

Prevalence and Persistence of Sleep Disordered Breathing Symptoms in Young Children: A 6-Year Population-Based Cohort Study

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Study Objectives: To describe the prevalence, persistence, and characteristics associated with sleep disordered breathing (SDB) symptoms in a population-based cohort followed from 6 months to 6.75 years.

Design: Avon Longitudinal Study of Parents and Children (ALSPAC).

Setting: England, 1991-1999.

Participants: 12,447 children in ALSPAC with parental report of apnea, snoring, or mouth-breathing frequency on any one of 7 questionnaires.

Measurements: Symptom prevalence rates—assessed as “Always” and “Habitually”—are reported at 0.5, 1.5, 2.5, 3.5, 4.75, 5.75, and 6.75 years of age. The proportion of children in whom symptoms develop, persist or abate between observation points is reported. Exploratory multivariate analyses identified SDB risk factors at 1.5, 4.75, and 6.75 years.

Results: The prevalence of apnea (“Always”) is 1%-2% at all ages assessed. In contrast, snoring “Always” ranges from 3.6% to 7.7%, and snoring “Habitually” ranges from 9.6% to 21.2%, with a notable increase from 1.5- 2.5 years. At 6 years old, 25% are habitual mouth-breathers. The “Always” and “Habitual” incidence of each symptom between time points is 1%-5% and 5%-10%, respectively. In multivariate analyses of combined symptoms, socioeconomic factors have stronger, more persistent effects upon increased SDB risk than gestational age, gender, or race (aside from 1.5 years); adenoidectomy decreases risk by 40%-50%.

Conclusions: This is the first natural history study of the primary symptoms of SDB across a key 6-year period in the development of SDB symptoms. Snoring rates are higher and spike earlier than previously reported. Symptoms are dynamic, suggesting the need for early and continued vigilance in early childhood.

Keywords: Epidemiological, sleep disordered breathing, snoring, apnea, mouth-breathing, children

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INTRODUCTION

Obstructive sleep apnea is estimated to affect about 1% to 4% of children. Yet many more may suffer significant medical consequences from less obvious forms of obstructive sleep disordered breathing (SDB) arising from variations in upper airway anatomy, local tissue compliance, and neurophysiological control. SDB disrupts nocturnal respiration and sleep, with adverse consequences for cognition,¹⁻⁴ behavior,²⁻⁴ cardiac function, and growth.³⁻⁶ For most children, adenotonsillar hypertrophy is a primary cause of SDB. Tonsillectomy and adenoidectomy is curative in many cases,^{7,8} though recent data suggest lower success rates than previously believed, particularly in children who are > 7 years and/or obese.⁹ SDB reportedly peaks between 2-6 years of age, given the adenotonsillar hypertrophy found at this time,¹⁰ but may be found in younger and older children.¹¹

Despite an exponential increase in research—a more than 10-fold increase in the number of scientific publications on sleep disordered breathing and children between 1990-1999 and 2000-2010—population-based data on the natural history of

SDB in children are scarce. Existing natural history studies have enrolled either preschool¹² or school-aged¹³⁻¹⁵ children, leaving important questions during the earliest years unresolved.¹⁶ Only one study follows children longer than 3 years,¹⁵ and only one was based upon a large population-based cohort.¹⁴

In contrast, longitudinal, population-based cohort studies have yielded data on behaviorally related sleep disorders in young¹⁷ and school-aged children,¹⁸ children transitioning from pre- to school-age,¹⁹ and adolescents²⁰ based upon reported symptoms. One reason for the gap in longitudinal population-based studies of SDB in children may be the infeasibility of employing polysomnography (PSG) for epidemiological purposes, given the expense, time, and possible selection bias of those undergoing PSG. However, as baseline SDB symptoms in comparison to PSG may predict treatment responses just as well,²¹ epidemiological studies of SDB symptoms may actually have considerable clinical relevance, at least until PSG methods can be made more informative and less cost-prohibitive for large samples.

This paper fills a critical gap in the literature by presenting the first-ever population-based cohort data on 3 key symptoms of SDB—snoring, mouth-breathing, and apnea—assessed at 7 time points from birth through 6.75 years of age. Two research questions were at the core of the study: (1) “What is the prevalence of snoring, mouth-breathing, and apnea in the cohort, over time?” and (2) “In what proportions of children do each of these symptoms develop, resolve, or persist in the shorter term (i.e., approximately 12-month period)?” Secondly, we conducted exploratory multivariate analyses to identify factors

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associated with the prevalence of each symptom prior to (1.5 years), during (4.75 years), and at the end (6.75 years) of the previously reported peak prevalence of symptoms.

METHODS

Population

The Avon Longitudinal Study of Parents and Children (ALSPAC), a geographically based cohort study of children, enrolled pregnant women residing in a defined part of the former county of Avon in southwest England with an expected date of delivery between April 1991 and December 1992. A total of 14,541 pregnant women were enrolled. The cohort has been described in detail elsewhere and is broadly representative of the UK population in terms of socioeconomic status (SES), although with a slight under-representation of ethnic minority families, and slight overrepresentation of wealthier families. Data for these analyses represent the 14,049 live births. Analyses were conducted on the ALSPAC sample because it is, to the best of our knowledge, the only existing population-based study to assess SDB symptoms in children from infancy through the early school years.

SDB Symptom Assessment

SDB symptoms were assessed through parent report of snoring, apnea, and mouth-breathing via preexisting questionnaires developed by ALSPAC that were mailed to participants. Snoring and apnea lie along the continuum of symptoms used to define SDB; mouth-breathing is a common clinical finding in younger²² and older²³ children with SDB, and often resolves post-tonsillectomy or adenoidectomy,²⁴ along with snoring and apnea. As a secondary data analysis, objective sleep evaluation measures were unavailable. However, items similar to, or the same as those used in ALSPAC have consistently been validated against polysomnographic data obtained from sleep laboratories. Some of these validation studies have employed parent report of all 3 SDB symptoms—snoring, mouth-breathing, and apnea,^{21,25-28} while a few have included only snoring and apnea.^{29,30} As data were collected in the 1990s, parent responses are unlikely to have been affected by the increased media and clinician attunement to pediatric sleep disorders since that time.

SDB symptoms were assessed as follows:

Mouth-Breathing: “Does she breathe through her mouth rather than her nose?” Through 3.5 years, mouth breathing was assessed at 4 levels: Always, Much of the Time, Rarely, Never. Beginning at 4.75 years, the scale was expanded to 5 levels.

Apnea: “When asleep, does she seem to stop breathing or hold breath for several seconds at a time?” Apnea was assessed in this manner at 3 levels (Yes/Often, Yes/Sometimes, No) except at 1.5 years, when the additional category “Yes, But Rarely” was included.

Snoring: “Does she snore for more than a few minutes at a time?” At 6 months, snoring was assessed at 3 levels: Most Nights, Quite Often, Rarely. At 1.5 years, responses were expanded to 4 levels: Most Nights, Quite Often, Sometimes, Rarely/Never. Options reverted to 3 levels at 2.5 years (Yes/Often, Yes/Sometimes, No) and 3.5 years (Most Nights, Quite Often, Rarely). From 4.75 years onward, snoring was assessed at 5 levels: Most Nights, Quite Often, Sometimes, Only Rarely, Never.

Covariate Assessment

We selected relevant covariates for examining potential attrition bias in our data on prevalence and persistence (primary aims), and for our exploratory multivariate analyses (secondary aim). Initially, we selected potential risk factors for SDB based upon existing literature and clinical judgment. Bivariate analyses of more than 300 such variables’ association with both “Always” and “Habitual” reduced these to:

Maternal and family characteristics

- *Maternal cigarette smoking:* defined as “ever” vs. “never” prior to pregnancy.
- *Ethnicity of child:* defined as white or non-white.
- *Housing inadequacy:* coded “Yes” if crowdedness (< 1 room/person); “Yes” for “homelessness”; “Yes” for the periods from the index child’s birth-2 years, and/or from 2-4 years. Otherwise, housing inadequacy was coded “No.”
- *Paternal social class:* assessed as manual vs. professional.
- *Maternal education:* assessed as low or high. “Low” was defined as “O” level education or less (the end of compulsory education, resulting in a school leaving certificate at 16 in the UK), from 5 original groupings.

Child characteristics

- *Birthweight and gestational age, analyzed as continuous and categorical variables.* For the latter, low birthweight was defined as < 2500 grams, and prematurity as < 37 weeks gestation.
- *Breastfeeding:* identifies whether the child was ever breast-fed or not.
- *Other children:* number of other children in the house when the index child was 6 months old.
- *Asthma:* On each questionnaire, parents were asked whether their child had wheezed in the prior 12 months and if he or she had, the total number of days. This number was used as the primary indicator for asthma.
- *Adenoidectomy/Tonsillectomy:* On the questionnaires for 4.75, 5.75, and 6.75 years, parents were asked whether their child had ever had their tonsils or adenoids removed. Exact surgery dates for ALSPAC participants were unavailable. In population-based data from another study begun in the 1990s in Northern Ireland, the median ages for these surgeries were 6.7 years and 5.6 years, respectively.³¹
- *BMI z-scores:* We computed age- and sex-specific BMI z-scores for ages 0.5, 1.5, and 3.5 years or younger,³² when universal measurements are taken by health visitors in U.K. homes, and recorded in personal child health records. If anthropometric data were available for the 10% subsample directly measured by ALSPAC staff at study clinics, those data were used instead of the home visitor measures, though the accuracy of the latter measures has been established.³³

Statistical Analyses

SDB symptom prevalence rates were derived from ALSPAC’s preexisting response options. As noted above, these response options were not uniform either across symptoms or over time. This is a common limitation in definitions of parent-reported snoring.³⁴ For dichotomous outcomes of symptom presence/absence, we addressed this problem by employing both the “Al-

ways” and “Habitual” terminology, consistent with prior work. “Always” was defined as the left-most extreme response option, while “Habitual” was defined as the 2 left-most extreme response options (e.g., “Yes/Often” and “Yes/Sometimes” for apnea). Note that this was not an issue for combined symptom outcomes in multivariate analyses, because we used standardized scores (see below), which mitigate the effects of varying response options. The cohort’s prevalence of “Always” and “Habitual” SDB symptoms is shown for each time point.

The persistence of symptoms was based upon children with non-missing data for 2 consecutive time points. Changes in “Always” having the symptom were described as: “Develops,” “Resolves,” or “Persists.” These changes reflect the differences in proportions from one time point to the next who go on to develop the symptom, in whom the symptom is no longer present, and in whom the symptom remains present. Corresponding data for “Habitual” transitions are in Supplemental Appendices.

Exploratory multivariate logistic regression analyses were employed to describe the characteristics associated with each of the 3 symptoms separately (i.e., having the symptom or not) at 1.5, 4.75, and 6.75 years. These 3 time points were selected to simplify data presentation, and because they reflect periods prior to, during, and at the end of the peak prevalence for SDB. (We note that given the complexity of the data, results from any one time point should not be overinterpreted; thus these are considered exploratory analyses). To analyze the effect of the 3 symptoms combined, we derived z-scores by extrapolating the codes across an interval from 0-100 with higher values denoting more symptoms (e.g., Apnea, 0 = No, 50 = Yes/sometimes, 100 = Yes/often). At each time point, the assigned scores of the 3 symptoms were summed, yielding a score from 0-300, which was then standardized to derive the SDB z-scores used as dependent variables in multiple linear regression models.

Both the multivariate logistic and regression analyses incorporate all putative covariates in the model. In Supplemental Tables S1-S2 we present the multivariate logistic regression analyses for the subsample of children with SDB data at all 7 time points.

First- and second-order interactions of wheezing, tonsillectomy (“ever” by 4.75 and 6.75 years), and adenoidectomy (“ever” by 4.75 and 6.75 years) were included in the above multivariate models given that (a) SDB is a prime indication for both surgeries, (b) wheezing history in this cohort is predictive of physician-diagnosed asthma,³⁵ which is a known risk factor for SDB,^{36,37} and (c) tonsillectomy medi-

Table 1—Characteristics of the study population with and without snoring data at 1.5, 4.75, and 6.75 years

Covariates	1.5 years		4.75 years		6.75 years	
	With Data N = 10,653	Missing N = 3,396	With Data N = 9,007	Missing N = 5,042	With Data N = 7,895	Missing N = 6,154
Wheezed, ever [†]	34.58%	60.75%*	49.24%	83.63%*	53.39%	87.89%*
LBW (< 2500 g)	4.99%	7.93%*	4.60%	7.66%*	4.48%	7.27%*
Preterm (< 37 weeks)	5.80%	7.86%*	5.33%	8.03%*	5.32%	7.56%
Housing, inadequate	9.34%	8.11%*	12.53%	12.25%	11.80%	13.52%
Girl	48.47%	46.67%	47.97%	48.81%	48.45%	48.05%
White [‡]	97.85%	95.21%*	98.11%	95.67%*	98.14%	96.14%*
Smoked, ever	48.66%	58.63%*	47.77%	56.83%*	47.29%	55.75%*
Other child, ≥ 1	54.82%	57.75%*	54.10%	57.76%*	53.70%	57.61%*
Breastfed, never	23.32%	34.71%*	22.32%	31.94%*	21.39%	31.41%*
Paternal employment, manual	35.12%	54.41%*	41.37%	50.97%*	40.53%	50.43%*
Maternal education, lower	62.29%	75.54%*	60.83%	73.55%*	59.47%	72.98%*

*Significant at P < 0.05. P values are from χ^2 test. [†]Based upon report of ever wheezing, prior 12 months. [‡]Participants reporting a race other than white are, in descending order: Black Caribbean (n = 75), Indian (n = 53), Other Black (n = 44), Chinese (n = 8), Pakistani (n = 22), Black African (n = 11), and Bangladeshi (n = 7).

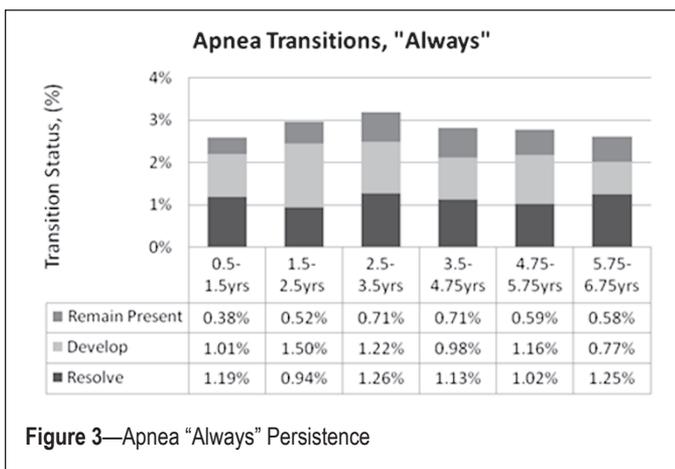
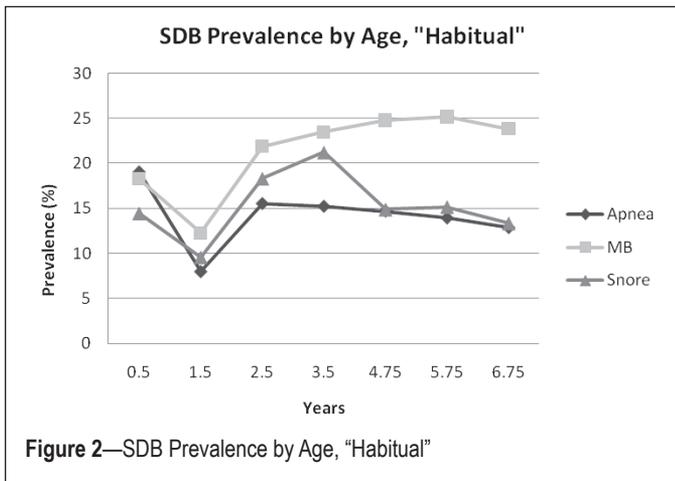
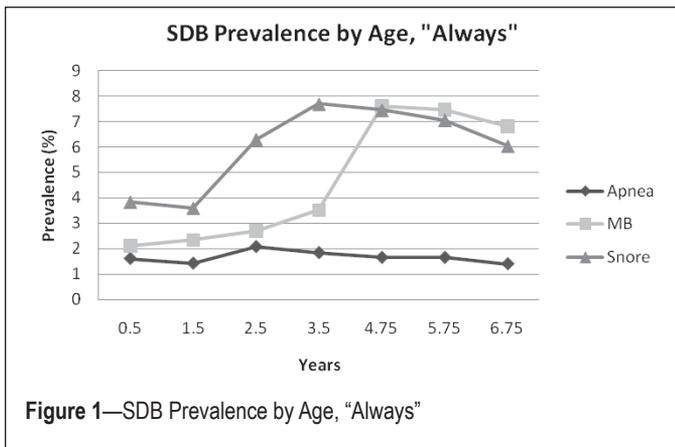
ates the effect of wheeze upon SDB.³⁶ Multivariate models were derived with the complete set of maternal, family, and child characteristics. Prior work found an association between low socioeconomic (SES) and increased risk of SDB, that was mediated by a third variable, high BMI.³⁸ Thus, to determine the effects of BMI, we incorporated BMI z-score changes from 0.6-1.5 years and from 1.5-3.5 years upon SDB outcomes at later time points for the subset of children with non-missing data for both BMI z-score changes and the SDB variables at these ages.

RESULTS

Data Completeness and Attrition Bias

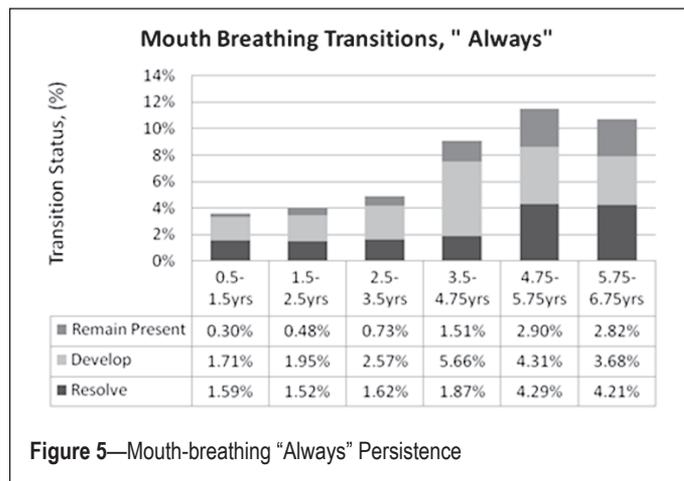
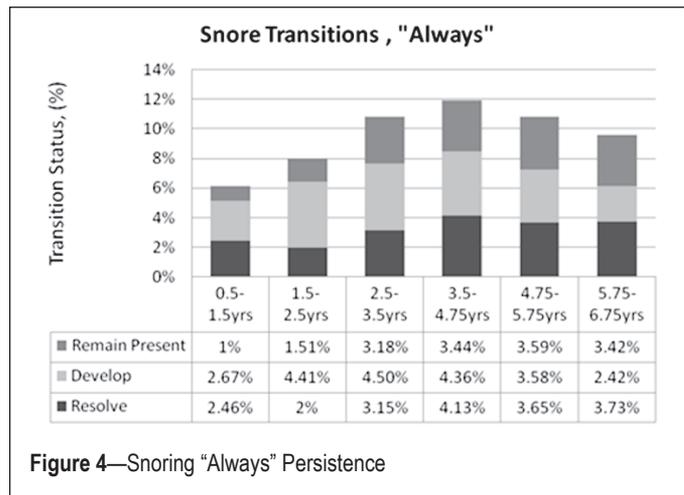
Of the base sample of 14,049 children, respondents with ≥ 1 SDB symptom assessed (not shown) were as follows: 0.5 years = 80.8%; 1.5 years = 78.5%; 2.5 years = 72.8%; 3.5 years = 70.8%; 4.75 years = 67%; 5.75 years = 61.2%; and 6.75 years = 59%. Of the base sample, 45.4% provided at least some SDB data for all 7 time points (n = 6,219). The following proportions of the sample provided partial data: ≥ 6/7 time points = 57.6%; ≥ 5/7 time points = 65.8%; ≥ 4/7 = 72.1%; ≥ 3/7 time points = 77.5%; ≥ 2/7 time points = 83.1%; and ≥ 1/7 time points = 88.7%. Of the base sample, 11.4% did not provide any SDB data. Note, overall ALSPAC questionnaire response rates were nearly identical to those for respondents with ≥ 1 SDB symptom.

Table 1 compares the characteristics of respondents with and without snoring data at 1.5, 4.75, and 6.75 years. Children with missing data were more likely to have SDB symptom risk factors, i.e., prior wheezing, low birthweight, preterm, born to primiparous mother, never breastfed, and lower SES. Children with mouth-breathing data (not shown) at 1.5 (n = 9,970), 4.75 (n = 8,525), and 6.75 (n = 7,460) years and with apnea data at 1.5 (n = 9,774), 4.75 (n = 8,102), and 6.75 (n = 6,998) years exhibited nearly identical patterns of attrition bias to those shown in Table 1.



Prevalence of SDB Across Early Childhood

The prevalence of "Always" snoring, mouth-breathing, and apnea is shown in Figure 1. "Always" apnea prevalence ranged from 1% to 2%; "Always" snoring ranged from 3.6% at 1.5 years, to a peak of 7.7% at 3.5 years, and "Always" mouth-breathing ranged from 2.1% at 0.5 years to 7.6% at 4.75 years, with a doubling from 3.5-4.75 years. As shown in Figure 2, "Habitual" apnea peaked at 19% at 0.5 years, fell to a nadir of 8% at 1.5 years (likely due to a one-time change in response categories as stated above), then plateaued at 12.9% at 6.75 years. Habitual snoring had a low of 9.6% at 1.5 years and reached its height at 3.5 years at 21%. Habitual mouth-breathing was at its lowest point at 1.5 years (12.3%), and then peaked later than either snoring or ap-



nea, at 5.75 years (25.2%). Prevalence data for the subsample of children with SDB symptom data for all 7 time points (n = 6,219) are shown in Supplemental Figures S1-S2. Snoring and mouth-breathing prevalence rates were approximately 1% lower in this subsample, while apnea rates appeared to be unchanged.

Persistence of SDB Symptoms Across Early Childhood

Figures 3-5 depict the proportions of the sample whose symptoms resolved, developed, or remained present between time points per the "Always" measure. Apnea remained stable throughout, at 1% to 2% (Figure 3). Snoring incidence peaked in the middle 4 intervals (Figure 4). Mouth-breathing patterns increased most from 3.5-4.75 years, resolved most from 4.75-5.75 years, and had the most overall shifts in the last 3 intervals (Figure 5). The primary differences for "Habitual" outcomes for all 3 symptoms (Supplemental Figures S3-S5) were relatively greater resolution in the first interval and relatively greater development in the second interval. Overall, each of the 3 "Always" symptoms developed in 1%-5% of the cohort from one time point to the next, while "Habitual" symptoms developed in approximately 5%-10% between time points.

Maternal, Family, and Child Characteristics Associated with Snoring, Mouth-Breathing, and Apnea

Table 2 shows risk factor associations with our "Always" outcomes in the full sample model (vs. the subset with non-

Table 2—Maternal, family, and child characteristics* associated with mouth-breathing, snoring, or apnea at 1.5, 4.75, and 6.75 years (“always” vs. “not always”), odds ratios (95% CIs)

Covariates # Always/Total #	1.5 years			4.75 years			6.75 years		
	Mouth-breathing 133/7672	Snoring 221/8116	Apnea 94/7457	Mouth-breathing 376/6264	Snoring 429/6561	Apnea 89/5910	Mouth-breathing 337/5506	Snoring 319/5774	Apnea 66/5120
Maternal and family characteristics:									
Maternal smoking, ever	1.07 (0.75, 1.52)	0.90 (0.68, 1.19)	0.74 (0.49,1.14)	0.98 (0.76,1.22)	1.11 (0.91,1.35)	1.88 (1.21,2.93)	1.10 (0.87,1.37)	1.11 (0.88,1.40)	1.20 (0.73,1.98)
Race (other v. white)	2.76 (1.09, 6.99)	2.80 (1.38, 5.70)	1.85 (0.56,6.06)	†	1.24 (0.57,2.71)	†	1.06 (0.38,2.95)	†	†
Housing, inadequate (yes v. no)	0.92 (0.50, 1.68)	1.49 (0.99, 2.25)	1.75 (0.97,3.16)	1.58 (1.17,2.12)	1.23 (0.92,1.65)	1.72 (0.99,2.99)	1.53 (1.10,2.12)	1.44 (1.03,2.01)	1.81 (0.93,3.50)
Paternal employment, manual v. professional	1.63 (1.13, 2.37)	1.19 (0.89, 1.59)	1.60 (1.03,2.50)	1.29 (1.03,1.61)	1.31 (1.06,1.62)	0.99 (0.63,1.57)	1.29 (1.01,1.64)	1.28 (1.00,1.64)	1.20 (0.71, 2.04)
Maternal education, lower v. higher	2.06 (1.32, 3.21)	1.82 (1.30, 2.55)	1.51 (0.92,2.47)	1.46 (1.15,1.87)	1.18 (0.94,1.48)	1.06 (0.65,1.71)	1.39 (1.08,1.80)	1.08 (0.84,1.40)	0.89 (0.52,1.53)
Other child:									
1 v. 0	1.33 (0.92, 1.94)	0.81 (0.61, 1.09)	0.92 (0.58,1.44)	0.86 (0.69,1.08)	1.06 (0.86,1.30)	0.74 (0.47,1.16)	0.59 (0.47,0.75)	1.07 (0.84,1.37)	1.33 (0.79,2.25)
> 1 v. 0	1.20 (0.51, 2.79)	1.82 (1.10, 3.00)	1.88 (0.90,3.93)	0.88 (0.52,1.49)	1.00 (0.60,1.65)	1.25 (0.52,2.96)	0.83 (0.48,1.43)	1.52 (0.90,2.57)	0.97 (0.27,3.47)
Child characteristics:									
Gestational age, (continuous, in weeks)	1.02 (0.91, 1.15)	1.00 (0.92, 1.09)	0.96 (0.84,1.10)	0.99 (0.92,1.06)	1.00 (0.94,1.07)	1.05 (0.91,1.22)	0.96 (0.89,1.04)	1.00 (0.92,1.08)	1.23 (1.02,1.47)
Gender (male v. female)	1.49 (1.04, 2.13)	1.46 (1.10, 1.93)	1.22 (0.81,1.86)	1.03 (0.83,1.27)	1.00 (0.82,1.22)	0.78 (0.51,1.20)	1.12 (0.89,1.41)	0.89 (0.71, 1.13)	0.84 (0.51,1.38)
Breastfed (no v. yes)	1.26 (0.86, 1.86)	1.64 (1.22, 2.21)	0.81 (0.49,1.34)	1.20 (0.93,1.53)	1.16 (0.92,1.47)	1.33 (0.81,2.17)	1.44 (1.11,1.87)	1.41 (1.08,1.84)	1.34 (0.76,2.38)
Adenoids removed	N/A†	N/A†	N/A†	0.52 (0.28,0.97)	0.38 (0.22,0.66)	0.33 (0.12,0.94)	0.33 (0.21,0.53)	0.39 (0.24,0.63)	0.49 (0.22,1.09)
Wheezing days	1.02 (0.98, 1.06)	1.06 (1.04, 1.09)	1.09 (1.06, 1.13)	1.04 (1.02,1.06)	1.05 (1.03,1.07)	1.09 (1.05,1.12)	1.05 (1.03,1.08)	1.06 (1.03,1.08)	1.09 (1.05,1.14)

*Only ORs (95% CIs) for putative risk factors significantly associated with ≥ 1 outcome measure in analyses of full sample data are shown (i.e., not the sample subset with BMI z-score change data at 0.5-1.5 years and 1.5-3.5 years). †Race not included in these models as the reported race for all children with SDB “Always” symptoms at these time points is white. ‡N/A because history of adenoidectomy was not assessed at 1.5 years. Bold indicates significant ORs at the level of 0.05.

missing BMI data); Table 3 presents corresponding data for “Habitual” outcomes. Significant ORs (95% CIs) are shown in bold. For maternal and family characteristics, 2- to 3-fold increases in race-associated risks of “Always” snoring and mouth-breathing, and “Habitual” snoring, mouth-breathing, and apnea at 1.5 years, were not significant at later outcomes. (NB: persons reporting race other than white were primarily Black Caribbean or Indian.) Manual paternal employment and lower maternal education increased most SDB symptoms risks by 20%-100% in “Always” models, with fewer and more modest significant “Habitual” effects, although inadequate housing became a significant risk factor (≈ 30% to 55%) in “Habitual” models across symptoms and time points.

Among the significant child characteristics in Tables 2 and 3, wheezing had the smallest (3%-9%)—albeit consistent—effects across symptoms and time points. Other putative SDB risk factors, e.g., gestational age and gender had only limited significance. In contrast, a history of adenoidectomy was associated with 50%-65% reduced “Always” and “Habitual” risks across all symptoms and time points, except apnea at 6.75 years. Not breastfeeding was associated with an increased risk of “Always” snoring at 1.5 (≈ 65%) and 6.75 (≈ 40%) years and “Habitual” snoring at 1.5 (≈ 50%) and 4.75 (≈ 30%) years. Outcomes for the subset of children with SDB data for all 7 time points (Supplemental Tables S1-S2) were quite similar to those in Tables 2 and 3 for maternal

Table 3—Maternal, family, and child characteristics associated* with mouth-breathing, snoring, or apnea at 1.5, 4.75, and 6.75 years (“habitual” vs. “not habitual”), odds ratios (95% CIs)

Covariates Habitual # Case/Total #	1.5 years			4.75 years			6.75 years		
	Mouth-Breathing 824/7672	Snoring 660/8116	Apnea 574/7457	Mouth-Breathing 1443/6246	Snoring 883/6561	Apnea 826/5910	Mouth-Breathing 1270/5506	Snoring 719/5774	Apnea 629/5120
Maternal and family characteristics:									
Maternal smoking, ever	1.17 (1.01,1.35)	0.95 (0.80,1.12)	1.07 (0.90,1.28)	1.06 (0.94, 1.19)	1.06 (0.92,1.23)	1.20 (1.03,1.39)	1.13 (0.99,1.28)	1.02 (0.87,1.20)	1.25 (1.05,1.48)
Race (other v. white)	2.06 (1.29,3.28)	1.89 (1.14,3.12)	1.85 (1.10,3.13)	1.16 (0.70,1.91)	1.38 (0.80,2.39)	1.13 (0.60,2.10)	0.76 (0.41,1.44)	0.91 (0.45,1.84)	0.91 (0.43,1.92)
Housing, inadequate (Yes v. No)	0.86 (0.66,1.13)	1.42 (1.09,1.84)	1.56 (1.18,2.06)	1.27 (1.05,1.54)	1.33 (1.07,1.66)	0.99 (0.78,1.26)	1.36 (1.10,1.67)	1.30 (1.01,1.66)	1.05 (0.79,1.39)
Paternal employment, manual v. professional	1.22 (1.04,1.42)	1.17 (0.98,1.39)	1.09 (0.90,1.31)	1.09 (0.96,1.24)	1.09 (0.93,1.27)	1.11 (0.94,1.30)	1.18 (1.03,1.36)	1.02 (0.85,1.21)	1.08 (0.90,1.30)
Maternal education, lower v. higher	1.48 (1.25,1.76)	1.23 (1.02,1.49)	1.12 (0.92,1.35)	1.47 (1.29,1.68)	1.04 (0.89,1.23)	1.13 (0.96, 1.34)	1.34 (1.16,1.54)	1.18 (0.99,1.40)	1.09 (0.90,1.31)
Other child:									
1 v. 0	1.02 (0.87,1.19)	0.89 (0.75,1.06)	0.91 (0.76,1.09)	0.77 (0.68,0.88)	0.94 (0.81,1.09)	0.85 (0.73,0.99)	0.78 (0.68,0.89)	0.90 (0.76,1.06)	0.91 (0.76,1.08)
> 1 v. 0	1.44 (1.03,2.01)	1.64 (1.17,2.29)	1.03 (0.69,1.54)	0.73 (0.52,1.01)	0.71 (0.48,1.06)	1.04 (0.71,1.53)	0.74 (0.52,1.06)	1.28 (0.86,1.89)	0.84 (0.52,1.35)
Child characteristics:									
Gestational age, (continuous, in weeks)	1.01 (0.96,1.06)	0.99 (0.94,1.04)	1.02 (0.97,1.08)	0.95 (0.91,0.99)	0.95 (0.90,0.99)	1.02 (0.97,1.07)	1.02 (0.97,1.06)	1.02 (0.96,1.07)	1.00 (0.95,1.06)
Gender (male v. female)	1.15 (0.99,1.33)	1.15 (0.98,1.35)	0.98 (0.83,1.17)	0.95 (0.84,1.07)	1.01 (0.87,1.17)	1.04 (0.89,1.21)	1.06 (0.93,1.21)	0.93 (0.79,1.09)	1.19 (1.01,1.42)
Breastfed (no v. yes)	1.32 (1.11,1.56)	1.47 (1.22,1.77)	0.99 (0.80,1.22)	1.26 (1.08,1.45)	1.28 (1.08,1.53)	1.04 (0.86,1.25)	1.29 (1.10,1.51)	1.20 (0.99,1.46)	1.09 (0.88,1.34)
Adenoids removed	N/A [†]	N/A [†]	N/A [†]	0.48 (0.32,0.71)	0.35 (0.23,0.52)	0.58 (0.36,0.95)	0.47 (0.34,0.65)	0.38 (0.27,0.55)	1.01 (0.63,1.61)
Wheezing days	1.03 (1.02,1.05)	1.06 (1.05,1.08)	1.06 (1.04, 1.08)	1.04 (1.03,1.05)	1.04 (1.03,1.06)	1.06 (1.05,1.08)	1.04 (1.03,1.06)	1.06 (1.04,1.08)	1.05 (1.03,1.07)

*Only ORs (95% CIs) for putative risk factors significantly associated with ≥ 1 outcome measure in analyses of full sample data are shown (i.e., not the sample subset with BMI Z score change data at 0.5-1.5 years and 1.5-3.5 years). [†]N/A because history of adenoidectomy was not assessed at 1.5 years. Bold indicates significant ORs at the level of 0.05.

education, adenoidectomy, and wheezing days, but differed markedly in the pattern and magnitude of effects for other variables.

We also conducted subsample analyses with BMI z-score change data (not shown). These found small but significant positive associations between the 0.5-1.5 year BMI z-score Δ and “Always” mouth-breathing at 4.75 years, and between the 0.5-1.5 year BMI z-score Δ and “Habitual” mouth-breathing at both 4.75 and 6.75 years. Given smaller sample sizes in these analyses—averaging $n = 4,500$ at 1.5 years, $n = 2,800$ at 4.75 years, and $n = 2,500$ at 6.75 years across SDB symptoms—risk factor effects were not directly comparable to those found in the full sample.

Maternal, Family, and Child Characteristics Associated with Combined SDB Outcomes

Factors associated with significant changes in mean combined SDB z-scores are shown in Table 4. Positive standardized β values (SE) indicate an increased combined SDB z-score, and negative standardized β values (SE) indicate a decreased combined SDB z-score, compared to the reference category. For example, the 1.5-year mean combined SDB z-score of non-white children was 0.415 higher than for white children, but race was not significant thereafter. Adenoidectomy had the greatest effects, lowering combined SDB z-scores by 0.656 at 4.75 years, and by 0.525 at 6.75 years. Tonsillectomy

Table 4—Maternal, family, and child characteristics associated with combined mouth-breathing, snoring, and apnea standardized scores at 1.5, 4.75, and 6.75 years*

	1.5 years		4.75 years		6.75 years	
	Z Score Parameter Estimate		Z Score Parameter Estimate		Z Score Parameter Estimate	
	Full Sample N = 8,393	Subsample, N = 4,895	Full Sample, N = 7,240	Subsample, N = 3,154	Full Sample, N = 6,673	Subsample, N = 2,957
Maternal and family characteristics:						
Maternal smoking, ever (yes v. no)	0.055 (0.021)	0.033 (0.028)	0.072 (0.029)	0.040 (0.035)	0.104 (0.024)	0.071 (0.036)
Race (other v. white)	0.415 (0.081)	0.308 (0.115)	0.054 (0.092)	0.0194 (0.164)	0.008 (0.099)	0.144 (0.167)
Housing, inadequate (yes v. no)	0.155 (0.039)	0.194 (0.053)	0.049 (0.037)	0.054 (0.059)	0.114 (0.040)	0.130 (0.061)
Paternal employment, manual v. professional	0.065 (0.023)	0.081 (0.030)	0.069 (0.025)	0.096 (0.037)	0.044 (0.026)	0.052 (0.038)
Maternal education, lower v. higher	0.078 (0.023)	0.064 (0.030)	0.100 (0.025)	0.092 (0.038)	0.060 (0.026)	0.041 (0.039)
Other child: 2 > 2, 1-1&2, 0-0	-0.006 (0.019)	-0.012 (0.025)	-0.087 (0.020)	-0.086 (0.031)	-0.088 (0.022)	-0.070 (0.032)
Child characteristics:						
Gestational age, (continuous, in weeks)	0.002 (0.007)	-0.002 (0.009)	-0.011 (0.008)	-0.014 (0.012)	0.006 (0.008)	-0.009 (0.012)
Gender (male v. female)	0.071 (0.021)	0.079 (0.027)	0.032 (0.023)	0.035 (0.035)	0.021 (0.024)	0.078 (0.036)
Breastfed (no v. yes)	0.081 (0.026)	0.059 (0.034)	0.053 (0.092)	0.040 (0.044)	0.112 (0.031)	0.072 (0.046)
BMI Z Δ, 0.05-1.5 y	N/A [†]	0.011 (0.118)	N/A [†]	0.038 (0.016)	N/A [†]	0.031 (0.016)
Tonsils removed (vs. not removed)	N/A [†]	N/A [†]	0.302 (0.123)	0.208 (0.192)	0.178 (0.090)	0.190 (0.133)
Adenoids removed (vs. not removed)	N/A [†]	N/A [†]	-0.656 (0.086)	-0.641 (0.126)	-0.525 (0.071)	-0.553 (0.099)
Wheezing days	0.039 (0.003)	0.039 (0.004)	0.032 (0.003)	0.030 (0.004)	0.036 (0.003)	0.035 (0.005)

*Significant β coefficient estimates and (standard errors) of risk factor effects upon standardized SDB scores. Positive β values signify an increase, and negative β values signify a decrease in mean combined SDB z-score compared to the reference group for categorical variables. [†]N/A for BMI Z Δ, 0.05-1.5 y, because BMI data were not available for all participants, and; for Tonsils Removed and Adenoids Removed because history of these procedures was not assessed at 1.5 years. Bold indicates significant ORs at the level of 0.05.

had the second greatest overall effect, *increasing* combined SDB z-scores by 0.302 at 4.75 years. Maternal smoking effects increased from 1.5, to 4.75, to 6.75 years, as did the lack of breastfeeding, from 1.5 to 6.75 years (not significant at 4.75 years), while inadequate housing effects became attenuated from 1.5 to 6.75 years (not significant at 4.75 years). Maternal smoking, maternal education, and wheezing days were the only significant variables at all 3 time points. In subsample analyses with BMI z-score data, only the 0.5-1.5 year change was significant, at 4.75 years

DISCUSSION

This is the first study to report the natural history of snoring, mouth-breathing, and apnea in a population-based cohort, with multiple observation points, across a key 6-year period in the development of SDB symptoms. The large spike in snoring (“Always”) prevalence from 1.5-2.5 years was earlier than previously reported. Similarly, this population’s rates of “Always” snoring (range = 3.6%-7.7%) and “habitually” snoring (range = 9.6%-21.2%) were considerably higher than analogous rates of 1.5%-6% and 5%-12%, respectively, from a systematic review

incorporating data from 2- to 18-year-olds.³⁴ The presence of apnea (“Always”) remained stable at 1% to 2%, consistent with the literature. Aside from being population-based, this study’s other considerable strengths include large sample size, extended follow-up, control for multiple potential confounders, and measurement of 3 different but commonly recognized symptoms of SDB.

SDB is dynamic, as shown by data for children in whom “Always” symptoms developed, resolved, or remained present between the approximate one-year age intervals. Overall, the persistence of symptoms on a population basis is less common than either their resolution or development. Snoring, mouth-breathing, and apnea each developed in roughly 1% to 5% of this population-based sample from one interval to the next per the “Always” measure, and in 5% to 10% per the “Habitual” measure. Absent a longitudinal analyses of combined symptom patterns—beyond the scope of this paper—our findings cannot discern phenotypes of children for whom (and for how long) “watchful waiting” is the optimal course.

As with any longitudinal data, ascertainment bias is possible. Families with missing data at a particular time point had more of the known risk factors for SDB: mothers who smoked; children who were preterm, low birthweight, and who had a history of wheezing; and families who were of lower SES. This bias was reflected in the lower rates (\approx 1%) of snoring and mouth-breathing in the subsample with SDB symptom data for all 7 time points, and in the symptom-specific analyses of this subsample (Supplemental Tables S1-S2). If this were a random subsample of the $n = 12,447$ in the study’s analytic sample, the ORs in Tables S1 and S2 would be the same as those in Tables 2 and 3, respectively, but with wider 95% CIs. However, this is not the case, with some ORs significant in the subsample not significant in the broader sample, and vice-versa. Thus, it appears that the subsample with SDB data at all 7 time points is a biased sample. For this reason, we present results for the broader sample in the main body of the paper.

A secondary goal of the study was to conduct exploratory analyses of putative risk factors. The complexity of these data—multiple observation points with varying schema for measuring symptoms—should caution against overinterpretation of results from one particular time point, in favor of examining consistent trends. Inadequate housing, paternal manual employment, maternal smoking, and lower maternal education significantly increased combined SDB risk at 1.5 years, and at either or both of the later time points. In contrast, initial race and gender effects did not persist. In a large English sample of 1- to 4-year-olds that measured parent report of multiple SES, environmental and biological risk factors, habitual snoring (7.9% prevalence) was positively associated with socioeconomic deprivation in bivariate analyses, but in analyses adjusted for wheeze and other atopic disorders, respiratory symptoms, BMI, and exposure to pollutants, SES was no longer significant.³⁹ Our SES findings may thus be proxies for other, unobserved clinical and environmental characteristics. Lower SES families are more likely to live in crowded housing, increasing the possibility of bedroom sharing, particularly among younger children, and therefore greater likelihood of symptom recognition.

Not breastfeeding increased the risk of combined SDB symptoms, an effect that intensified from 1.5 to 6.75 years, but,

curiously, was not significant at 4.75 years (data complexity cited above may be a factor). In a study of snoring children undergoing polysomnography, having been breastfed for \geq 2 months reduced SDB severity on every measure assessed. This may occur via breastfeeding reducing infections that lead to adenotonsillar hypertrophy, or anatomically, by promoting an upper airway less vulnerable to narrowing and collapse during sleep.⁴⁰ Prematurity increased SDB risk among 8- to 11-year olds,⁴¹ while very low birthweight increased risk for SDB in young adulthood.⁴² In contrast, neither birthweight nor gestational age was associated with a significant increase in combined SDB symptoms.

Adenoidectomy had the strongest effect upon reducing combined SDB symptoms; this is particularly notable given tonsillectomy’s lesser but opposite effect. We speculate that this is because adenoidectomy alone is performed earlier than either tonsillectomy or adenotonsillectomy (and has fewer risks than those surgeries)⁴³ to relieve chronic nasal obstruction. Such nasal obstruction can lead to remodeling of the upper airway, predisposing to obstructive sleep apnea. In contrast, tonsillectomies and adenotonsillectomies may be performed later, as often for suspected apnea as for recurrent pharyngitis (perhaps with comorbid undiagnosed SDB). Waiting periods longer than 12 months for either surgery were common in England during the study period, thus surgeries were preferentially performed in the more severe and absolute indications. That likely would have included demonstrable SDB, though SDB related morbidity was not as widely recognized at the time.

Our findings have implications for clinical care. They suggest that SDB risk, as identified by chronic nasal obstruction at age 4 years or earlier, may merit treatment well before SDB actually develops later in childhood. Once SDB develops, treatment by tonsillectomy and even adenotonsillectomy may not as reliably eliminate SDB, especially in the context of obesity. Although such conclusions, from a cohort study rather than a randomized trial are speculative, they align with data showing that snoring at baseline is more predictive of hyperactive behavior (an important SDB outcome) 4 years later than are concurrent snoring patterns at that 4-year follow-up.⁴⁴

The study has several limitations. First, results are based upon parent-report of each symptom, by a single item. Objective data may yield different results; newer cohort studies in schoolchildren employing polysomnography yielded a 1.2% prevalence of moderate SDB⁴⁵ and a 2.8% prevalence of apnea. However, our parent-reported SDB symptom prevalence data are consistent with results from a systematic review.³⁴ Furthermore our epidemiological study of symptoms aligns with current clinical practice in the US and abroad, which relies primarily upon symptoms—vs. PSG or other objective tests—regarding decisions about adenotonsillectomy.^{46,47}

Second, the ALSPAC question on observed apneas was not phrased to elicit a distinction between obstructive and central apneas. Brief, generally benign central apneas are not uncommon in the youngest children.^{48,49} While the 19% prevalence of “Habitual” apneas in 6-month-olds could reflect parent observation of central apneas, one would not expect central (vs. obstructive) apneas to occur in a similar pattern as both snoring and mouth-breathing at this time. Given that all three symptoms were “Habitually” present at comparable rates at this point, this

suggests that physiological central apneas were not the major component of those reported by parents.

Third, there was inconsistency in the SDB item response categories across symptoms and over time. We sought to address this by presenting dichotomous SDB outcomes in two ways (“Always” and “Habitual”) and by standardizing combined SDB scores.

Fourth, anthropometric data were only available for three time points, the latest being 3.5 years. This may be one reason why BMI z-score changes between 0.5, 1.5, and 3.5 years had only minimal effects upon SDB. Alternatively, controlling for SES may have attenuated the effects of BMI upon SDB risk, as found by others.³⁹

Understanding the trajectory of pediatric SDB has significant clinical implications for deciding whether and in whom watchful waiting might be a valid long-term strategy for children with mild SDB.⁵⁰ Findings from this large, population-based cohort study suggest the necessity for early and continued screening for SDB symptoms. Secondly, our findings reaffirm that modifiable characteristics such as those related to SES and infant feeding, as well as adenoidectomy may have a substantial impact upon SDB risk.

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SDB Prevalence by Age, "Always," Children with Complete SDB Data only

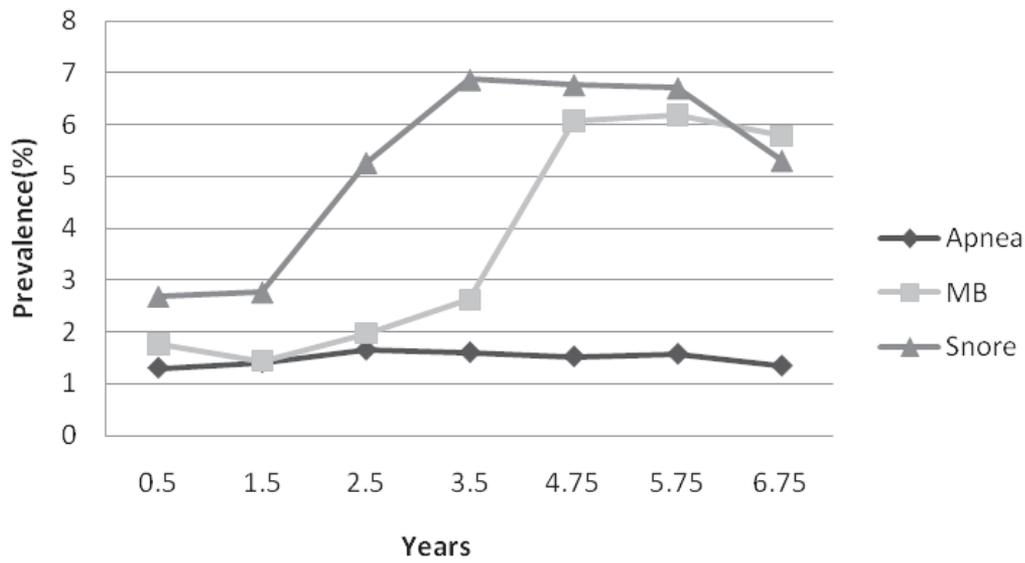


Figure S1—SDB Prevalence by Age, "Always," Children with Complete SDB Data only

SDB Prevalence by Age, "Habitual," Children with Complete SDB Data Only

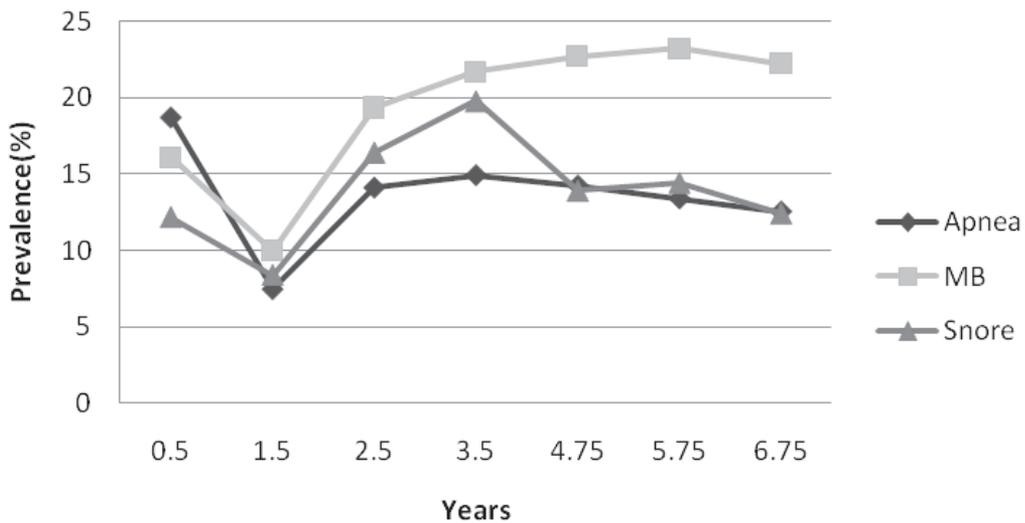


Figure S2—Prevalence by Age, "Habitual," Children with Complete SDB Data only

Apnea Transitions, "Habitual"

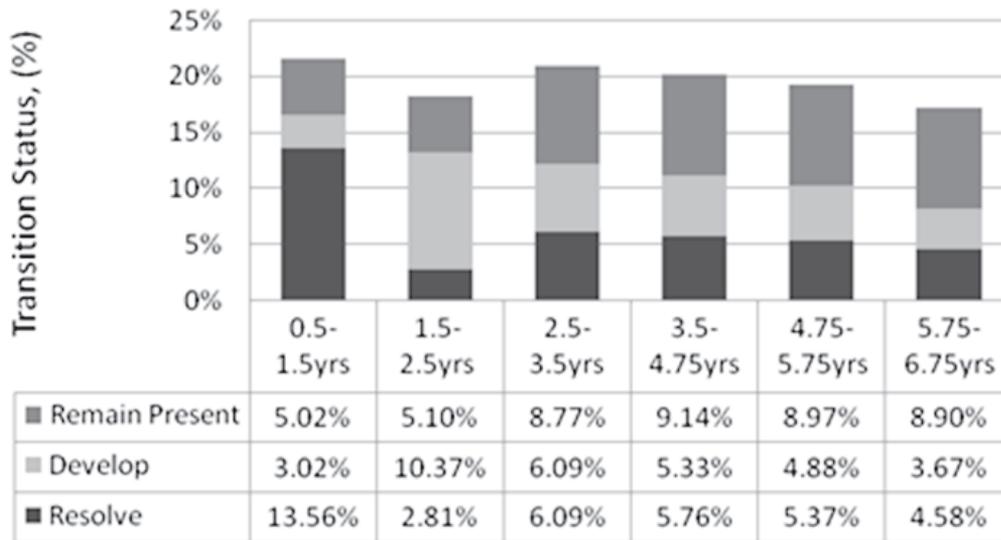


Figure S3—Apnea Transitions for "Habitual"

Mouth Breathing Transitions, "Habitual"

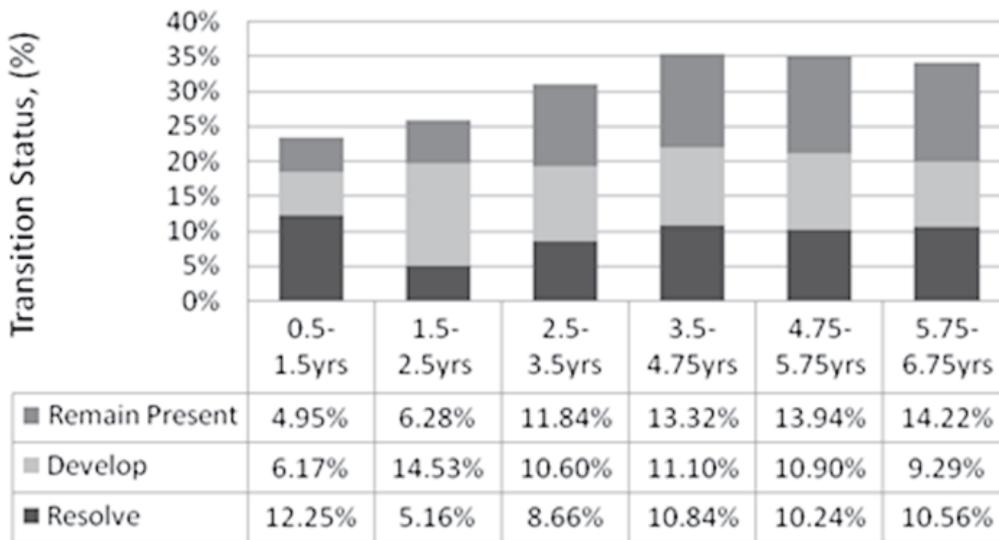


Figure S4—Mouth-Breathing Transitions for "Habitual"

Snore Transitions, "Habitual"

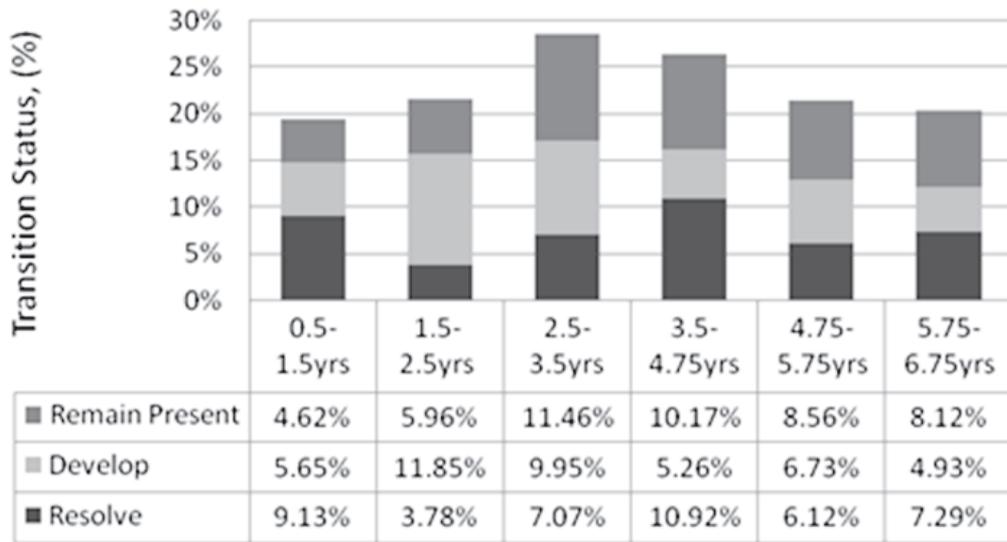


Figure S5—Snore Transitions for "Habitual"

Table S1—Maternal, Family, and Child Characteristics Associated* with Mouth-Breathing, Snoring, or Apnea at 1.5, 4.75, and 6.75 years (“Always” vs. “Not Always”), Odds Ratios (95% CIs) of Subsample with SDB Data for 7/7 Timepoints

Covariates Habitual # Case/Total #	1.5 years			4.75 years			6.75 years		
	Mouth-Breathing 63/5022	Snoring 129/5249	Apnea 64/4894	Mouth-Breathing 280/4930	Snoring 324/5122	Apnea 70/4724	Mouth-Breathing 273/4743	Snoring 261/4901	Apnea 60/4423
Maternal and Family Characteristics:									
Maternal Smoking, Ever	1.00 (0.60,1.66)	0.75 (0.52,1.08)	0.81 (0.49,1.36)	1.03 (0.81,1.32)	1.02 (0.81,1.28)	2.07 (1.26,3.40)	1.11 (0.86,1.42)	1.15 (0.89,1.48)	1.42 (0.84,2.41)
Race (Other v. White)	3.20 (0.75,13.77)	3.69 (1.42,9.59)	2.58 (0.60,11.06)	0.57 (0.14,2.34)	1.25 (0.49,3.15)	N/A [†]	1.56 (0.55,4.42)	0.29 (0.04,2.12)	N/A [†]
Housing, Inadequate (Yes v. No)	0.92 (0.35,2.41)	1.60 (0.91,2.79)	1.01 (0.42,2.42)	1.67 (1.18,2.37)	1.19 (0.84,1.70)	1.71 (0.89,3.29)	1.61 (1.12,2.32)	1.72 (1.20,2.47)	1.68 (0.82,3.46)
Paternal Employment, Manual v. Professional	1.19 (0.70,2.02)	1.18 (0.81,1.72)	1.55 (0.91,2.65)	1.41 (1.09,1.83)	1.25 (0.98,1.60)	0.85 (0.51,1.44)	1.30 (0.99,1.70)	1.30 (0.99,1.71)	1.32 (0.76,2.29)
Maternal Education, Lower v. Higher	1.82 (1.01,3.29)	2.00 (1.31,3.04)	1.77 (0.99,3.17)	1.48 (1.12,1.96)	1.27 (0.99,1.64)	1.07 (0.63,1.83)	1.41 (1.06,1.86)	1.06 (0.80,1.41)	0.87 (0.49,1.55)
Other Child:									
1 v. 0	1.50 (0.87,2.57)	0.77 (0.53,1.13)	0.81 (0.48,1.38)	0.73 (0.57,0.95)	0.95 (0.75,1.20)	0.57 (0.34,0.95)	0.57 (0.44,0.74)	1.06 (0.81,1.38)	1.25 (0.73,1.27)
> 1 v. 0	1.05 (0.23,4.80)	1.72 (0.83,3.53)	1.53 (0.53,4.39)	0.70 (0.37,1.34)	1.03 (0.57,1.86)	1.42 (0.56,3.64)	1.05 (0.60,1.85)	1.45 (0.81,2.59)	1.05 (0.29,3.87)
Child Characteristics:									
Gestational Age, (Continuous, in weeks)	1.01 (0.85,1.20)	0.95 (0.85,1.06)	0.87 (0.74,1.02)	0.98 (0.90,1.06)	1.00 (0.93,1.08)	1.08 (0.91,1.29)	1.00 (0.92,1.09)	1.03 (0.95,1.13)	2.21 (0.99,1.46)
Gender (Male v. Female)	1.76 (1.04,2.99)	1.55 (1.07,2.24)	0.73 (0.44,1.21)	1.03 (0.81,1.32)	0.85 (0.68,1.07)	0.79 (0.49,1.28)	1.17 (0.91,1.51)	0.86 (0.66,1.11)	0.86 (0.51,1.46)
Breastfed (No v. Yes)	1.51 (0.85,2.66)	1.21 (0.80,1.84)	0.97 (0.53,1.78)	1.18 (0.88,1.58)	1.12 (0.85,1.48)	1.29 (0.73,2.29)	1.51 (1.13,2.02)	1.34 (0.99,1.81)	1.36 (0.75,2.49)
Adenoids Removed	N/A [‡]	N/A [‡]	N/A [‡]	0.44 (0.23,0.87)	0.28 (0.16,0.49)	0.26 (0.09,0.74)	0.35 (0.21,0.60)	0.36 (0.21,0.66)	0.51 (0.16,1.57)
Wheezing Days	0.95 (0.87,1.04)	1.07 (1.03,1.10)	1.09 (1.05,1.14)	1.04 (1.02,1.06)	1.05 (1.03,1.07)	1.08 (1.04,1.12)	1.06 (1.03,1.09)	1.06 (1.03,1.09)	1.10 (1.06,1.14)

*Only ORs (95% CIs) for putative risk factors significantly associated with ≥1 outcome measure in analyses of full sample data are shown (i.e., not the sample subset with BMI Z score change data at 0.5-1.5 years and 1.5-3.5 years). [†]Race not included in these models as the reported race for all children with SDB “Always” symptoms at these timepoints is White. [‡]N/A because history of adenoidectomy was not assessed at 1.5 years.

Table S2—Maternal, Family, and Child Characteristics Associated* with Mouth-Breathing, Snoring, or Apnea at 1.5, 4.75, and 6.75 years (“Habitual” vs. “Not Habitual”), Odds Ratios (95% CIs) for Subsample with SDB Data for 7/7 Timepoints.

Covariates Habitual # Case/Total #	1.5 years			4.75 years			6.75 years		
	Mouth- Breathing 479/5022	Snoring 396/5249	Apnea 353/4894	Mouth- Breathing 1083/4930	Snoring 677/5122	Apnea 655/4724	Mouth- Breathing 1046/4743	Snoring 601/4901	Apnea 551/4423
Maternal and Family Characteristics:									
Maternal Smoking, Ever	1.16 (0.96,1.41)	0.89 (0.72,1.10)	1.07 (0.85,1.33)	1.07 (0.93,1.23)	1.00 (0.85,1.18)	1.26 (1.06,1.49)	1.17 (1.02,1.35)	1.05 (0.88,1.25)	1.32 (1.10,1.59)
Race (Other v. White)	1.51 (0.71,3.21)	2.99 (1.60,5.58)	2.12 (1.03,4.38)	1.16 (0.64,2.09)	1.43 (0.75,2.70)	1.07 (0.50,2.27)	0.79 (0.35,1.63)	0.97 (0.43,2.16)	1.23 (0.57,2.63)
Housing, Inadequate (Yes v. No)	0.84 (0.57,1.22)	1.46 (1.03,2.08)	1.28 (0.86,1.89)	1.22 (0.97,1.52)	1.32 (1.01,1.71)	1.05 (0.79,1.38)	1.32 (1.05,1.67)	1.24 (0.94,1.65)	1.05 (0.77,1.42)
Paternal Employment, Manual v. Professional	1.05 (0.86,1.29)	1.03 (0.82,1.29)	1.14 (0.89,1.44)	1.07 (0.92,1.24)	1.05 (0.88,1.26)	1.06 (0.88,1.27)	1.14 (0.98,1.33)	1.02 (0.84,1.23)	1.11 (0.91,1.35)
Maternal Education, Lower v. Higher	1.33 (1.07,1.64)	1.29 (1.02,1.63)	1.00 (0.79,1.27)	1.40 (1.21,1.63)	1.06 (0.88,1.27)	1.15 (0.96,1.38)	1.33 (1.14,1.55)	1.20 (0.99,1.45)	1.11 (0.91,1.36)
Other Child:									
1 v. 0	1.06 (0.87,1.29)	0.87 (0.70,1.09)	0.85 (0.68,1.07)	0.70 (0.61,0.81)	0.88 (0.74,1.04)	0.83 (0.70,0.99)	0.75 (0.65,0.87)	0.86 (0.72,1.03)	0.91 (0.75,1.09)
> 1 v. 0	1.27 (0.77,2.09)	1.49 (0.92,2.42)	0.99 (0.56,1.75)	0.75 (0.51,1.09)	0.69 (0.43,1.11)	1.02 (0.65,1.59)	0.69 (0.46,1.03)	1.30 (0.84,1.99)	0.86 (0.52,1.44)
Child Characteristics:									
Gestational Age, (Continuous, in weeks)	1.02 (0.96,1.09)	0.95 (0.89,1.02)	1.02 (0.95,1.10)	0.95 (0.91,0.99)	0.96 (0.91,1.01)	1.04 (0.98,1.10)	1.01 (0.97,1.06)	1.03 (0.97,1.09)	1.01 (0.95,1.07)
Gender (Male v. Female)	1.11 (0.92,1.35)	1.24 (1.00,1.53)	0.94 (0.76,1.18)	0.95 (0.83,1.09)	0.93 (0.79,1.09)	1.00 (0.85,1.19)	1.06 (0.92,1.22)	0.90 (0.75,1.07)	1.23 (1.03,1.48)
Breastfed (No v. Yes)	1.34 (1.07,1.69)	1.26 (0.98,1.62)	1.10 (0.83,1.45)	1.23 (1.04,1.46)	1.21 (0.99,1.49)	1.09 (0.88,1.34)	1.29 (1.09,1.54)	1.18 (0.95,1.47)	1.03 (0.82,1.29)
Adenoids Removed	N/A†	N/A†	N/A†	0.43 (0.28,0.67)	0.32 (0.20,0.50)	0.60 (0.35,1.02)	0.45 (0.31,0.64)	0.40 (0.27,0.60)	1.15 (0.68,1.93)
Wheezing Days	1.03 (1.01,1.05)	1.06 (1.04,1.08)	1.06 (1.04,1.09)	1.03 (1.02,1.04)	1.05 (1.03,1.06)	1.06 (1.05,1.08)	1.05 (1.03,1.07)	1.06 (1.04,1.08)	1.06 (1.04,1.08)

*Only ORs (95% CIs) for putative risk factors significantly associated with ≥ 1 outcome measure in analyses of full sample data are shown (i.e., not the sample subset with BMI Z score change data at 0.5-1.5 years and 1.5-3.5 years). †N/A because history of adenoidectomy was not assessed at 1.5 years.