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Atopy, but Not Obesity is Associated with Asthma Severity Among Children with Persistent Asthma

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Abstract

Background and Objective—Obesity is associated with an increased risk of asthma in children. Atopic sensitization is a major risk factor for asthma including severe asthma in children. It is unclear if obesity is associated with worse asthma control or severity in children and how its effects compare to atopy. We sought to examine relationships of weight status and atopy to asthma control and severity among a population of predominantly low income, minority children and adolescents with persistent asthma.

Methods—A cross-sectional analysis of 832 children and adolescents, age range 5–17 years, with persistent asthma was performed. Clinical assessments included asthma questionnaires of symptoms, asthma severity score, health care utilization and medication treatment step, lung function testing, and skin prick testing as well as measures of adiposity. Data were collected between December 2010 and August 2014 from Johns Hopkins Hospital in Baltimore, MD and Children's Hospital of Boston, MA.

Results—Obesity was not associated with worse asthma control or severity in this group of predominantly low income, minority children and adolescents with persistent asthma. However, a greater degree of atopy was associated with lower lung function, higher asthma severity score, and higher medication treatment step.

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Declaration of Interest

All of the authors have indicated they have no potential conflicts of interest to disclose.

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Conclusion—Atopy may be a more important risk factor for asthma severity than obesity among low-income minority children and adolescents with persistent asthma living in Northeastern cities in the United States.

Keywords

asthma; obesity; atopy

INTRODUCTION

Asthma and obesity are common conditions in pediatrics that have both had a dramatic increase in prevalence over the past few decades in the United States, suggesting that these conditions may be linked.(1;2) The mechanism(s) linking obesity and asthma are not fully understood but may include genetic factors, mechanical effects of obesity on the lung, chronic systemic inflammation and lifestyle factors (3). Among adult asthmatics, obesity is associated with worse quality of life, poor asthma control, and increased healthcare utilization and decreased responsiveness to inhaled corticosteroids, the mainstay of therapy in asthma.(4–7) While obesity is associated with increased risk of developing asthma in children, the relationship between obesity and asthma health (i.e. asthma control, severity, symptoms) in children and adolescents are conflicting.(8–14)

In children, atopic sensitization is a well-established and major risk factor for severe asthma (15–18), but it is unclear whether obesity is also a risk factor; and if so, how its effects on asthma control and severity compare to those of atopy. While some studies of children have found that being overweight or obese is associated with markers of worse asthma control or increased severity including exacerbations, poor control, and symptoms (8–11), other studies have not.(12–14) How the risk associated with obesity compares to that associated with atopy is important to understand to help guide pediatricians in targeting their management of children with asthma. These questions are especially important in high-risk populations, such as low-income an minority children who have worse asthma than their non-low-income, non-minority counterparts, and are more likely to be overweight or obese and atopic (19–21). A better understanding of the risks (obesity vs atopy) on asthma in this high risk population will inform public health approaches to reducing asthma morbidity in this high-risk population.

We therefore sought to examine relationships of weight status and atopy to asthma control and severity among a population of predominantly low income, minority children and adolescents with persistent asthma.

METHODS

Study Design and Population

Relationships between weight status, atopy and asthma characteristics were examined in an Institutional Review Board-approved, cross-sectional analysis of children and adolescents drawn from the baseline screening visit for a clinical trial performed in the clinical research clinics at two sites, The Johns Hopkins Children’s Center in Baltimore, Maryland, and

Children's Hospital of Boston in Boston, Massachusetts from December 2010 through August 2014. The clinical trial is the Mouse Allergen and Asthma Intervention Trial, whose primary objective is to test the effect of an integrated pest management intervention on asthma among mouse sensitized and exposed children and adolescents with asthma. The participants met NAEPP criteria for persistent asthma and had had an exacerbation in the previous 12 months (22). Written consent was obtained from parents/guardians of participants and assent was obtained from participants.

Four thousand and fifty-six potential participants were phone screened. Two thousand one hundred and thirty-nine of the 4056 were interested and underwent telephone screening for eligibility assessment. Age and race/ethnicity were not available for the majority of the potential participants. One thousand two hundred and twenty-eight children were identified as eligible for the baseline clinic visit. Nine hundred of the 1228 came in for the screening clinic visit. Of the 908 who came in for screening clinic visit, 814 were included in the analysis population of this study and 94 participants were excluded due to pregnancy, were smokers, underweight (BMI $<5^{th}$ percentile), or did not have sufficient symptoms at the clinic visit to meet criteria for persistent asthma. Overall, those who were included in this analysis were similar to those who were eligible to be in the study after completing telephone screening (Table S1. Online Repository). All study visit procedures were performed on the same day during the screening visit.

Study Visit Procedures

Skin prick testing was performed to 14 allergens at the study visit using the MultiTest II device (Lincoln Diagnostics, Decatur, IL), with positive histamine control and a negative glycerol control. A positive skin test was defined as a net orthogonal wheal size of 3mm or greater. Atopy was defined as ≥ 1 positive skin test. The allergens tested were: dog, cat, *Dermataphagoides pteronyssinus*, *Dermataphagoides farinae*, rat epithelia, German cockroach, American cockroach, mouse epithelia, tree mix, grass mix, *Alternaria tenius*, *Aspergillus fumigatus*, common ragweed, and *Cladosporium*. (Greer Laboratories, Lenoir, NC) Participants who were wheezing or on anti-histamines at the time of visit did not undergo skin testing. Skin prick testing was considered invalid if there was an inadequate histamine response.

Spirometry was performed using a Koko spirometer according to American Thoracic Society (ATS) standards.(23;24) Fractional exhaled nitric oxide (F_eNO) was measured using the Niox MINO (Aerocrine, Uppsala, Sweden) according to the manufacturer's instruction and ATS standards.(25)

Questionnaires were administered that captured demographic information, pulmonary and allergic history, medications, symptoms, and asthma-related health care utilization. The Asthma Control Test (ACT, 12 years and older) and the Childhood Asthma Control Test (c-ACT, 4–11 years) were used to determine asthma control status; a score of >19 indicated well-controlled asthma.(26;27) Height was measured twice to the nearest 0.1cm using a stadiometer. Weight was measured twice to the nearest 0.1kg using a digital scale. Height and weight measurements were averaged and BMI was calculated. BMI percentiles were calculated based on Centers for Disease Control (CDC) BMI calculator.(28) Underweight

was defined as BMI <5%ile, healthy weight was defined as 5th to <85%ile, overweight was defined as BMI 85th to <95th percentile and obesity was defined as BMI ≥95th percentile. (29) Waist circumference was measured twice to the nearest 0.1cm at minimal inspiration in standing position at the high point of the iliac crest and parallel to the floor.

Statistical Analyses

Underweight participants were excluded from the analyses as there were too few (n=18) to perform meaningful analyses. Asthma characteristics were examined across groups of interest (e.g. BMI categories, atopic groups and waist circumference) using binomial regression models for asthma symptoms, logistic regression models for healthcare utilization or linear regression models for lung function, medication treatment step and severity score. Analyses were also stratified by race, gender, and age to determine if body mass was associated with clinical features of asthma among specific demographic groups. Interactions between race (black vs. non-black), gender, age (<12 vs. ≥12 years), and BMI category were tested by inclusion of interaction terms in the final models, with obese/nonobese as the BMI variable. A variable indicating the number of positive skin prick tests (SPT) was constructed to create an ordinal measure of atopy. We created four atopy groups as follows: (1) non-atopic (0 +SPTs), (2) atopic with 1–3 +SPTs, (3) atopic with 4–7 +SPTs, and (4) atopic with ≥8 +SPTs. To create these groups the atopic participants (defined as having at least one positive skin test) were divided into tertiles and non-atopics were considered as their own group. Asthma characteristics were also examined across atopic groups using appropriate models. Because the atopy variable was an ordinal variable, models were created to estimate the relationship between atopy and the outcomes in two different ways. First, models were created to estimate the change in odds of the outcome with each step-up in atopy category. Second, the atopy variable was modeled using dummy variables, which results in an estimated difference in odds of the outcome among participants in any given atopy category relative to the non-atopic category. Models were adjusted for race, ethnicity, age, gender, study site, controller medication, household income, and atopy groups or BMI category. Controller medication as a covariate was a dichotomous variable (yes/no) based on reported use in the past 2 weeks prior to visit. Waist circumference was transformed into a normal distribution and then a z-score was created. We examined relationships between waist circumference z-score and asthma characteristics using appropriate models.

The Composite Asthma Severity Index (CASI) was used to determine asthma severity which included symptoms, lung function measures, controller treatment and exacerbations (30). The CASI is a validated instrument for asthma severity that takes into account impairment, risk and amount of medication needed to maintain control. Controller medication treatment step was derived from information collected from medications brought to screening visit and reported use of medications in the previous two weeks including inhaled corticosteroid (ICS) +/− long-acting beta-agonist (LABA). Treatment steps are defined as: 1 (albuterol only), 2 (low dose ICS), 3 (low dose ICS with LABA or medium dose ICS), 4 (medium dose ICS with LABA), and 5 (high dose ICS +/− LABA). The composite asthma severity index and controller medication treatment step was adapted from Wildfire et al.(30)

Analyses were performed with STATA 11.0/SE (StataCorp, College Station, TX). A p value < 0.05 was considered statistically significant for main effects and interactions.

RESULTS

The study population was predominantly male, African American, and low income with a mean age of 9.9 years (range of 5.0–17.98) (Table 1). Fifty-two percent of the participants were healthy weight, 17% were overweight, and 31% were obese. The majority of the participants were atopic (84.5%). The obese participants were more likely to be female and have either private insurance or self-pay than the non-obese participants. Overall, groups by BMI category were similar in terms of almost all measures of asthma control and severity, as well as atopy (Tables 2 and 3). In bivariate analyses, overweight and obese participants had a lower FEV_1/FVC compared to healthy weight participants (mean 80.9% (SD ±8.0) and 80.4% (SD ±8.3) vs. 82.1% ((SD ±9.1), p= 0.02) and obese participants had fewer days of nocturnal symptoms compared to healthy weight and overweight participants (mean 1.2 days (SD ±1.6) vs. 2.0 days (SD ±3.3) and 2.7 days (SD ±4.1), p = 0.02). However, there was no association between BMI group and FEV_1/FVC or nocturnal symptoms after adjusting for covariates. Children who did not have skin test data were included in the analyses of weight status (n=135). Sensitivity analyses were performed by excluding those who did not have valid skin test data and the results were similar (data not shown).

Relationships between atopy groups and measures of asthma control and severity were also examined (Table 4). A greater degree of atopy was associated with lower lung function, higher asthma severity score, and higher medication treatment step. For example, participants in the highest atopic group (≥8 +SPTs) had a mean FEV_1/FVC of 79.1% (SD ±8.9) compared to non-atopic participants who had a mean FEV_1/FVC of 84.1% (SD ±7.9) (p≤0.001). Medication treatment step also increased with greater atopy, for example 49% of participants who were non-atopic had been prescribed treatment step 3 or higher (equivalent to low dose ICS with LABA or medium dose ICS or higher) compared to 68% in the highest atopic group (p=0.001). Asthma severity was also increased with greater atopy. Non-atopic participants had a mean asthma severity score of 6.0 (SD ±3.5) compared to a mean score of 7.2 (SD ±3.5) among the highest atopic group (8+ SPTs) (p=0.003). These results were consistent when atopic groups were compared to non-atopic group using multivariate models (Table 5). There was no difference in asthma symptoms or acute care utilization among atopic groups (Tables 4 and 5).

Relationships between BMI categories and clinical features of asthma were also examined by race, gender, and age to determine if body mass was a risk factor for asthma control or severity for certain demographic groups (Tables S2, S3, and S4. Online Repository). Overall, there was little evidence that relationships between body mass and measures of asthma control or severity differed by race, gender, or age. Analyses were also performed examining associations between waist circumference and asthma symptoms, acute care utilization, or lung function and findings were similar to those when BMI categories were used (Tables S5. Online Repository). Medications were not held prior to spirometry; however, we collected information about whether the participant had used albuterol in the previous 24 hours

(n=147). We performed a sensitivity analysis by excluding those who had and found that results were similar (data not shown).

DISCUSSION

In this urban, predominantly low income, minority population, greater weight status was not associated with measures of asthma control or severity. However, we found that atopic sensitization was strongly associated with measures of more severe asthma, including higher treatment step, higher asthma severity score, and lower lung function. Our results suggest that obesity is not a major risk for asthma control or severity in this population, particularly when viewed in the context of the strong relationships between atopy and asthma severity.

In contrast to adult studies (31–33), our findings suggest that obesity is not a major risk factor for uncontrolled asthma or more severe asthma, but that atopy is a clear risk factor for asthma severity, in low-income, minority pediatric populations. We did not, however, find associations between atopy and asthma symptoms. The reasons for the lack of an association with symptoms are not clear, but we speculate that the degree of atopy influences the more subacute and chronic manifestations of asthma such as lung function and controller medication requirements rather than the more acute changes captured by days of asthma symptoms. The differences between our findings and those in adult populations may be due to the fact that atopy is a less prominent feature of asthma in adults than children. In addition, our findings highlight differences between the pathophysiology of asthma in children and that in adults as childhood asthma, at least in the population studied here, appears to be characterized by a less prominent role for obesity and a more prominent role of atopy.

In contrast to our study, some studies of children have found that being overweight or obese is associated with markers of worse asthma health including exacerbations, poor control, and symptoms. Black et al found that in children and adolescents, obesity was associated with an increased risk of asthma exacerbations requiring ED visits or oral corticosteroids. However this study was a longitudinal analysis of a group of children and adolescents enrolled in Kaiser Permanente in Southern California, which included children with newly diagnosed asthma followed for one year (9). Not only did this population have milder asthma overall than ours, but the demographic characteristics were also different from those of our population. Approximately half of the study population was Hispanic and only 10% African-American, with the majority of the participants having private health insurance. In another study that used data from NHANES, Michelson et al found that an elevated BMI z score was associated with more severe asthma; however, asthma severity was based on reported symptom burden from questionnaires and did not include any lung function or medication data.(8) At least 50% of the participants with asthma were classified as mild with little/no symptoms and no acute care visits or exacerbations over a three month period. In a study of minority children in the U.S., Borrell et al found worse asthma control in boys.(34) However, in girls, this association varied with race/ethnicity with obese Mexican American girls having greater odds of worse asthma control. The study population from the studies mentioned included a greater percentage of white and/or Hispanic children, which differs from our population of predominantly urban, low-income, minority children and adolescents

in Boston and Baltimore City and may reflect racial or ethnic differences in asthma and obesity that we were not able to study in our population. Additionally, these studies included children with mild intermittent asthma, which were excluded from our study. Lastly, these studies did not report or assess atopy and may have included children with no or a lesser degree of atopy compared to our study. In a study from major urban areas in the U.S that included Baltimore and Boston, Kattan et al found that increased adiposity was associated with reduced asthma control and increased exacerbations among girls only; however, this study differed from ours as it was among adolescents aged 12–20 years of age and from a more geographically heterogeneous sample.(35) With a mean age of 14 years, the study participants were likely pubertal or post-pubertal and would more likely resemble the adult population in which there are stronger associations between obesity and asthma health. However, we did not see associations between body mass and asthma outcomes even among the adolescent subset of our study population. Although one study found that atopy may mediate the relationship between obesity and asthma morbidity,(36), our findings are not consistent with these as obesity and measures of atopy were not associated in our population.

While our study suggests that obesity is not a major risk factor for worse asthma health, obesity is important to consider in asthma health in children and adolescents in other ways. The preponderance of epidemiologic studies indicates that overweight/obesity is a risk factor of the development of asthma throughout the lifespan.(37–40) In addition, even though obesity may not be associated with more severe asthma, it may be a marker of an asthma endotype in that the pathophysiology of asthma among overweight and/or obese children may differ from that among healthy weight children. Indeed, being overweight is a susceptibility factor for environmental exposure, including pollutant exposure (41–43) and obesity in children may be associated with steroid resistance or immune/metabolic abnormalities.(44;45) Lastly, obesity may be important in some asthmatics that are not captured by our study population, such as Caucasians, those who are non-atopic, or those with milder asthma as suggested in previous studies.(8–10)

The strength of our study is that it contains a relatively large sample population with well-characterized asthma measures including lung function testing and pulmonary inflammation (F_eNO), symptoms, health care utilization, skin prick testing and medications. Additionally, our study included a predominantly low income, minority population that is at high risk for asthma morbidity and mortality. There are several potential limitations to our study. Because our study was cross-sectional, we cannot make any temporal associations related to changes in weight over time that may affect asthma control or severity. Additionally, it is possible that we did not measure a particular outcome affected by BMI however, we did include a wide range of variables that captured asthma symptoms, exacerbations, medications, lung function, inflammation, and asthma severity. It is important to note that there are limitations to using BMI as a marker of adiposity as it may not accurately reflect the relative amount of body fat.(46) Other measures of adiposity include waist to hip ratios, skin fold thickness and dual-energy X-ray absorptiometry. However, we did not see any relationships between waist circumference and asthma morbidity in our study, consistent with other studies that used additional measures of adiposity to look at effects of adiposity on asthma control and/or severity.(35;36) Lastly, we studied a population that was predominantly minority, low-

income, and resided in Baltimore and Boston. One the one hand, this is a strength of the study as it is important to understand asthma in this population specifically given their high burden of disease, but on the other hand, our findings may not be generalizable to populations with different characteristics.

In summary, atopy may be a more important risk factor for asthma severity than obesity among low-income minority children and adolescents with persistent asthma. While interventions aimed at obesity are important, particularly for future cardiovascular disease and diabetes risks, our study suggests that it is not likely to reduce asthma severity in these populations. Instead, a more effective approach to reducing asthma severity may include targeting atopy, potentially through interventions aimed at allergen exposure reduction or medications, such as omalizumab, that target IgE.

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Table 1

Baseline Characteristics, n=814

	All n=814	Healthy Weight (5th–<85th percentile) n=426	Overweight (85th–<95th percentile) n=138	Obese (≥95th percentile) n=250	P value	P value (trend)
Age, mean (range)	9.9 (5.0–17.98	9.7 (5.0–17.8)	9.9 (5.1–17.5)	10.2 (5.0–17.8)	0.09	0.03
Male, n (%)	486 (59.7)	270 (63.4)	82 (59.4)	134 (53.6)	0.37	0.01
Race, n (%)						
Black	567 (69.7)	290 (68.1)	100 (72.5)	177 (70.1)	0.37	0.35
White	135 (16.6)	70 (16.4)	21 (15.2)	44 (17.6)		
Asian/multi/other	112 (13.8)	66 (15.5)	17 (12.3)	29 (11.6)		
Hispanic, yes (%)	171 (21.0)	80 (19.0)	29 (21.3)	62 (25.1)	0.17	0.06
Maternal education, n (%)						
Less than high school	139 (17.3)	75 (17.9)	15 (11.1)	49 (19.8)	0.18	0.68
High school graduate	284 (35.4)	156 (37.1)	44 (32.6)	84 (34.0)		
Some college or more	380 (47.3)	189 (45)	76 (56.3)	114 (46.2)		
Household income, n (%)						
Less than 20,000	356 (44.4)	187 (44.3)	52 (38.2)	117 (47.2)		
20,000 to 39,999	206 (25.6)	97 (23)	36 (26.5)	73 (29.4)	0.14	0.35
40,000 or more	155 (19.2)	92 (21.8)	31 (22.8)	32 (12.9)		
Refused/don’t know	89 (11.0)	46 (10.9)	17 (12.5)	26 (10.5)		
Insurance, n (%)						
Private/self-pay	135 (16.6)	73 (17.1)	34 (24.6)	28 (11.2)	< 0.01	0.10
Public	670 (82.3)	349 (81.7)	101 (73.2)	220 (87.7)		
unknown	9 (1.1)	5 (1.2)	3 (2.2)	3 (1.2)		
Atopic sensitization, # of positive skin prick tests						
0	105 (15.5)	49 (13.8)	20 (17.0)	36 (17.5)	0.51	0.25
1–3	194 (28.6)	105 (29.6)	30 (25.4)	59 (28.6)		

	All n=814	Healthy Weight (5th–<85th percentile) n=426	Overweight (85th–<95th percentile) n=138	Obese (≥95th percentile) n=250	P value	P value (trend)
4–7	246 (36.2)	129 (36.3)	39 (33.1)	78 (37.9)		
8+	134 (19.7)	72 (20.3)	29 (24.6)	33 (16.0)		
Skin Test Sensitivities						
Pollens (tree, grass or weeds)	411 (60.5)	228 (64.2)	66 (55.9)	117 (56.8)	0.11	0.06
Mouse	370 (54.5)	199(56.1)	69 (58.5)	102 (49.5)	0.19	0.15
Rat	287 (42.3)	158 (44.6)	57 (48.3)	72 (35.0)	0.03	0.04
Cat	271 (39.9)	137 (38.6)	53 (44.9)	81 (39.3)	0.46	0.79
Cockroach	266 (39.2)	141 (39.7)	48 (40.7)	77 (37.4)	0.78	0.59
Molds (*Cladosporium, Aspergillus*, or *Alternaria*)	265 (39.0)	139 (39.2)	54 (45.8)	72 (35.0)	0.18	0.47
Dust mite	255 (37.6)	125 (35.2)	47 (39.8)	83 (40.3)	0.44	0.23
Dog	110 (16.2)	63 (17.8)	15 (12.7)	32 (15.5)	0.41	0.41

1st p value for difference between BMI groups using Kruskal-Wallis or Chi Square.

2nd p value test for trend between BMI groups.

Table 2

BMI Categories and Measures of Asthma Control and Severity

	Healthy weight n=427	Overweight n=137	Obese n=251	p value	p value (trend)
Asthma Symptoms	Mean days (SD)/past 2 weeks				
Cough, wheeze or shortness of breath	3.3 (3.8)	3.0 (3.8)	3.6 (4.2)	0.30	0.82
Nocturnal	2.0 (3.3)	2.7 (4.1)	1.2 (1.6)	0.02	0.19
SABA use *	4.5 (5.0)	4.3 (5.1)	4.8 (5.2)	0.58	0.65
Uncontrolled asthma **, %	43.8	50.4	41.9	0.27	0.77
Acute care utilization	Yes (%) over past 12 months				
Hospitalization	22.9	23.2	26.4	0.57	0.32
ED	79.1	80.4	80.8	0.85	0.59
Lung function	Mean (SD)				
FEV_1, % predicted	95.4 (18.8)	94.2 (18.9)	94.0 (18.0)	0.35	0.17
FVC, % predicted	99.0 (16.1)	99.0 (14.9)	100.0 (16.0)	0.98	0.99
FEV_1/FVC %	82.1 (9.1)	80.9 (8.0)	80.4 (8.3)	0.02	<0.01
F_eNO, median (IQR)	18 (9–35)	19 (8–41)	14 (8–33)	0.26	0.12
Medications and Severity, Mean (SD)					
Treatment step, n (%)				0.83	0.35
1	72 (18.4)	24 (19.1)	42 (17.9)		
2	85 (21.7)	31 (24.6)	43 (18.3)		
3	70 (17.9)	18 (14.3)	39 (16.6)		
4	16 (4.1)	4 (3.2)	13 (5.5)		
5	148 (37.9)	49 (38.9)	98 (41.7)		

	Healthy weight n=427	Overweight n=137	Obese n=251	p value	p value (trend)
Asthma Severity Score	6.5 (3.4)	6.6 (3.6)	7.0 (3.5)	0.87	0.11

*SABA - Short-acting beta agonist use

**uncontrolled=ACT (Asthma Control Test) score ≤ 19

1st p value for difference between groups using Kruskal-Wallis or Chi Square.

2nd p value test for trend.

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Table 3

Asthma Control and Severity by Weight Status

	Healthy weight N=427	Overweight N=137	Obese N=251	Estimated effect across BMI Categories	p value*
Asthma Symptoms, Adjusted OR (95% CI)					
Cough, wheeze or shortness of breath	ref	0.81 (0.57,1.16)	1.09 (0.83,1.45)	1.04 (0.90,1.19)	0.63
Nocturnal	ref	0.71 (0.43,1.17)	1.27 (0.88,1.82)	1.11 (0.92,1.34)	0.28
SABA use**	ref	0.86 (0.59,1.24)	1.02 (0.77,1.36)	1.00 (0.87,1.16)	0.98
Uncontrolled asthma†	ref	1.39 (0.90,2.14)	0.92 (0.64,1.32)	0.98 (0.82,1.17)	0.80
Acute Care Utilization, Adjusted OR (95% CI)					
Hospitalization	ref	0.93 (0.55,1.56)	1.31 (0.87,1.97)	1.13 (0.92,1.39)	0.23
ED	ref	1.09 (0.64,1.88)	1.09 (0.70,1.70)	1.05 (0.84,1.31)	0.69
Lung Function, β coefficient (95% CI)					
FEV_1	ref	−0.01 (−0.05,0.03)	−0.002 (−0.03,0.03)	−0.001 (−0.02,0.01)	0.86
FEV_1/FVC %	ref	−0.01 (−0.03,0.004)	−0.01 (−0.02,0.005)	−0.01 (−0.01,0.002)	0.15
Log 10(F_eNO)	ref	−0.11 (−0.32,0.10)	−0.17 (−0.35,0.001)	−0.09 (−0.17, −0.001)	0.05
Medications and Severity, β coefficient (95% CI)					
Treatment Step	ref	−0.05 (−0.38,0.28)	0.15 (−0.13,0.42)	0.68 (−0.07,0.20)	0.33
Asthma Severity Score	ref	−0.11 (−0.86,0.64)	0.31 (−0.32,0.95)	0.14 (−0.17,0.46)	0.36

*p value for trend across BMI groups

**SABA - Short-acting beta agonist use

†uncontrolled=ACT (Asthma Control Test) score ≤ 19

All analyses adjusted for race, ethnicity, age, gender, study site, controller medication, household income, and atopy groups.

Asthma characteristics were examined across atopic groups using binomial regression models for asthma symptoms, logistic regression models for healthcare utilization or linear regression models for lung function, medication treatment step and severity score.

Table 4

Atopy and Measures of Asthma Control and Severity

	Non atopic n=105	Atopic (1–3 +SPT) n=194	Atopic (4–7+ SPT) n=246	Atopic (8+ SPT) n=134	p value	p value (trend)
Asthma Symptoms	Mean days (SD)/past 2 weeks					
Cough, wheeze or shortness of breath	3.5 (4.1)	3.1 (3.9)	2.7 (3.5)	3.4 (4.1)	0.09	0.58
Nocturnal	2.4 (3.8)	2.3 (4.0)	1.8 (3.4)	1.8 (3.0)	0.20	0.07
Days of SABA use	4.1 (4.7)	4.4 (5.0)	4.2 (5.0)	4.5 (4.9)	0.74	0.89
Uncontrolled asthma, % *	57.0	50.3	55.5	54.6	0.64	0.87
Acute care utilization	Yes (%) over past 12 months					
Hospitalization,	18 (17.1)	40 (20.6)	71 (29.0)	28 (20.9)	0.05	0.17
ED	88 (83.8)	160 (82.5)	184 (74.8)	105 (78.4)	0.14	0.09
Lung function	Mean (SD)					
FEV_1 % predicted	97.9 (18.4)	97.9 (16.5)	95.4 (17.4)	92.7 (20.3)	0.14	0.04
FVC % predicted	99.2 (16.2)	101.0 (15.1)	100.0 (16.2)	97.9 (15.9)	0.24	0.43
FEV_1/FVC	84.0 (7.9)	82.4 (7.9)	81.6 (8.4)	79.1 (8.7)	<0.001	<0.001
F_eNO, median (IQR)	8 (5,13)	13 (8,32)	21 (11,38)	25 (13,46)	<0.001	<0.001
Medications and Severity, Mean (SD)						
Treatment Step, n (%)						
1	29 (29.0)	40 (22.5)	29 (12.7)	20 (16.3)		
2	22 (22.0)	47 (26.4)	43 (18.9)	20 (16.3)	0.005	0.001
3	12 (12.0)	28 (15.7)	43 (18.9)	24 (19.5)		
4	1 (1.0)	5 (2.8)	14 (6.1)	7 (5.7)		
5	36 (36.0)	58 (32.6)	99 (43.4)	52 (42.3)		

	Non atopic n=105	Atopic (1–3 +SPT) n=194	Atopic (4–7+ SPT) n=246	Atopic (8+ SPT) n=134	p value	p value (trend)
Asthma Severity Score	6.0 (3.5)	6.0 (3.4)	6.6 (3.3)	7.2 (3.5)	0.02	0.003

*SABA - Short-acting beta agonist use

**uncontrolled=ACT (Asthma Control Test) score ≤ 19

1st p value test for difference between groups using Kruskal-Wallis or Chi Square.

2nd p value for trend

Table 5

Asthma Control and Severity by Atopy Group

	Non atopic n=105	Atopic (1–3 +SPT) n=194	Atopic (4–7+ SPT) n=246	Atopic (8+ SPT) n=134	Estimated effect across groups	p value†
Asthma Symptoms (past 2 weeks), Adjusted OR (95% CI)						
Cough, Wheeze or Shortness of Breath	ref	0.93 (0.62,1.39)	0.74 (0.51,1.09)	1.06 (0.68,1.63)	0.98 (0.86,1.13)	0.82
Nocturnal	ref	0.99 (0.60,1.62)	0.72 (0.44,1.18)	0.72 (0.43,1.23)	0.87 (0.74,1.02)	0.09
Days of SABA use *	ref	1.08 (0.72,1.63)	0.98 (0.66,1.45)	1.04 (0.66,1.61)	0.99 (0.87,1.13)	0.89
Uncontrolled asthma **	ref	1.15 (0.69,1.89)	0.95 (0.58,1.55)	1.00 (0.57,1.75)	0.97 (0.82,1.14)	0.70
Acute care utilization (past 12 months), Adjusted OR (95% CI)						
Hospitalization	ref	1.20 (0.64,2.27)	1.88 (1.04,3.41)	1.28 (0.64,2.55)	1.14 (0.94,1.39)	0.18
ED	ref	1.03 (0.52,2.03)	0.55 (0.29,1.04)	0.64 (0.31,1.30)	0.79 (0.64,0.98)	0.03
Lung Function, β coefficient (95% CI)						
FEV_1	ref	0.01 (−0.03,0.5)	−0.003 (−0.04,0.04)	−0.01 (−0.04,0.04)	−0.01 (−0.02,0.01)	0.41
FEV_1/FVC	ref	−0.01 (−0.03,0.02)	−0.02 (−0.04,0.003)	−0.04 (−0.6,−0.01)	−0.01 (−0.02,−0.004)	0.002
Log 10(F_eNO)	ref	0.65 (0.40,0.91)	0.96 (0.72,1.21)	1.13 (0.85,1.40)	0.35 (0.27,0.43)	<0.001
Medications and Severity, β coefficient (95% CI)						
Treatment Step	ref	0.02 (−0.36,0.39)	0.55 (0.18,0.91)	0.56 (0.14,0.98)	0.25 (0.12,0.37)	<0.001
Asthma Severity Score	ref	0.11 (−0.77,0.99)	0.64 (−0.20,1.48)	1.06 (0.10,2.02)	0.39 (0.10,0.68)	0.009

* SABA - Short-acting beta agonist use

** uncontrolled=ACT (Asthma Control Test) score ≤ 19

† p value for trend across BMI groups

Adjusted for race, ethnicity, age, gender, study site, controller medication, household income, and atopy groups.

Asthma characteristics were examined across atopic groups using binomial regression models for asthma symptoms, logistic regression models for healthcare utilization or linear regression models for lung function, medication treatment step and severity score.