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Prevalence of high fractional exhaled nitric oxide among US youth with asthma

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Abstract

BACKGROUND: High fractional exhaled nitric oxide (FeNO) is an indicator of poor asthma control and has been proposed as a non-invasive assessment tool to guide asthma management.

OBJECTIVE: We aimed to describe the prevalence of and factors associated with high FeNO among US youth with asthma.

METHODS: Data from 716 children and adolescents with asthma ages 6–19 years who participated in the 2007–2012 National Health and Nutrition Examination Survey were analyzed. Using American Thoracic Society guidelines, high FeNO was defined as >50 ppb for ages 12–19 years and >35 ppb for ages 6–11 years. Multivariate logistic regression examined associations between high FeNO and age, sex, race/Hispanic origin, income status, weight status, tobacco smoke exposure, and other factors associated with asthma control (recent use of inhaled corticosteroids, recent respiratory illness, asthma-related respiratory signs/symptoms, and spirometry).

RESULTS: About 16.5% of youth with asthma had high FeNO. The prevalence of high FeNO was higher among non-Hispanic black (27%, $P < 0.001$) and Hispanic (20.2%, $P = 0.002$) youth than non-Hispanic white (9.7%) youth. Differences in high FeNO prevalence by sex (girls < boys), weight status (obese < normal weight), tobacco smoke exposure (smokers < home exposure < no exposure), and FEV1/FVC (normal < abnormal) were also observed. No differences were noted between categories for the remaining covariates.

CONCLUSION: High FeNO was observed to be associated with sex, race/Hispanic origin, weight status, tobacco smoke exposure, and abnormal FEV1/FVC, but was not associated with

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CONFLICTS OF INTEREST

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asthma-related respiratory symptoms. These findings may help inform future research and clinical practice guidelines on the use of high FeNO in the assessment of asthma control.

Keywords

Asthma; exhaled nitric oxide; National Health and Nutrition Examination Survey; pediatrics

1 | INTRODUCTION

Childhood asthma is a significant public health problem, affecting 8.6% of US children less than 18 years of age in 2014.[1] Asthma morbidity is high despite national clinical practice guidelines that seek to improve asthma care and the quality of life for persons with asthma.[2] Airway inflammation has long been recognized as a main underlying determinant of impairment and risks related to asthma.[2] Fractional exhaled nitric oxide (FeNO), a noninvasive method of measuring eosinophilic airway inflammation, may be elevated in allergic conditions, including asthma and atopy.[3,4]

In 2011, the American Thoracic Society (ATS) published clinical practice guidelines that recommended use of FeNO for a variety of reasons, including to assess asthma control.[5] In addition, FeNO has been shown to have clinical utility in supporting the diagnosis of asthma,[5] predicting risk of asthma onset,[6] and response to preventive therapy.[7] Multiple factors can impact airway inflammation, and therefore FeNO levels. These include weight status, tobacco smoke exposure, recent steroid use, and recent respiratory illness.[5] Historically, assessment of asthma control has been aided by clinical tools such as spirometry,[2] and/or patient report of signs/symptoms. However, neither of these assessments, unlike FeNO, directly assess inflammation.[8] Within a clinical framework, FeNO levels are an additional indicator of asthma control to aid in the management of asthma.

The National Health and Nutrition Examination Survey (NHANES) provides an opportunity to assess FeNO levels in a nationally representative sample of children and adolescents with asthma and to thereby add to the understanding of variation in FeNO levels among youth with asthma. In this study, we describe factors associated with high FeNO among youth with asthma and assess whether high FeNO levels are associated with measures of asthma control.

2 | MATERIALS AND METHODS

2.1 | Study design

The National Health and Nutrition Examination Survey (NHANES) is administered by the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention (CDC). NHANES is a continuous cross-sectional survey that obtains a nationally representative sample of the noninstitutionalized civilian US population via a stratified and multistage probability cluster design. We examined 2007–2012 data for children and adolescents with asthma aged 6–19 years. The examination response rates for this age group was between 74% and 85%.[9] Informed consent was obtained for persons aged 18 and 19 years. Participation of children aged younger than 18 years required written parental consent

and written assent from children aged 7–17 years. The NCHS Research Ethics Review Board approved the survey protocols. Further information regarding NHANES methods can be found elsewhere.[9]

2.2 | Analytic sample and missing data

Youth aged 6–19 years with current asthma were eligible for inclusion ($n = 877$). Current asthma status was determined by affirmative responses to both of two survey questions: "Has a doctor or other health professional ever told you that (you have/your child has) asthma?" and "(Do you/does your child) still have asthma?"

Of the eligible 877 participants, 161 were excluded because of missing FeNO measurements, resulting in a sample size of 716 youth. Missing FeNO did not differ by current asthma status. However, a higher percentage of non-Hispanic (NH) blacks had missing FeNO compared to NH whites (20.7% vs. 12.3%, $P < 0.02$). Children aged 6–11 years had more missing values than adolescents aged 12–19 years (24.8% vs. 9.5%, $P < 0.001$). Missing FeNO was not associated with any other of the characteristics included in the analysis. NHANES produces examination weights for public use data files, but these weights do not account for nonresponse to individual variables such as FeNO. To assess item nonresponse bias, we adjusted the examination weights using SAS-callable SUDAAN's PROC WTADJUST[10] and included age, sex, race/Hispanic origin in the model. The difference in FeNO prevalence estimates between the adjusted examination weights and the original weights was less than 1%. Thus, we report FeNO prevalence estimates calculated using the original examination weights.

2.3 | FeNO measurement

FeNO concentration was measured in exhaled air prior to the spirometry exam. Measurements were determined using the NIOX MINO® (Aerocrine AB, Solna, Sweden), a hand-held nitric oxide analyzer. Details for procedures on obtaining FeNO can be found elsewhere.[9,11] The mean of two FeNO measurements was used as the main outcome variable. High FeNO for this analysis was defined using the ATS age-specific criteria: >50 ppb for adolescents aged 12–19 years and >35 ppb for those aged 6–11 years.[5] Previous studies have produced race-specific FeNO reference values,[11] however, our analysis defined high FeNO based on published ATS clinical practice guidelines.[5]

2.4 | Categorization of study variables

The association between FeNO and demographic and environmental characteristics, in addition to asthma-related signs/symptoms, were examined.

Age group was categorized as 6–11 years and 12–19 years. Race/Hispanic origin was based on the reported responses from participants, or their proxy, and categorized as NH white, NH black, Hispanic, and "other." The "other" category included Asians, results for whom are not separately reported because of insufficient sample sizes. Family income-to-poverty ratio (FIPR) was calculated by dividing family income by the federal poverty threshold specific for family size.[9] Participants were categorized as low income if their FIPR was less

than 1.85, a cut-point used to determine income eligibility for some federal programs, including reduced price school lunches.[12]

Weight status was determined using BMI percentiles calculated from the 2000 CDC BMI-for-age growth charts[9] and categorized as: <5th (underweight), ≥5th to <85th (normal weight), ≥85th to <95th (overweight), and ≥95th (obese). Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared rounded to one decimal place.[9] Height and weight were measured using standardized protocols.[9]

Tobacco smoke exposure was examined in three categories—smokers, home exposure, and no exposure. Smokers were defined as participants aged 12–19 years answering affirmative to smoking cigarettes, cigars, or pipes within the last 5 days or having serum cotinine levels >10 ng/mL, a level used to define smoking in previous studies.[13] Home exposure was defined by report of household members smoking inside the home. We also examined the association between FeNO and cotinine levels (using a cut-point of 0.05 ng/mL[13]), rather than reported home exposure. Prevalence of high FENO was similar for participants with reported home exposure and high cotinine levels. The reported home exposure variable had less missing data and therefore was used in the final analysis.

Use of oral or inhaled steroids in the last 2 days was categorized dichotomously. Reporting a recent cough, cold, or respiratory illness in the last 7 days was also categorized dichotomously.

FeNO is associated with asthma control, a complex measure affected by underlying disease severity, exposure to factors that trigger airway inflammation and reactivity, and preventive management actions.[2] Per the National Asthma Education and Prevention Program (NAEPP) guidelines, asthma control assessment is a composite measure of symptom frequency, airway function, and adverse outcomes.[2] Asthma control measures examined in this analysis included reported wheezing over the preceding 12 months (yes/no) and the following health consequences due to wheezing over the last 12 months: missed school days (none/1+ days), number of medical visits (no visits, one visit, or 2 + visits), disturbed sleep (none, <1 night per week, or 1+ nights per week), limited activity (none, a little, or a fair/moderate/lot amount), and wheezing during exercise (yes/no).

Spirometry was obtained using standardized protocols[14] and was completed by 651 of our 716 eligible participants. Youth were excluded from spirometry for any of the following conditions: any physical limitation preventing forceful exhalation; current chest pain; congenital heart disease; recent surgery to the eye, chest, or abdomen; reported histories of exposure to tuberculosis or coughing up blood; or painful ear infections. The spirometry measures included in this analysis were forced expiratory volume at 1 s (FEV1) and the ratio of FEV1 to forced vital capacity (FEV1/FVC).[2] FEV1 is expressed as percent predicted values (FEV1%) based on Hankinson's equations for participants aged 8–19 years and Wang's equation for children aged 6–7 years,[15,16] which are sex- and race-specific, and similarly used in previous studies.[17] NAEPP cut-points of ≤80% and ≤0.80 were used to categorize FEV1% and FEV1/FVC, respectively.[2]

2.5 | Statistical methods

Statistical analyses were conducted using SAS-callable SUDAAN (SAS version 9.3, SAS Institute, Cary, NC; SUDAAN, version 10.0, RTI, Research Triangle Park, NC) which accounts for the complex sample design. NHANES survey examination weights were used to produce national estimates. Differences between groups were tested using a *t*-test. Statistical significance was determined at a *P* value of <0.05.

Bivariate analyses examined the association between high FeNO and age, sex, race/Hispanic origin, family income, weight status, tobacco smoke exposure, recent steroid use, and recent respiratory illness, underlying factors previously identified as affecting FeNO.[5,18] Multivariate logistic regression analysis was conducted using FeNO status as the dependent variable and all the factors from the bivariate analyses as the independent variables.

To analyze the association between high FeNO and NHANES measures of asthma control, we conducted separate multivariate logistic regression analyses with FeNO status (dependent variable) and wheezing symptoms and lung function as measured by FEV1% and FEV1/FVC (independent variables). Adjusted models for each of these associations included age, sex, race/Hispanic origin, family income, weight status, tobacco smoke exposure, recent steroids use, and recent respiratory illness. We also examined the agreement between FeNO status and spirometry, using SUDAAN's PROC Crosstab with AGREE statement to generate a kappa coefficient. While the two measures capture different aspects of asthma control, there is overlap (spirometry measures airflow through small airways that is affected by inflammation and additional factors, while FeNO is primarily a measure of airway inflammation).

Given that prevalence of high FeNO was greater than 10%, odds ratios (OR) may overestimate the relative risk (RR).[19] To investigate the differences between OR and RR, we used SUDAAN's PROC rlogist PREDMARG/adjrr statement.[10] Our assessment of RR found the association to be similar to that of the OR. The largest difference was in comparing NH blacks to NH whites, where adjusted OR = 3.4 and adjusted RR = 2.6 (24% lower for RR). Therefore, we report the adjusted odds ratio.

3 | RESULTS

There were 716 eligible participants aged 6–19 years for our analysis (Table 1). Approximately, 65% of those with asthma were 12–19 years of age, 53.1% were boys, and 56.1% were NH white, 20.5% were NH black, and 16.1% were Hispanic. Approximately, 49% of youth with asthma were members of families with a FIPR <1.85% and 41% were overweight or obese.

Overall, 16.5% of youth with asthma had high FeNO (Table 2), while those without asthma had a high FeNO prevalence of 5.3% (data not shown). Among our study population of youth with asthma, prevalence of high FeNO was similar among children aged 6–11 years and adolescents aged 12–19 years (16.1% vs. 16.8%, $P = 0.8324$). High FeNO prevalence was greater in boys than girls (21.5% vs. 10.9% respectively, $P < 0.01$), and greater in NH black (27%, $P < 0.001$) and Hispanic (20.2%, $P < 0.01$) compared to NH white (9.7%)

youth. The prevalence of high FeNO did not differ by income group. Prevalence of high FeNO was greater in youth with normal weight (20.1%) compared to those with obesity (10.6%, $P < 0.01$). Prevalence of high FeNO was higher in those with no tobacco smoke exposure (19.6%) compared with smokers (3.6%, $P < 0.001$) and those with home exposure (9.4%, $P = 0.001$). Prevalence of high FeNO in participants with recent steroid use (15.2%) was similar to those that did not report recent steroid use (17%, $P = 0.5985$), and there was no difference in the prevalence of high FeNO by recent respiratory illness status (18.8% vs. 16%, $P = 0.4822$). In adjusted analyses, significant associations between high FeNO and sex, race/Hispanic origin, weight status, and tobacco smoke exposure remained significant.

For each of the wheezing-related symptom measures representing components of asthma control, there were no significant differences in the prevalence of high FeNO (Table 3). For example, high FeNO prevalence for participants with no medical visits and 2+ visits within the last 12 months was 15.3% and 18% (P=0.5297), respectively. Similar results were observed after adjustment for underlying characteristics and other components of asthma control.

With regard to spirometry measures (Table 3), approximately one quarter of youth with abnormal FEV1% (≤80) had high FeNO, and 15.9% of youth with normal FEV1% (>80) had high FeNO, but this difference was not significant. High FeNO prevalence for participants with abnormal FEV1/FVC (≤0.80) was 27% while those with normal FEV1/FVC (>0.80) was significantly lower (12.5%, P<0.05). In the adjusted logistic regression models, the association between FeNO status and FEV1% was not statistically significantly different, while that with FEV1/FVC was significantly different.

The percent of youth with normal and abnormal results for FeNO and FEV1% and FEV1/FVC are shown in Table4A and B, respectively. Overall, 76.1% had both normal FeNO and FEV1% while 2.4% had abnormal results (high FeNO and FEV1% ≤80). The relationship between FeNO and FEV1/FVC showed a similar pattern. The kappa agreement between high FeNO and abnormal FEV1% and FEV1/FVC was 0.07 and 0.17, respectively.

4 | DISCUSSION

Minority populations have higher prevalence of asthma and, among the population of children with asthma, are more likely to have adverse events of ER visits, hospitalizations, and death.[20] Our study showed that, similarly, NH black and Hispanic youth with asthma have greater prevalence of high FeNO than NH white children. Researchers have noted differences in FeNO by race/Hispanic origin in children and have called for studies with larger statistical power.[21,22] To our knowledge, no studies have examined differences in the prevalence of high FeNO by race/Hispanic origin, in addition to other asthma risk factors, with a nationally representative sample of youth with asthma.

The association between FeNO levels and environmental tobacco smoke (ETS) exposure, obesity, and asthma control measures such as spirometry and patient assessment questionnaires have been previously investigated.[3,5,23–25] Smokers are known to have low FeNO levels,[5] while the relationship between ETS exposure and FeNO has been inconsistent

in the literature.[23–25] For example, ETS exposure has been associated with lower FeNO levels,[25] but a study examining children less than 2 years of age showed an association with higher FeNO levels.[23] Differences in the sample population and methods of obtaining FeNO values could account for these different findings. Differences between our study and previous studies in ascertainment of exposure variables may also account for some differences. Participants who smoked or with home exposure to tobacco smoke had lower prevalence of high FeNO than those with no tobacco exposure. While this finding may be secondary to a physiologic etiology,[26] there is also a possibility of selection bias, where families with youth with higher severity of asthma go to greater lengths to eliminate any ETS exposure.[27]

The association of asthma and obesity was summarized by a 2010 ATS Workshop statement.[28] There is evidence that obesity is a risk factor for asthma[28] as well as a possible risk factor for poor asthma control.[29] Few studies examining FeNO level as a concomitant biomarker have been conducted. A Hong Kong study investigating youth with asthma did not show any FeNO differences between the obese and non-obese.[30] However, this study used the Hong Kong Growth Survey definition of obesity of >120% of median weight for height, which has been shown to classify a greater proportion of children as obese when compared to World Health Organization and CDC obesity definitions using BMI percentile.[31] A study found that overweight/obese children with low FeNO were more likely to have asthma.[32] We found that participants classified as obese have lower prevalence of high FeNO when compared to those with normal weight.

NAEPP guidelines recommend use of spirometry to aid in the assessment of asthma control.[2] ATS guidelines recommend measuring airway inflammation with FeNO to help determine asthma control and management.[5] We found a low agreement[33] between abnormal FeNO and spirometry, results that are consistent with a previous study.[8] Comparison of two measures that may capture different biologic processes contributing to asthma symptoms could explain the low agreement. As part of a comprehensive evaluation, FeNO[5] and spirometry[2] can help determine the overall clinical picture for the asthma patient.

Patient self-assessment questionnaires have been employed to aid clinicians in determining asthma control. These questionnaires assess symptoms such as disturbed sleep, limitation of activities, and presence of wheezing but can be limited by poor symptom recognition by patients and caregivers.[34] We analyzed similar wheezing-related respiratory symptoms, although the time frame of recall differs,[34] and found similar prevalence of high FeNO among those with and without respiratory symptoms. Studies examining subjective patient assessment questionnaires and objective FeNO measurements have found no significant association[35] and poor agreement[8] between asthma control and FeNO. Another study found no correlation between FeNO levels and missed school days.[36] Our study, in conjunction with previous studies, suggests that patient perception of symptoms and FeNO levels may be capturing different aspects of asthma control.

A primary contribution of this analysis of a nationally representative, population-based sample of children with asthma is to increase understanding of the variation of FeNO levels in a non-clinical setting. Because NHANES is a multipurpose health survey, these findings

can neither support nor refute observed associations between FeNO and more precisely defined outcomes found in clinical studies (such as risk of frequent medication use or prediction of an asthma exacerbation).[37] There are also limitations to consider when comparing results to those obtained in clinical studies. Asthma status is defined by self or proxy report (although respondents are asked about receiving an asthma diagnosis from a physician). In addition, there is a long recall period for asthma symptoms (12 months) in NHANES that differs from symptom data typically collected in clinical studies. Furthermore, report of symptoms occurred in the household interview while FeNO measurement was conducted up to several weeks later during their physical assessment. In determining FeNO values for those reporting ICS use, we cannot ensure that there was proper compliance with ICSs and previous studies have shown adherence to be suboptimal.[39] A previous study has shown FeNO to be a biomarker for severity of "allergic asthma," whereas no difference in FeNO levels was observed among those with non-atopic asthma and those without allergies or asthma.[40] Serum IgE measurement and FeNO were not collected concurrently. Thus the associations observed in our study do not account for any variation in FeNO by atopy status. Small sample sizes with some analyses may impact significance of results. In addition, while we performed weight adjustment to assess the likelihood of non-response bias by sex, age, and race/Hispanic origin, missing data could be related to other characteristics and the possibility of non-response bias may still exist.

Despite these limitations, results of this study generally support the patterns observed in clinical studies.[8,21,22,25,32,35,36] As noted in the 2011 ATS guidelines and by others assessing the clinical utility of FeNO, no single measure can be used to assess and manage asthma, which is a complex, episodic, and variable disease.[5,37] When combined with physical examination and other asthma assessment tools, FeNO measurement can provide an additional data point that may be useful for clinicians in asthma management. Results from this study provide further context to continue to refine the role of FeNO in asthma management.

5 | CONCLUSION

FeNO is a noninvasive point-of-care measurement of eosinophilic airway inflammation. Our study demonstrated that approximately one in six youth with asthma had high FeNO values, a finding not previously demonstrated using a nationally representative sample of the US population. High FeNO was associated with sex, race/Hispanic origin, weight status, tobacco smoke exposure, FEV1/FVC but not predicted FEV1%. ATS guidelines discuss the usefulness of FeNO as a complementary tool in the diagnosis and management of asthma[5] and future research focusing on the clinical utility of FeNO[38] may provide further evidence to inform its use. While other clinical tools assess patient history or degree of lung function, FeNO is a non-invasive means to assess degree of airway inflammation in patients with asthma. These population-based findings may help inform future research and stakeholders who determine clinical practice guidelines on the use of high FeNO in the assessment of asthma control.

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Abbreviations:

ATS	American Thoracic Society
CDC4	Centers for Disease Control and Prevention
ETS	environmental tobacco smoke
FeNO	fractional exhaled nitric oxide
FIPR4	family income-to-poverty ratio
ICS	inhaled corticosteroid
NCHS	National Center for Health Statistics
NHANES	National Health and Nutrition Examination Survey
NH	non-Hispanic
OR	odds ratio
RR	relative risk.

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TABLE 1

Sample size and characteristics of youth aged 6–19 years with current asthma

	Unweighted numbr	Weighted %
Total sample size	**716**	**100**
Characteristics associated with FeNO		
Age		
6–11 years	318	34.9
12–19 years	398	65.1
Sex		
Boys	396	53.1
Girls	320	46.9
Race/His panic origin[a]		
NH White	201	56.1
NH Black	250	20.5
Hispanic	198	16.1
Family income status (FIPR)		
<1.85	402	48.9
1.85+	260	51.1
Weigit states[a]		
Normal weight	375	54.9
Overweight	111	14.2
Obese	207	26.7
Smoking exposure		
No smoke exposure	541	74.8
Home exposure	112	14.7
Smoker	60	10.6
Oral or inhaled steroids in past 2 days		
Yes	156	21.91
No	556	78.09
Respiratory illness in past 7 days		
Yes	172	21.9
No	543	78.1
Wheezing-related measures of asthma control		
Wheezing in last year		
No	293	38.9
Yes	423	61.1
Missed school days in last year		
None	499	74
1+days	216	26
# Medical visits in last year		
No visits	468	67.7

	Unweighted numbr	Weighted %
Total sample size	**716**	**100**
1 visits	95	12.4
2+ visits	150	19.9
Disturbed sleep in last year		
None	475	68.7
<1 nights/wk	129	18.6
1+ nights/wk	108	12.7
Wheezing limiting activity in last year		
None	503	71.9
a little	129	18.6
fair, moderate, or a lot	83	9.4
Wheezing during activity/exercise in last year		
No	420	58.8
Yes	287	41.2
Lung function		
Predicted FEV1%		
≤80%	77	9.6
>80%	574	90.4
FEV1/FVC		
≤0.80	199	29.2
>0.80	452	70.8

SOURCE: National Health and Nutrition Examination Survey.

NOTE: FIPR (family income poverty ratio) is calculated by dividing family income by a poverty measure specific for family size and accounts for inflation. A FIPR of 1.85 is the eligibility criteria to enroll in some federal programs, including reduced priced school lunches.

Weight status was based on body mass index (BMI) percentiles calculated as weight in kilograms divided by height in meters squared. The 2,000 CDC BMI-for-age growth charts were used to calculate BMI percentiles.

[a]Persons with race/Hispanic origin classified as “other” and weight status classified as “underweight” were included in overall estimates but not separately reported due to insufficient sample size.

TABLE 2

Prevalence and adjusted odds ratios of high FENO among children with current asthma, NHANES 2007–2012

	High FeNO prevalence		Adjusted odds ratio	
Category	**Percent (95%CI)**	***P* values**	**aOR**	**95% Cl**
Total	16.5 (13.6–19.8)			
Age				
6–11 years	16.1 (11.5–21.6)	Ref	1	-
12–19 years	16.8 (13.0–21.1)	0.8324	1.5	0.8–2.6
Sex				
Boys	21.5 (16.9–26.8)	Ref	1	-
Girls	10.9 (6.4–17.1)	0.0079	0.4	02–0.8
Race/Hispanic origin[a]				
NH White	9.7 (5.9–15.0)	Ref	1	-
NH Black	27.0 (20.5–34.3)	<0.001	3.4	1.7–7
Hispanic	202 (15.3–25.7)	0.0019	1.9	1–3.8
Family income status (FIPR)				
<1.85	19.4 (14.5–25.2)	Ref	1	-
1.85+	132 (8.3–19.6)	0.1523	0.6	0.3–12
Weight status[a]				
Normal weight	20.1 (15.7–25.2)	Ref	1	-
Overweight	13.8 (6.3–25.1)	0.1783	0.5	0.2–1.5
Obese	10.6 (7.1–15.1)	0.0038	0.4	02–0.6
Smoke exposure				
No smoke exposure	19.6 (16.1–23.5)	Ref	1	-
Home exposure	9.4 (4.7–16.3)	0.0013	0.4	02–0.6
Smoker	3.6 (1.0–8.8)	<0.001	0.1	0.0–0.4
Oral or inhaled steroids in past 2 days				
Yes	152 (11.0–20.2)	Ref	1	-
No	17.0 (13.0–21.7)	0.5985	1.2	0.7–2.3
Respiratory illness in past 7 days				
Yes	18.8 (129–26.1)	Ref	1.3	0.7–2.3

	High FeNO prevalence		Adjusted odds ratio	
Category	**Percent (95%CI)**	***P* values**	**aOR**	**95% CI**
No	16.0 (123–20.3)	0.4822	1	-

SOURCE: National Health and Nutrition Examination Survey.

NOTE: FIPR (family income poverty ratio) was calculated by dividing family income by a poverty measure specific for family size and accounts for inflation. A FIPR of 1.85 is the eligibility criteria to enroll in some federal programs, including reduced priced school lunches.

High FeNO is defined as >50 ppb for adolescents ages 12–19 years and >35 ppb for those 6–11 years.

Weight status was based on body mass index (BMI) percentiles calculated as weight in kilograms divided by height in meters squared. The 2,000 CDC BMI-for-age growth charts were used to calculate BMI percentiles.

Odds ratio were adjusted for age, sex, race/Hispanic origin, family income status, weight status, tobacco smoke exposure, recent steroid use, and recent respiratory illness.

[a]Persons with race/Hispanic origin classified as “other” and BMI classified as “underweight” were included in overall estimates but not separately reported due to insufficient sample size.

TABLE 3

Prevalence of high FeNO by wheezing-related measures of asthma control and lung function

	High FeNO prevalence		Adjusted odds ratio	
Category	**Percent (95% CI)**	***P* value**	**aOR**	**95% CI**
Wheezing in last year				
No	13.6 (8.0–19.3)	Ref	1	
Yes	18.4 (14.2–226)	02234	1.6	0.8–32
Missed school days due to wheezing in last year				
None	15.5(11.3–19.8)	Ref	1	
1+ days	19.2(123–26.1)	0.4317	1.3	0.6–2.5
# Medical visits in last year for wheezing				
No visits	15.3 (11.3–19.2)	Ref	1	
1 visits	20.6 (8.8–32.4)	0.3828	1.8	0.6–5.1
2+ visits	18.0 (11.0–25.0)	0.5297	1.6	0.8–3.4
Wheezing disturbed sleep in last year				
None	14.8(10.5–19.1)	Ref	1	
< 1 nights/wk	22.6(121–33.1)	0207	2.3	0.9–5.9
1+ nights/wk	17.0 (10.7–23.4)	0.5747	1.1	0.5–2.3
Wheezing limiting activity in last year				
not at all	16.3 (123–20.4)	Ref	1	
a little	17.4 (9.9–24.8)	0.8145	1.4	0.7–2.9
fair, moderate, or a lot	15.9 (9.4–22.5)	0.9204	0.9	0.5–1.7
Wheezing during activity/exercise in last year				
No	14.6 (10.0–19.3)	Ref	1	
Yes	19.2 (13.5–24.8)	02815	1.6	0.8–32
Lung function				
Predicted FEV1%				
≤80%	25.2 (13.5–40.5)	0.1483	1.5	0.7–32
>80%	15.9 (126–19.6)	Ref	1	
FEV1/FVC				
≤0.80	27.0 (19.7–35.4)	0.0029	2.9	1.4–5.7

	High FeNO prevalence		Adjusted odds ratio	
Category	**Percent (95% CI)**	***P* value**	**aOR**	**95% CI**
>0.80	12.5 (8.6–17.5)	Ref	1	

Source: National Health and Nutrition Examination Survey.

NOTE: Odds ratios adjusted for age, sex, race/Hispanic origin, family income, weight status, tobacco smoke exposure, recent steroids use, and recent respiratory illness. FEV1% and FEV1/FVC cut point values based on NAEPP age-specific criteria.

TABLE 4

Percent (with 95% confidence interval) of children and adolescents with normal and abnormal FeNO and FEV1 cut point values

(A)		
	Normal FeNO	**High FeNO**
Normal lung function (>80% predicted FEV1)	76.1 (72.2–79.7)	14.3 (11.2–18.0)
Abnormal lung function (≤80% predicted FEV1)	7.2 (4.7–10.4)	2.4 (0.5–6.8)
(B)		
Normal lung function (>0.80 predicted FEV1/FVC)	62.0 (56.3–67.4)	8.9 (5.8–12.9)
Abnormal lung function (≤0.80 predicted FEV1/FVC)	21.3 (16.4–26.9)	7.9 (5.5–10.9)

Source: National Health and Nutrition Examination Survey.

NOTE: High FeNO is defined as >50 ppb for adolescents ages 12–19 years and >35 ppb for those ages 6–11 years.

FEV1% and FEV1/FVC cut point values based on NAEPP age-specific criteria.

Percentages weighted to estimate national percentages.