EJ. Status of childhood asthma in the United States, 1980-2007. *Pediatrics*. 2009;123(suppl 3):S131–S145

46. Moorman JE, Akinbami LJ, Bailey CM, et al. National surveillance of asthma: United States, 2001-2010. *Vital Health Stat 3*. 2012;(35):1–58

47. Rudd RA, Moorman JE. Asthma incidence: data from the National Health Interview Survey, 1980-1996. *J Asthma*. 2007;44(1):65–70

48. Winer RA, Qin X, Harrington T, Moorman J, Zahran H. Asthma incidence among children and adults: findings from the Behavioral Risk Factor Surveillance system asthma call-back survey–United States, 2006-2008. *J Asthma*. 2012;49(1):16–22

49. Rosser FJ, Forno E, Cooper PJ, Celedón JC. Asthma in Hispanics. An 8-year update. *Am J Respir Crit Care Med*. 2014;189(11):1316–1327

50. Lang JE, Fitzpatrick AM, Mauger DT, et al; National Institutes of Health/National Heart, Lung and Blood Institute AsthmaNet. Overweight/obesity status in preschool children associates with worse asthma but robust improvement on inhaled corticosteroids. *J Allergy Clin Immunol*. 2018;141(4):1459–1467.e2

51. Lang JE, Hossain MJ, Lima JJ. Overweight children report qualitatively distinct asthma symptoms: analysis of validated symptom measures. *J Allergy Clin Immunol*. 2015;135(4):886–893.e3

52. Quinto KB, Zuraw BL, Poon KY, Chen W, Schatz M, Christiansen SC. The association of obesity and asthma severity and control in children. *J Allergy Clin Immunol*. 2011;128(5):964–969

53. Ogden CL, Fryar CD, Hales CM, Carroll MD, Aoki Y, Freedman DS. Differences in obesity prevalence by demographics and urbanization in US children and adolescents, 2013-2016. *JAMA*. 2018;319(23):2410–2418

54. Lang JE, Bunnell T, Hossain MJ, et al. Demonstrating the value of PEDSnet EHR-generated data: defining key determinants on the path from obesity to asthma in children (KOACH). 2017. Available at: https://pedsnet.org/research/pedsnet-studies-active/demonstrating-value-pedsnet-ehr-generated-data-defining-key-determinants-path-obesity-asthma-children-koach/. Accessed November 14, 2017

Downloaded from www.aappublications.org/news by guest on December 1, 2018

Being Overweight or Obese and the Development of Asthma

Jason E. Lang, H. Timothy Bunnell, Md Jobayer Hossain, Tim Wysocki, John J. Lima, Terri H. Finkel, Leonard Bacharier, Amanda Dempsey, Lisa Sarzynski, Matthew Test and Christopher B. Forrest

Pediatrics 2018;142;
DOI: 10.1542/peds.2018-2119 originally published online November 26, 2018;

Updated Information & Services	including high resolution figures, can be found at: http://pediatrics.aappublications.org/content/142/6/e20182119
References	This article cites 51 articles, 12 of which you can access for free at: http://pediatrics.aappublications.org/content/142/6/e20182119#BIBL
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): **Pulmonology** http://www.aappublications.org/cgi/collection/pulmonology_sub **Asthma** http://www.aappublications.org/cgi/collection/asthma_subtopic **Obesity** http://www.aappublications.org/cgi/collection/obesity_new_sub
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.aappublications.org/site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: http://www.aappublications.org/site/misc/reprints.xhtml

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Downloaded from www.aappublications.org/news by guest on December 1, 2018

PEDIATRICS®
OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Being Overweight or Obese and the Development of Asthma

Jason E. Lang, H. Timothy Bunnell, Md Jobayer Hossain, Tim Wysocki, John J. Lima, Terri H. Finkel, Leonard Bacharier, Amanda Dempsey, Lisa Sarzynski, Matthew Test and Christopher B. Forrest

Pediatrics 2018;142;
DOI: 10.1542/peds.2018-2119 originally published online November 26, 2018;

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://pediatrics.aappublications.org/content/142/6/e20182119

Data Supplement at:
http://pediatrics.aappublications.org/content/suppl/2018/11/19/peds.2018-2119.DCSupplemental

Pediatrics is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. Pediatrics is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2018 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 1073-0397.

American Academy of Pediatrics
DEDICATED TO THE HEALTH OF ALL CHILDREN™

Downloaded from www.aappublications.org/news by guest on December 1, 2018

Supplemental Information

SUPPLEMENTAL TABLE 6 Epidemiological Formulas Used in KOACH Analyses

Statistic	Formula	Description
AR	$(\text{Incidence}_{exposed}) - (\text{incidence}_{unexposed})$	Also called excess risk; the difference in the rate of asthma incidence between an exposed population (with obesity) and an unexposed (without obesity) population; also the portion of the incidence in the exposed (with obesity) population due to the exposure (obesity), which would be eliminated if obesity were not present in the population
AR%	$([\text{Incidence}_{exposed}] - [\text{incidence}_{unexposed}])/\text{incidence}_{exposed}$	The percent of the incidence of asthma in the population with obesity that is due to obesity or the percent of the incidence of asthma in the population with obesity that would be eliminated if obesity were eliminated
PAR	$(\text{Incidence}_{population}) - (\text{incidence}_{unexposed})$	PAR is the portion of the incidence of asthma in the population (with and without obesity) that is due to obesity or the incidence of asthma in the population that would be eliminated if obesity were eliminated.
PAR%	$([\text{Incidence}_{population}] - [\text{incidence}_{unexposed}])/\text{incidence}_{population}$	The percent of the incidence of asthma in the population (with or without obesity) that is due to obesity; the percent of the incidence of asthma in the population that would be eliminated if obesity were eliminated

AR%, attributable risk percent; KOACH, Key Determinants on the Path from Obesity to Asthma in Children study; PAR%, population attributable risk percent.

SUPPLEMENTAL TABLE 7 Asthma Medications

Type of Medication	Asthma Medications
Controller	Fluticasone propionatea,[a] beclomethasone dipropionatea, flunisolide inhalant, budesonidea,[a] mometasonea,[a] ciclesonide, montelukast, zafirlukast, and zileuton
Systemic steroid	Prednisone, prednisolone, and dexamethasone

[a] Includes individual products and those with combination long-acting β-agonists.