

Original Article

Associations of Snoring and Asthma Morbidity in the School Inner-City Asthma Study

Sigfus Gunnlaugsson, MD^{a,b,*}, Mehtap Haktanir Abul, MD^{a,b,*}, Lakiea Wright, MD^{b,c,*}, Carter R. Petty, MA^d, Perdita Permaul, MD^e, Diane R. Gold, MD, MPH^{b,f,g}, Jonathan M. Gaffin, MD, MMSc^{a,b}, and Wanda Phipatanakul, MD, MS^{b,h} *Boston, Mass; and New York, NY*

What is already known about this topic? Asthma and sleep-disordered breathing are associated conditions with a bidirectional relationship. They are common in childhood and disproportionately affect those of minority race and ethnicity.

What does this article add to our knowledge? Expands the knowledge of the association of asthma and sleep-disordered breathing assessed by report of snoring frequency in relation to asthma morbidity and health care utilization among school-age children of minority racial and ethnic background.

How does this study impact current management guidelines? Report of snoring frequency is easily assessed and can identify those at risk for worse asthma morbidity and increased health care utilization. Given the variation in snoring frequency over time, repeated assessments of snoring should be performed.

BACKGROUND: Inner-city children are disproportionately affected by asthma and sleep-disordered breathing (SDB). However, little is known about the association of SDB symptoms with asthma morbidity in this vulnerable population. **OBJECTIVE:** Assess the relationship between snoring frequency and asthma morbidity. **METHODS:** This study was part of the School Inner-City Asthma Study, a longitudinal prospective cohort study of children with persistent asthma who attended schools in the Northeast United States from 2008 to 2013. Participants had baseline assessments of asthma symptoms, snoring, and allergy status. Caregivers completed quarterly surveys for 12 months on symptoms of asthma, snoring, and health care outcomes.

Snoring frequency (non-, rare-, sometimes-, habitual-snoring) and its relationship with asthma symptoms and asthma morbidity were assessed by mixed-effects models. RESULTS: There were 1186 observations from 339 subjects. Mean age was 7.9 years; roughly half were male, and most were of minority race. Half were overweight or obese, and 65.5% had atopy. At initial snoring assessment, 24.8% reported habitual snoring, but report of snoring frequency varied over the study period. Multivariate analyses revealed increased odds of maximum asthma symptom days for habitual snoring compared with nonsnoring (1.58; 95% CI, 1.19-2.10; $P < .002$) and all other snoring categories. Habitual snoring was associated with greater odds of health care utilization (incidence rate ratio, 1.72;

^aDivision of Pulmonary Medicine, Boston Children's Hospital, Boston, Mass

^bHarvard Medical School, Boston, Mass

^cDivision of Allergy and Immunology, Brigham and Women's Hospital, Boston, Mass

^dInstitutional Centers for Clinical and Translational Research, Boston Children's Hospital, Boston, Mass

^eDivision of Pulmonology, Allergy and Immunology, NY-Presbyterian Hospital/Weill Cornell Medicine, Weill Cornell Medical College, New York, NY

^fDepartment of Environmental Health, Harvard T.H. Chan School of Public Health, Boston, Mass

^gChanning Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, Mass

^hDivision of Allergy and Immunology, Boston Children's Hospital, Boston, Mass
* Co-first authors.

This study was supported by the National Institutes of Health (grant nos. R01HL137192, U01 AI 110397, R01 AI 073964, and K24 AI 106822 to W.P.; grant no. R01030100 to J.M.G.; grant no. K23 AI123517 to P.P.; and grant nos. F32 HL124919-01 and 3 U01 AI110397-02S1 SICAS2 Diversity Supplement to L.W.). This work was conducted with support from Harvard Catalyst | The Harvard Clinical and Translational Science Center (National Center for Research Resources and the National Center for Advancing Translational Sciences, National Institutes of Health Award UL1 TR001102) and financial contributions from

Harvard University and its affiliated academic health care centers. The content is solely the responsibility of the authors and does not necessarily represent the official views of Harvard Catalyst, Harvard University and its affiliated academic health care centers, or the National Institutes of Health. Additional acknowledgment goes to Allergy, Asthma Awareness Initiative, Inc.

Conflict of interest: L. Wright is Medical Director of US Clinical Affairs in the ImmunoDiagnostics Division at Thermo Fisher Scientific. J. M. Gaffin, D. R. Gold, P. Permaul, and L. Wright have received grants from the National Institutes of Health. W. Phipatanakul does consulting with Genentech, Novartis, Regeneron, and Sanofi, for asthma-related therapeutics, and has received clinical trial support in asthma studies from these companies. The rest of the authors declare that they have no relevant conflicts of interest.

Received for publication February 5, 2021; revised April 30, 2021; accepted for publication May 13, 2021.

Available online ■ ■

Corresponding author: Wanda Phipatanakul, MD, MS, Division of Allergy and Immunology, Boston Children's Hospital, 300 Longwood Ave, Boston, MA 02115. E-mail: wanda.phipatanakul@childrens.harvard.edu.

2213-2198

© 2021 American Academy of Allergy, Asthma & Immunology

<https://doi.org/10.1016/j.jaip.2021.05.022>

Abbreviations used
 BMI- Body mass index
 OR- Odds ratio
 SDB- Sleep-disordered breathing
 URI- Upper respiratory tract infection

95% CI, 1.10-2.69; $P = .02$) and worse asthma control (odds ratio, 1.49; 95% CI, 1.05-2.11; $P = .03$) compared with nonsnoring.

CONCLUSIONS: Snoring is common among inner-city school-age children with asthma, and habitual snoring is associated with increased asthma symptom burden and health care utilization. © 2021 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2021;■:■-■)

Key words: Habitual snoring; Sleep-disordered breathing; Asthma

INTRODUCTION

Childhood asthma has a prevalence of 8.3% in the United States.¹ Although the trend in overall childhood asthma prevalence has plateaued, children from minority races and disadvantaged communities continue to be disproportionately affected.² Disadvantaged populations are also vulnerable to sleep disturbances and poor sleep habits.³ Sleep-disordered breathing (SDB), of which snoring is the primary symptom, is a known comorbidity of asthma and is associated with worse asthma control⁴ and asthma severity.⁵ The prevalence of snoring is estimated to be almost 3 times higher in children with asthma than in children without asthma.⁶⁻⁸ However, little is known about the relationship of snoring or symptoms of SDB and asthma morbidity among inner-city children. Identifying risk factors for poor asthma control and health care utilization for this vulnerable population is extremely important. We evaluated the relationship between snoring frequency and asthma morbidity in children enrolled in the School Inner-City Asthma Study. We hypothesized that greater frequency of snoring was associated with higher asthma morbidity in inner-city school-age children.

METHODS

The School Inner-City Asthma Study is a longitudinal prospective cohort study of children with persistent asthma who attended schools in the Northeast United States from 2008 to 2013. It was designed to assess the relationship of environmental exposures with asthma morbidity. The study design and the characteristics of the study population were previously published.⁹ Briefly, screening questionnaires were distributed each spring in participating schools to identify eligible participants. After obtaining written informed consent from the subject's guardian and assent from the child, enrolled participants underwent a baseline assessment at a research clinic visit during the summer before the academic year in which sociodemographic information, medical history, and symptom profiles were assessed by questionnaire. Aeroallergen sensitization was tested by allergy skin testing (MultiTest device, Lincoln Diagnostics, Decatur, Ill) and/or serum specific IgE (ImmunoCAP, Phadia AB, Uppsala, Sweden). Sensitization was defined by a wheal 3 mm or larger than the negative saline control on skin prick testing or a specific-IgE level of 0.35 kU/L or greater. The tested allergens

included tree pollen, grass, ragweed, dust mites, cat, dog, mouse, rat, cockroach, and molds (Greer, Lenoir, NC). Subjects performed spirometry with a Koko spirometer (Ferraris Respiratory, Louisville, Colo) using American Thoracic Society guidelines.¹⁰ Body mass index (BMI) was calculated using the weight data (kg) and dividing it by height (m) squared (kg/m^2) measured at the initial clinical research visit. Follow-up surveys were administered to a parent/guardian during telephone interviews at 3, 6, 9, and 12 months to evaluate asthma and sleep symptoms, health care use, and effect on the parent/guardian. The study was approved by the Boston Children's Hospital Institutional Review Board and the participating schools.

Study population

Children with asthma from participating schools attending kindergarten through sixth grade were enrolled between 2008 and 2013. Children were included if they had a history of physician-diagnosed asthma and symptoms of cough, wheezing, shortness of breath, or whistling in the chest in the past 12 months; daily asthma controller medication use; or unscheduled medical visits for asthma in the past year. Children were excluded from the study if they had a chronic lung disease other than asthma and cardiovascular disease.

Snoring assessment

As part of our already established protocol,⁹ questionnaire data on sleep habits were assessed through caregiver report at the baseline visit and each quarterly phone interview. The guardian was asked "How often does your child snore?" and the possible responses were "Never," "Rarely (1-2 nights a week)," "Sometimes (3-5 nights a week)," "Always or almost always (6-7 nights a week)," or "Don't know." Snoring category for each observation was determined on the basis of these 4 potential responses.

Outcome measures

The primary outcome was maximum symptom days in the previous 2 weeks. This outcome was used and validated in previous urban home-based studies^{11,12} and school studies.¹³⁻¹⁶ Maximum asthma symptom days were determined by the largest value among the following 3 variables in the 14 days before each survey: (a) number of days with wheezing, chest tightness, or cough, (b) number of days on which child had to slow down or stop his or her play or activities because of wheezing, chest tightness, or cough, and (c) number of nights the participant woke up because of wheezing, chest tightness, or cough leading to disturbed sleep.

Secondary outcomes included health care utilization, defined as the number of hospitalizations and unscheduled health care visits for asthma (including emergency room visits), and asthma morbidity in the previous 14 days assessed as the number of days a caregiver needed to change plans because of the child's asthma, number of missed school days due to asthma, and number of nights the caregiver lost sleep because of the child's asthma. A composite outcome of poor asthma control over the previous 4 weeks was defined by any of the following: shortness of breath more than twice weekly, nighttime awakenings owing to asthma at least once, limitation in activity level, or use of rescue asthma medication 2 or more times weekly.

Covariates

Pediatric age and sex-adjusted BMI percentiles were calculated using the Centers for Disease Control and Prevention classification category: (underweight, BMI < 5th percentile; normal weight, 5th percentile \leq BMI < 85th percentile; overweight, 85th percentile \leq

BMI < 95th percentile; obese, BMI \geq 95th percentile).¹⁷ Atopy was defined as a binomial variable based on allergen sensitization, either present or not. Prematurity was defined as being born before or at and after 37 weeks of gestation. Household income was assessed as a binomial variable as household income below \$45,000 or equal and above \$45,000. Presence of viral upper respiratory tract infection (URI) and allergic rhinitis symptoms was determined on the basis of a 2-week recall (same time period as primary outcome of asthma symptom days) for the questions “During the past 14 days, has [CHILD] had a problem with sneezing, or a runny, or a blocked nose from a cold or the flu?” and “During the past 14 days, has [CHILD] had a problem with sneezing, or a runny, or a blocked nose that was NOT from a cold or the flu?” respectively.

Statistical analysis

Descriptive statistics were used to characterize the snoring groups. The relationship between snoring and asthma morbidity was assessed for each study assessment in which both observations were obtained. Sankey plots were used to demonstrate longitudinal changes in snoring category over time. We evaluated the snoring-asthma morbidity outcome relationship using snoring as a 4-level categorical variable while adjusting for confounders using generalized estimating equations with an exchangeable correlation structure, robust variance estimates, and clustered at the participant level. Binomial family generalized estimating equations with a logit link and an overdispersion parameter were used for 2-week outcomes (ie, 2-week outcomes were modeled as the sum of 14 binomial “successes”) and poor asthma control, negative binomial family, and log link were used for health care utilization and school absences. Age, sex, race/ethnicity, annual household income, BMI, environmental tobacco smoke exposure, history of prematurity, and history of rhinitis were all considered as potential confounders and assessed as categorical variables. BMI and annual household income were the only covariates associated with snoring (predictor) at $P < .01$ and $P < .05$, respectively, and therefore included in the final model. Viral URI and allergic rhinitis symptoms were included in all models given their potential to confound the relationship of snoring and asthma symptoms.

RESULTS

In total, 1186 observations from 339 subjects were included in this analysis. Baseline demographic and clinical characteristics of the study population and by snoring category are summarized in Table I. The mean age of the study population was 7.9 years, roughly half (53.4%) were male, and 16.2% were born prematurely. About half the subjects were on a controller medication at baseline assessment. On average, subjects had normal lung function with mean FEV₁ % predicted 101.6 ± 18.7 and mean FEV₁/forced vital capacity 0.87 ± 0.07 . The study population was predominantly Black (35.1%) and Hispanic (36.3%), and almost three-quarters (72.2%) were from low-income households. At their first report of snoring symptoms, 24.8% reported habitual snoring, 20.4% reported sometimes snoring, 24.5% rare snoring, and 30.4% reported no snoring. Half (49.3%) of the subjects were either overweight or obese. Those reporting habitual snoring at initial assessment were more likely to be obese compared with nonsnorers and rare snorers ($P = .003$ and $P = .04$, respectively). One-third of the children had environmental tobacco exposure. Two-thirds (65.5%) of the subjects were classified as atopic; however, there were no significant differences in atopy status between the snoring groups. Rhinitis was present

in 72.3% of subjects, and there were no statistical differences between the groups. The average maximum asthma symptom days at baseline were 3.4 ± 4.2 days per 14-day recall.

We then assessed whether reported snoring changed over time during the study period (see Figure E1 in this article’s Online Repository at www.jaci-inpractice.org). Of those who initially reported no snoring ($n = 103$), 52 reported rare snoring, 20 reported sometimes snoring, and 12 reported habitual snoring on at least 1 assessment during the study period. Of those who initially reported rare snoring ($n = 83$), 38 reported no snoring, 27 reported sometimes snoring, and 11 reported habitual snoring at least once during follow-up visits. Of those who initially reported sometimes snoring ($n = 69$), 24 reported no snoring, 34 reported rare snoring, and 21 reported habitual snoring at least once during the follow-up visits. Lastly, of those who initially reported habitual snoring ($n = 84$), 12 reported no snoring, 21 reported rare snoring, and 32 reported sometimes snoring at least once during the follow-up visits. During the study period, 52.2% reported no snoring, 56.0% reported rare snoring, 43.7% sometimes snoring, and 37.8% habitual snoring on at least 1 assessment.

We assessed the association of snoring and asthma morbidity at each observation. Multivariate analyses, adjusting for BMI, income, symptoms of viral URI, and symptoms of allergic rhinitis, revealed that predicted means for maximum asthma symptom days by snoring frequency were 2.7 (2.3-3.1) days for nonsnoring observations, 2.7 (2.2-3.1) days for rare snoring observations, 2.7 (2.3-3.2) days for sometimes snoring, and 3.8 (3.2-4.4) days for habitual snoring (Table II).

Compared with nonsnoring observations, the odds ratio (OR) for maximum symptom days was 0.98 (95% CI, 0.75-1.27; $P = .87$) for rare snoring, 1.01 (95% CI, 0.77-1.33; $P = .92$) for sometimes snoring, and 1.58 (95% CI, 1.19-2.10; $P < .002$) for habitual snoring observations. Habitual snoring was also associated with significantly greater odds of an asthma symptom day compared with each of the other snoring frequency categories (rare snoring [OR, 1.62; 95% CI, 1.20-2.17; $P = .001$] and sometimes snoring groups [OR, 1.56; 95% CI, 1.17-2.07; $P = .002$]) (Table III).

Habitual snoring was also associated with significantly increased health care use (incidence rate ratio, 1.72; 95% CI, 1.10-2.69; $P = .02$) compared with nonsnoring. Habitual snoring (OR, 1.49; 95% CI, 1.05-2.11; $P = .03$) was associated with increased odds of higher composite asthma control scores than nonsnoring. In addition, caregivers were affected such that all snoring frequencies were associated with increased odds of missed sleep compared with no snoring. There was a stepwise increase in which the rare snoring observations had OR 1.45 (95% CI, 1.01-2.08; $P = .04$), sometimes snoring OR 1.69 (95% CI, 1.07-2.66; $P = .02$), and habitual snoring OR 2.35 (95% CI, 1.55-3.56; $P < .001$). Habitual snoring was associated with greater odds of missed caregiver sleep compared with rare snoring (OR, 1.62; 95% CI, 1.10-2.39; $P = .02$), as well. Habitual snoring was associated with greater odds of changed caregiver plans compared with no snoring (OR, 2.63; 95% CI, 1.50-4.62; $P = .001$). In addition, habitual snoring was associated with greater odds of changed plans compared with rare snoring (OR, 1.78; 95% CI, 1.06-2.98; $P = .03$) and sometimes snoring (OR, 1.79; 95% CI, 1.04-3.09; $P = .04$). School absences did not differ by snoring frequency.

TABLE I. Characteristics of the study population by snoring category at initial assessment

Characteristic	Total cohort (N = 339)	Snoring categories*			
		No snoring (N = 103)	Rare snoring (N = 83)	Sometimes snoring (N = 69)	Habitual snoring (N = 84)
Age (y)	7.9 ± 1.9	8.0 ± 1.8	8.1 ± 1.8	7.9 ± 1.9	7.6 ± 2.1
Sex: male	181 (53)	56 (54)	44 (53)	34 (49)	47 (56)
Race					
White	15 (4)	4 (4)	5 (6)	5 (7)	1 (1)
Black	119 (35)	37 (36)	34 (41)	19 (28)	29 (35)
Latino	123 (36)	38 (37)	30 (36)	23 (33)	32 (38)
Mixed	58 (17)	16 (16)	10 (12)	17 (25)	15 (18)
Other	24 (7)	8 (8)	4 (5)	5 (7)	7 (8)
Income <45k	203 (72)	61 (73)	45 (63)	41 (73)	56 (80)
Weight					
Underweight	4 (1)	0 (0)	1 (1)	0 (0)	3 (4)
Normal	165 (49)	60 (59)	45 (55)	31 (45)	29 (35)
Overweight	48 (14)	10 (10)	13 (16)	11 (16)	14 (17)
Obese	119 (35)	32 (31)	23 (28)	27 (39)	37 (45)
Viral URI symptoms past 2 wk†	97 (29)	22 (22)	25 (30)	24 (34)	26 (31)
Allergic rhinitis symptoms past 2 wk†	176 (52)	45 (44)	44 (53)	34 (50)	53 (63)
ETS	111 (33)	31 (30)	20 (24)	30 (43)	30 (36)
Prematurity	55 (16)	17 (17)	11 (13)	11 (16)	16 (19)
History of rhinitis	245 (72)	68 (66)	58 (70)	53 (77)	66 (79)
Atopy	222 (66)	74 (73)	57 (73)	42 (66)	49 (64)
Asthma medications					
SABA only	150 (44)	46 (45)	33 (40)	30 (43)	41 (49)
ICS and/or montelukast	189 (56)	57 (55)	50 (60)	39 (57)	43 (51)
FEV ₁ , % predicted	101.6 ± 18.7	105.6 ± 19.1	102.1 ± 17.0	96.0 ± 16.8	101.1 ± 20.6
FVC, % predicted	100.3 ± 17.4	102.4 ± 17.6	101.8 ± 17.5	97.4 ± 14.1	98.8 ± 19.3
FEV ₁ /FVC	0.87 ± 0.07	0.88 ± 0.06	0.86 ± 0.08	0.85 ± 0.09	0.87 ± 0.07

Atopy, Sensitization to any aeroallergen; ETS, environmental tobacco smoke exposure; FVC, forced vital capacity; ICS, inhaled corticosteroid; prematurity, history of birth before 37 wk of gestation; SABA, short-acting β -agonist.

*Data presented as N (%).

†Viral URI symptoms were defined as sneezing, or a runny, or a blocked nose due to a cold or the flu, and allergic rhinitis symptoms were defined as sneezing, or a runny, or a blocked nose that was not from a cold or the flu.

DISCUSSION

In this study, we aimed to examine the relationship of snoring frequency and asthma morbidity in school-age children. We found that inner-city school-age children with asthma who reported habitual snoring had higher asthma symptom burden compared with those who reported never, rarely, or sometimes snoring at the same assessment. We also found that health care utilization was significantly increased for those with habitual snoring, which has not been previously reported. These are particularly important findings given that snoring is an easy symptom to screen for and, as demonstrated here, can have important health implications. In addition, the within-subject snoring prevalence varied over time during the study period, which is important to consider in clinical practice and suggests that snoring frequency assessment should be performed regularly.

The prevalence of snoring in children varies broadly from 2.4% to 34.5% depending on what definitions are used.¹⁸ The prevalence of SDB in general pediatric populations ranges from 0.7% to 13.0% owing similarly to varying definitions and methods of testing.¹⁹ Prevalence data for SDB among children with asthma vary even more, with numbers ranging from 7% to 70%.²⁰ However, the prevalence of snoring and SDB in inner-city children with asthma has not been extensively studied, and

thus our findings enrich the understanding of sleep-related comorbidity in this high-risk group.²¹ Within our cohort, we found that the prevalence of habitual snoring at initial report was 24.8% and that more than one-third of the subjects reported habitual snoring during at least 1 assessment, which is on the higher end of what has been reported.

We have shown that, within our cohort of inner-city school-age children, increasing frequency of snoring was associated with higher asthma morbidity. Habitual snoring was associated with higher odds of having asthma symptom days, worse asthma control, and increased caregiver burden evident by missed sleep and changed plans compared with nonsnorers. Specifically, habitual snoring was associated with greater odds of having an asthma symptom day compared with each of the less frequent snoring categories. Our findings are in concordance with those from a large inner-city cohort of predominantly ethnic minority adolescents, in which self-reported SDB was associated with increased asthma burden.²² That study was the first to examine the relationship of symptoms of SDB and asthma severity in predominantly minority race adolescents. Although the relationship of asthma and SDB has been studied in various pediatric cohorts,²³⁻²⁷ our findings extend this knowledge base by including school-age children of minority racial and ethnic

TABLE II. Predicted means of health outcomes adjusted for BMI category, income, and nasal symptoms with a cold/flu and without a cold/flu

Health outcomes	No snoring	Rare snoring	Sometimes snoring	Habitual snoring
Primary outcome				
Maximum symptom days	2.7 (2.3- 3.1)	2.7 (2.2-3.1)	2.7 (2.3-3.2)	3.8 (3.2-4.4)
Secondary outcomes				
Health care use	0.21 (0.14-0.28)	0.25 (0.17-0.33)	0.25 (0.17-0.34)	0.37 (0.25-0.48)
School absences	0.9 (0.6-1.1)	1.0 (0.7-1.2)	1.1 (0.8-1.4)	1.1 (0.8-1.5)
Missed sleep	0.7 (0.5-0.9)	0.9 (0.7-1.2)	1.1 (0.8-1.4)	1.5 (1.1-1.8)
Changed plans	0.2 (0.1-0.3)	0.4 (0.2-0.5)	0.4 (0.2-0.5)	0.6 (0.4-0.9)
Composite asthma control	0.43 (0.37-0.49)	0.50 (0.44-0.56)	0.52 (0.45-0.58)	0.53 (0.47-0.60)

Primary outcome: Maximum asthma symptom days were determined by the largest value among the following 3 variables in the 14 d before each survey: (a) number of days with wheezing, chest tightness, or cough; (b) number of days on which child had to slow down or stop his or her play or activities because of wheezing, chest tightness, or cough; and (c) number of nights the participant woke up because of wheezing, chest tightness, or cough leading to disturbed sleep.

Secondary outcomes: Health care use was defined as number of hospitalizations and unscheduled health care visits; school absences and changed plans were defined as number of days of missed school or change in caregiver plans; missed sleep was defined as number of nights caregiver lost sleep because of child's asthma; a composite outcome of poor asthma control over the previous 4 wk was defined by any of the following: shortness of breath more than twice weekly, nighttime awakenings owing to asthma at least once, limitation in activity level, or use of rescue asthma medication 2 or more times weekly.

TABLE III. Multivariate analysis of snoring and asthma morbidity

Health outcomes	How often does your child snore?			
	No snoring (N = 363) (177 subjects)	Rare snoring (N = 319) (190 subjects)	Sometimes snoring (N = 239) (148 subjects)	Habitual snoring (N = 265) (128 subjects)
Maximum symptom days	Reference group	OR = 0.98 (0.75-1.27) <i>P</i> = .87	OR = 1.01 (0.77-1.33) <i>P</i> = .92	OR = 1.58 (1.19-2.10) <i>P</i> = .002*†
Health care use	Reference group	IRR = 1.17 (0.74-1.84) <i>P</i> = .49	IRR = 1.18 (0.72-1.92) <i>P</i> = .52	IRR = 1.72 (1.10-2.69) <i>P</i> = .02
School absences	Reference group	IRR = 1.12 (0.78-1.61) <i>P</i> = .54	IRR = 1.24 (0.82-1.88) <i>P</i> = .31	IRR = 1.28 (0.84-1.93) <i>P</i> = .25
Missed sleep	Reference group	OR = 1.45 (1.01-2.08) <i>P</i> = .04	OR = 1.69 (1.07-2.66) <i>P</i> = .02	OR = 2.35 (1.55-3.56) <i>P</i> < .001‡
Changed plans	Reference group	OR = 1.48 (0.91-2.40) <i>P</i> = .11	OR = 1.47 (0.79-2.72) <i>P</i> = .22	OR = 2.63 (1.50-4.62) <i>P</i> = .001§,
Composite asthma control	Reference group	OR = 1.24 (0.91-1.69) <i>P</i> = .17	OR = 1.29 (0.93-1.80) <i>P</i> = .13	OR = 1.49 (1.05-2.11) <i>P</i> = .03

IRR, Incidence rate ratio.

Primary outcome: Maximum asthma symptom days were determined by the largest value among the following 3 variables in the 14 d before each survey: (a) number of days with wheezing, chest tightness, or cough; (b) number of days on which child had to slow down or stop his or her play or activities because of wheezing, chest tightness, or cough; and (c) number of nights the participant woke up because of wheezing, chest tightness, or cough leading to disturbed sleep. The outcome is a score from 0 to 14 d. Secondary outcomes: Health care use was defined as number of hospitalizations and unscheduled health care visits; school absences and changed plans were defined as number of days of missed school or change in caregiver plans; missed sleep was defined as number of nights caregiver lost sleep because of child's asthma; a composite outcome of poor asthma control over the previous 4 wk was defined by any of the following: shortness of breath more than twice weekly, nighttime awakenings owing to asthma at least once, limitation in activity level, or use of rescue asthma medication 2 or more times weekly.

*Significantly different than Rare snoring (OR, 1.62 [1.20-2.17]; *P* = .001).

†Significantly different than Sometimes snoring (OR, 1.56 [1.17-2.07]; *P* = .002).

‡Significantly different than Rare snoring (OR, 1.62 [1.10-2.39]; *P* = .02).

§Significantly different than Rare snoring (OR, 1.78 [1.06-2.98]; *P* = .03).

||Significantly different than Sometimes snoring (OR, 1.79 [1.04-3.09]; *P* = .04). All results adjusting for BMI category, income, nasal symptoms with a cold/flu, and nasal symptoms without a cold/flu.

backgrounds. The high prevalence of SDB symptoms among inner-city children and the strong relationship with asthma morbidity indicate the importance of identifying those patients who are at risk of SDB because its treatment can lead to significant improvement in asthma morbidity, control, and health care utilization.^{25,28,29}

A particularly novel finding of our study is that habitual snoring was associated with increased health care utilization, a finding that has not been previously reported. This is an important finding to consider in a pediatric population of inner-city children who are already disproportionately affected by

asthma. The fact that the OR for health care utilization was highest, and only statistically significant, for habitual snoring may indicate that this category of frequency truly separated those with SDB from those without clinically significant snoring. SDB in children with asthma has been associated with increased asthma burden,⁵ worsened asthma control,^{4,30} and prolonged hospitalizations,³¹ consistent with our findings for habitual snoring. Treatment of SDB can lead to improved asthma control²⁸ and fewer exacerbations²⁵ among children with asthma and SDB. This is clinically applicable because report of snoring is easy to screen for, and therefore children at risk for worse health

outcomes can be found without requiring the significant time or resources associated with formal polysomnography, which may not always be available.

Our study highlights other important findings related to SDB and asthma in inner-city children. First, we did not find an association between BMI and snoring frequency. This is likely secondary to the fact that SDB and snoring in school-age children are primarily related to adenotonsillar hypertrophy³² rather than obesity. Second, there was no relationship between snoring frequency and rhinitis or allergic sensitization. Although rhinitis is a risk factor for asthma and SDB, there is paucity of literature on its role in the relationship of these 2 common conditions. Two pediatric studies on children with asthma found an association between allergic rhinitis and prevalence of questionnaire-based SDB³³ and polygraphy-diagnosed obstructive sleep apnea.³⁴ The lack of association in our study may be related to different definitions of rhinitis and allergic rhinitis among the studies and varying definitions of SDB. Third, we did not identify a relationship between snoring and race. Snoring and SDB are more common in minority populations,^{35,36} but it is plausible that because our study cohort was of majority Hispanic and Black, there was not enough diversity to detect a difference between the snoring groups.

The finding of within-subject variability in snoring frequency over the course of the study period is an important finding to consider, as well, particularly in regard to clinical practice. This may be related to seasonal variability and risk factors that can fluctuate over time, such as environmental allergens and viral infections.³⁷ It highlights the need for repeatedly assessing snoring; a 1-time assessment of SDB symptoms would frequently misclassify a patient and potentially fail to identify those children at risk for worse asthma morbidity.

One of the strengths of our study is a large sample size of children with persistent asthma, particularly within a cohort of children who were mostly of minority race. Also, with the time-varying assessments we were able to evaluate for fluctuations in snoring frequency over the course of the year. This allowed for a more dynamic evaluation of snoring burden and its relationship with asthma health outcomes as opposed to a 1-time baseline cross-sectional assessment. We were also able to evaluate various domains of asthma morbidity, in regard to symptoms, asthma control, health care utilization, and caregiver burden, which allowed for a comprehensive assessment of the relationship between snoring and asthma morbidity.

We acknowledge that lack of objective assessments of SDB is a limitation that may cause overestimation or underestimation of the problem. Although polysomnography is the criterion standard diagnostic test in children, it is not always feasible in large-scale studies, or clinical practice, due to access, time, and cost. However, the significant associations of snoring frequency with asthma outcomes suggests that this symptom assessment is an acceptable, and clinically useful, surrogate for SDB in relation to asthma morbidity. Our cohort primarily consisted of Black and Hispanic children with asthma from disadvantaged neighborhoods, thereby limiting the generalizability of our findings to some degree. Recall bias in questionnaire-based assessments may influence the association of snoring frequency and asthma-related health care outcomes. It is possible that parents attributed some symptoms to asthma incorrectly. Nevertheless, the primary outcome of maximum asthma symptom days is a validated tool that has been widely used in

epidemiologic studies of asthma with high reliability.¹¹⁻¹⁶ In addition, although snoring assessments were performed at each quarterly visit, the questions did not reflect a specific time frame, potentially affecting the interpretation of the association between snoring and asthma morbidity for each observation. It is also a limitation that most of the covariates we adjusted for in our models were collected only at baseline so we were unable to account for variability in these factors during the study period and the potential effect on the association between snoring and asthma morbidity. However, it is unlikely that many of the covariates would have changed in clinically meaningful ways during the study period. We also included viral URI and allergic rhinitis symptoms based on 2-week recall, which were assessed at each quarterly visit, in all our models given their potential confounding effect on the relationship of snoring and asthma symptoms. We did not find these symptoms to confound our results. However, we did not collect data on nasal corticosteroids or antihistamines.

CONCLUSIONS

Within our cohort of inner-city school-age children with asthma, we found that snoring was highly prevalent and was associated with higher asthma morbidity and increased health care. In addition, symptoms of SDB fluctuate substantially over time, which is important to consider in clinical practice when assessing for comorbidities of asthma. Our findings highlight the need to screen children with asthma for symptoms of SDB, particularly snoring frequency, at each encounter. Treatment of this underlying comorbidity may significantly improve their asthma-related outcomes.

Acknowledgments

We thank the following companies for their generous donations. Lincoln Diagnostics, Inc, Decatur, Ill, Multi-Test II devices; Greer, Inc, Lenoir, NC, allergenic extracts for skin testing; Thermo Fisher, Inc, ImmunoCAP testing; Monaghan Medical, Inc, aerochambers; and Aerocrine, Inc, Solna, Sweden, NiOx Machines.

REFERENCES

- Zahran HS, Bailey CM, Damon SA, Garbe PL, Breyse PN. Vital signs: asthma in children—United States, 2001-2016. *MMWR Morb Mortal Wkly Rep* 2018; 67:149-55.
- Akinbami LJ, Simon AE, Rossen LM. Changing trends in asthma prevalence among children. *Pediatrics* 2016;137:1-7.
- Grandner MA, Petrov MER, Rattanaumpawan P, Jackson N, Platt A, Patel NP. Sleep symptoms, race/ethnicity, and socioeconomic position. *J Clin Sleep Med* 2013;9:897-905. 905A-D.
- Ginis T, Akcan FA, Capanoglu M, Toyran M, Ersu R, Kocabas CN, et al. The frequency of sleep-disordered breathing in children with asthma and its effects on asthma control. *J Asthma* 2017;54:403-10.
- Ross KR, Storfer-Isser A, Hart MA, Kibler AMV, Rueschman M, Rosen CL, et al. Sleep-disordered breathing is associated with asthma severity in children. *J Pediatr* 2012;160:736-42.
- Goldstein NA, Abramowitz T, Weedon J, Koliskor B, Turner S, Taioli E. Racial/ethnic differences in the prevalence of snoring and sleep disordered breathing in young children. *J Clin Sleep Med* 2011;7:163-71.
- Goldstein NA, Aronin C, Kantrowitz B, Hershcopf R, Fishkin S, Lee H, et al. The prevalence of sleep-disordered breathing in children with asthma and its behavioral effects. *Pediatr Pulmonol* 2015;50:1128-36.
- Kaditis AG, Alonso Alvarez ML, Boudewyns A, Alexopoulos EI, Ersu R, Joosten K, et al. Obstructive sleep disordered breathing in 2- to 18-year-old children: diagnosis and management. *Eur Respir J* 2016;47:69-94.

9. Phipatanakul W, Bailey A, Hoffman EB, Sheehan WJ, Lane JP, Baxi S, et al. The school inner-city asthma study: design, methods, and lessons learned. *J Asthma* 2011;48:1007-14.
10. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. *Eur Respir J* 2005;26:319-38.
11. Morgan WJ, Crain EF, Gruchalla RS, O'Connor GT, Kattan M, Evans R III, et al. Results of a home-based environmental intervention among urban children with asthma. *N Engl J Med* 2004;351:1068-80.
12. Busse WW, Morgan WJ, Gergen PJ, Mitchell HE, Gern JE, Liu AH, et al. Randomized trial of omalizumab (anti-IgE) for asthma in inner-city children. *N Engl J Med* 2011;364:1005-15.
13. Lai PS, Sheehan WJ, Gaffin JM, Petty CR, Coull BA, Gold DR, et al. School endotoxin exposure and asthma morbidity in inner-city children. *Chest* 2015; 148:1251-8.
14. Gaffin JM, Hauptman M, Petty CR, Sheehan WJ, Lai PS, Wolfson JM, et al. Nitrogen dioxide exposure in school classrooms of inner-city children with asthma. *J Allergy Clin Immunol* 2018;141:2249-2255.e2.
15. Baxi SN, Sheehan WJ, Sordillo JE, Muilenberg ML, Rogers CA, Gaffin JM, et al. Association between fungal spore exposure in inner-city schools and asthma morbidity. *Ann Allergy Asthma Immunol* 2019;122:610-615.e1.
16. Sheehan WJ, Permaul P, Petty CR, Coull BA, Baxi SN, Gaffin JM, et al. Association between allergen exposure in inner-city schools and asthma morbidity among students. *JAMA Pediatr* 2017;171:31-8.
17. Barlow SE. Expert committee recommendations regarding the prevention, assessment, and treatment of child and adolescent overweight and obesity: summary report. *Pediatrics* 2007;120:S164-92.
18. Lumeng JC, Chervin RD. Epidemiology of pediatric obstructive sleep apnea. *Proc Am Thorac Soc* 2008;5:242-52.
19. Bixler EO, Vgontzas AN, Lin H-M, Liao D, Calhoun S, Vela-Bueno A, et al. Sleep disordered breathing in children in a general population sample: prevalence and risk factors. *Sleep* 2009;32:731-6.
20. Brockmann PE, Bertrand P, Castro-Rodriguez JA. Influence of asthma on sleep disordered breathing in children: a systematic review. *Sleep Med Rev* 2014;18:393-7.
21. Ross K. Sleep-disordered breathing and childhood asthma: clinical implications. *Curr Opin Pulm Med* 2013;19:79-83.
22. Zandieh SO, Cespedes A, Ciarleglio A, Bourgeois W, Rapoport DM, Bruzzese J-M. Asthma and subjective sleep disordered breathing in a large cohort of urban adolescents. *J Asthma* 2017;54:62-8.
23. Sulit LG, Storfer-Isser A, Rosen CL, Kirchner HL, Redline S. Associations of obesity, sleep-disordered breathing, and wheezing in children. *Am J Respir Crit Care Med* 2005;171:659-64.
24. Ramagopal M, Mehta A, Roberts DW, Wolf JS, Taylor RJ, Mudd KE, et al. Asthma as a predictor of obstructive sleep apnea in urban African-American children. *J Asthma* 2009;46:895-9.
25. Kheirandish-Gozal L, Dayyat EA, Eid NS, Morton RL, Gozal D. Obstructive sleep apnea in poorly controlled asthmatic children: effect of adenotonsillectomy. *Pediatr Pulmonol* 2011;46:913-8.
26. Fagnano M, van Wijngaarden E, Connolly HV, Carno MA, Forbes-Jones E, Halterman JS. Sleep-disordered breathing and behaviors of inner-city children with asthma. *Pediatrics* 2009;124:218-25.
27. Ross KR, Hart MA, Storfer-Isser A, Kibler AMV, Johnson NL, Rosen CL, et al. Obesity and obesity related co-morbidities in a referral population of children with asthma. *Pediatr Pulmonol* 2009;44:877-84.
28. Goldstein NA, Thomas MS, Yu Y, Weaver DE, Watanabe I, Dimopoulos A, et al. The impact of adenotonsillectomy on pediatric asthma. *Pediatr Pulmonol* 2019;54:20-6.
29. Levin JC, Gagnon L, He X, Baum ED, Karas DE, Chupp GL. Improvement in asthma control and inflammation in children undergoing adenotonsillectomy. *Pediatr Res* 2014;75:403-8.
30. Dooley AA, Jackson JH, Gatti ML, Fanous H, Martinez C, Prue DC, et al. Pediatric sleep questionnaire predicts more severe sleep apnea in children with uncontrolled asthma [published online ahead of print September 14, 2020]. *J Asthma*, <https://doi.org/10.1080/02770903.2020.1818775>.
31. Shanley LA, Lin H, Flores G. Factors associated with length of stay for pediatric asthma hospitalizations. *J Asthma* 2015;52:471-7.
32. Kang K-T, Chou C-H, Weng W-C, Lee P-L, Hsu W-C. Associations between adenotonsillar hypertrophy, age, and obesity in children with obstructive sleep apnea. *PLoS One* 2013;8:e78666.
33. Perikleous E, Steiropoulos P, Nena E, Iordanidou M, Tzouveleki A, Chatzimichael A, et al. Association of asthma and allergic rhinitis with sleep-disordered breathing in childhood. *Front Pediatr* 2018;6:250.
34. Nguyen-Hoang Y, Nguyen-Thi-Dieu T, Duong-Quy S. Study of the clinical and functional characteristics of asthmatic children with obstructive sleep apnea. *J Asthma Allergy* 2017;10:285-92.
35. Pranathiageswaran S, Badr MS, Severson R, Rowley JA. The influence of race on the severity of sleep disordered breathing. *J Clin Sleep Med* 2013; 9:303-9.
36. Rosen CL, Larkin EK, Kirchner HL, Emancipator JL, Bivins SF, Surovec SA, et al. Prevalence and risk factors for sleep-disordered breathing in 8- to 11-year-old children: association with race and prematurity. *J Pediatr* 2003;142:383-9.
37. Gozal D, Shata A, Nakayama M, Spruyt K. Seasonal variability of sleep-disordered breathing in children. *Pediatr Pulmonol* 2011;46:581-6.

ONLINE REPOSITORY

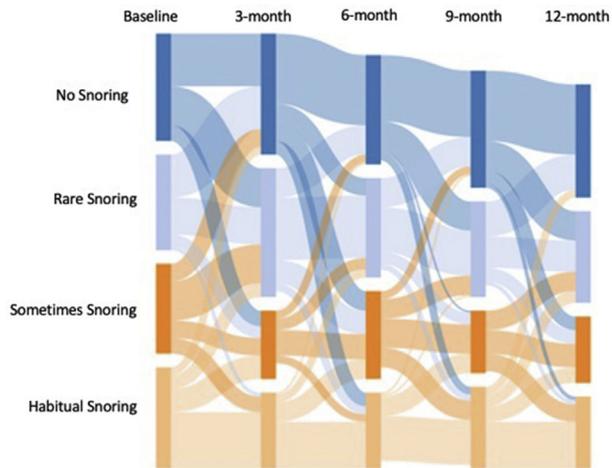


FIGURE E1. Snoring frequency over time by quarterly assessments period. Figure depicting variation in snoring frequency during the study period. Stacked bars represent the percentage of subjects within each snoring category at each quarterly assessment. Connecting lines represent the proportion of subjects changing categories between each assessment.