Quality of Life and Obstructive Sleep Apnea Symptoms After Pediatric Adenotonsillectomy

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abstract

BACKGROUND AND OBJECTIVES: Data from a randomized, controlled study of adenotonsillectomy for obstructive sleep apnea syndrome (OSAS) were used to test the hypothesis that children undergoing surgery had greater quality of life (QoL) and symptom improvement than control subjects. The objectives were to compare changes in validated QoL and symptom measurements among children randomized to undergo adenotonsillectomy or watchful waiting; to determine whether race, weight, or baseline OSAS severity influenced changes in QoL and symptoms; and to evaluate associations between changes in QoL or symptoms and OSAS severity.

METHODS: Children aged 5 to 9.9 years with OSAS (N = 453) were randomly assigned to undergo adenotonsillectomy or watchful waiting with supportive care. Polysomnography, the Pediatric Quality of Life inventory, the Sleep-Related Breathing Scale of the Pediatric Sleep Questionnaire, the 18-item Obstructive Sleep Apnea QoL instrument, and the modified Epworth Sleepiness Scale were completed at baseline and 7 months. Changes in the QoL and symptom surveys were compared between arms. Effect modification according to race and obesity and associations between changes in polysomnographic measures and QoL or symptoms were examined.

RESULTS: Greater improvements in most QoL and symptom severity measurements were observed in children randomized to undergo adenotonsillectomy, including the parent-completed Pediatric Quality of Life inventory (effect size [ES]: 0.37), the 18-item Obstructive Sleep Apnea QoL instrument (ES: –0.93), the modified Epworth Sleepiness Scale score (ES: –0.42), and the Sleep-Related Breathing Scale of the Pediatric Sleep Questionnaire (ES: –1.35). Effect modification was not observed by obesity or baseline severity but was noted for race in some symptom measures. Improvements in OSAS severity explained only a small portion of the observed changes.

CONCLUSIONS: Adenotonsillectomy compared with watchful waiting resulted in significantly more improvements in parent-rated generic and OSAS-specific QoL measures and OSAS symptoms.

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This trial has been registered at www.clinicaltrials.gov (identifier NCT00560859).

www.pediatrics.org/cgi/doi/10.1542/peds.2014-0620

DOI: 10.1542/peds.2014-0620

Accepted for publication Nov 4, 2014

WHAT'S KNOWN ON THIS SUBJECT: Pediatric obstructive sleep apnea syndrome (OSAS) has been associated with decreased health-related quality of life (QoL). Observational studies suggest that adenotonsillectomy for pediatric OSAS improves QoL, but these studies did not use a randomized study design or a control group of children with OSAS managed nonsurgically.

WHAT THIS STUDY ADDS: A prospective, randomized controlled study of adenotonsillectomy for pediatric OSAS showed significantly greater QoL and symptom improvements in children undergoing adenotonsillectomy than in the nonsurgical control arm. The extent of improvement was not appreciably influenced by baseline OSAS severity or obesity.

Obstructive sleep apnea syndrome (OSAS) affects ~1% to 3% of children[1,2] and has been associated with an increased risk for developing cardiovascular and other systemic morbidities.[3,4] Even milder forms of sleep-disordered breathing have been associated with behavioral disturbances in children.[5–9] Pediatric OSAS has also been associated with decreased health-related quality of life (QoL). Studies (including a recent meta-analysis) demonstrated that children with OSAS had generic health-related QoL scores lower than healthy children and similar to children with juvenile rheumatoid arthritis.[10–13] Validated QoL instruments have shown moderate to large impairment of disease-specific QoL in more than one-half of surveyed children.[14]

The first-line surgical treatment of pediatric OSAS is adenotonsillectomy (AT). Rising health care costs and emphasis on evidence-based medicine have resulted in scrutiny of common surgical procedures, including measurement of outcomes meaningful to patients. Observational studies have suggested that in pediatric OSAS, AT improves both short-term and longer term QoL.[15–18] However, none of these studies used a randomized study design or a control group of children with OSAS who were not treated surgically.

The recently completed CHAT (Childhood Adenotonsillectomy Trial) was the first multisite, prospective, randomized controlled study on the effects of AT for the treatment of pediatric OSAS. Although the primary cognitive test outcome did not differ significantly between the surgical and observational treatment arms, children randomized to early AT (eAT) rather than watchful waiting had improved behavior and QoL as well as higher rates of OSAS resolution on polysomnography (PSG).[19] For the present report, the impact of AT on QoL was quantified (including specific domains of function) and on OSAS symptoms. The extent to which race, baseline OSAS severity, or obesity affected treatment responses was also explored. Finally, we characterized relationships between changes in PSG indices of OSAS severity and changes in symptom and QoL measures.

METHODS

As part of the CHAT study, 453 children 5 to 9.9 years of age with OSAS were randomly assigned to either AT within 1 month (eAT) or watchful waiting with supportive care (WWSC). A detailed description of the methods of the CHAT study has been published.[20] In brief, children with OSAS were recruited from pediatric sleep centers, otolaryngology and pediatric clinics, and the general community from 6 clinical sites from 2007 to 2011. Institutional review board approval was obtained from participating clinical centers, children provided assent if old enough, and caregivers provided written informed consent.

All children underwent standardized PSG; studies were scored at a central reading center to ensure uniformity.[19] PSG inclusion criteria included OSAS, defined as an obstructive apnea index (OAI) $\geq$1 or obstructive apnea hypopnea index (AHI) $\geq$2. OAI is the number of obstructive apneic events per hours of total sleep time and AHI is the number of mixed or obstructive apneic events and hypopneic events associated with a $\geq$50% reduction in airflow and either $\geq$3% oxygen desaturation or electroencephalographic arousal per hours of total sleep time. Children with severe OSAS as defined by an OAI $>$20, an AHI $>$30, or oxygen saturation $\leq$90% for $>$2% of total sleep time were excluded. All children were deemed appropriate surgical candidates by otolaryngologists.

In addition to PSG data, physical examination and validated survey information were collected at baseline and 7 months later.

Demographic information included age, gender, race, height, weight, ethnicity, maternal education, and family income. BMI and *z* scores were calculated by using standardized formulas.[21]

Generic and disease-specific health-related QoL and severity of OSAS symptoms were assessed with survey instruments validated for these ages. Generic health-related QoL was measured by using the parent and child versions of the Pediatric Quality of Life (PedsQL) inventory that assess physical, emotional, social, and school functioning.[22] The parallel child and parent-proxy forms differ only in use of age-appropriate language. For children ages 5 to 7 years, the survey was administered by an interviewer. Scoring is performed by linear transformation of the 23 item scores to a scale of 0 to 100. Higher values indicate better QoL.

Disease-specific health-related QoL was assessed by caregivers by using the 18-item Obstructive Sleep Apnea (OSA-18) tool. This instrument focuses on perceived impact of OSAS on 5 domains: sleep disturbance, physical suffering, emotional distress, daytime problems, and caregiver concerns.[23] Items are scored on a 7-point scale and totaled, providing a severity score of 18 to 126, with lower scores representing higher QoL. Mean scores for healthy children with no OSAS symptoms are in the range of 31.2 $\pm$ 10.4.[24] Scores $>$60 suggest a moderate impact.

To assess OSAS symptom severity, caregivers completed the Sleep-Related Breathing Disorder (SRBD) scale of the Pediatric Sleep Questionnaire (PSQ) and the Epworth Sleepiness Scale modified for children (mESS). The PSQ SRBD scale contains 22 yes/no questions and provides both a total score, as the proportion of all symptoms endorsed by the caregiver, and subscale scores for snoring, daytime sleepiness, and behavior. The mean of yes (1) and no (0) responses generates a score

between 0 and 1, with higher scores indicating greater symptom severity. Values ≥0.33 have been proposed as identifying higher risk for pediatric OSAS.[25] The sleepiness subscale has been validated against objective sleepiness in children.[26] On the mESS, caregivers rate the likelihood of their child falling asleep from 0 (never) to 3 (almost always) in 8 situations. Scores range from 0 to 24, with higher scores indicating more sleepiness.[27]

PSG parameters used to assess OSAS severity were the AHI and oxygen desaturation index (ODI [ie, number of episodes of oxygen desaturation ≥3% per hour of sleep]). The AHI reflects both sleep fragmentation and hypoxemia, whereas the ODI more specifically assesses intermittent hypoxemia.

Baseline demographic variables are summarized according to treatment arm (ie, eAT, WWSC) as mean ± SD values for continuous variables or frequency (%) for categorical variables. Baseline comparisons of QoL and symptom measurements according to study arm were examined by using 2-sample independent *t* tests (unadjusted *P* value) or analysis of covariance (ANCOVA). These and all other ANCOVA models were adjusted for site, race (African American versus non–African American), age (5–7 vs 8–10 years), and overweight status (≥85th vs <85th BMI percentile) as the primary analysis and site. Race (African American versus non–African American), gender, age (continuous), obesity (≥95th vs <95th BMI percentile), maternal education (less than high school, high school or higher, or missing), income (<$30 000, ≥$30 000, or missing), and baseline log AHI were included in the secondary analysis.[19] To assess whether the WWSC and eAT arms experienced a differential change in QoL and symptom measurements, unadjusted analysis of variance and adjusted ANCOVA models were fit with the QoL and symptom outcomes expressed as change from baseline to follow-up. Additional ANCOVA models included interaction terms to assess effect modification for treatment response according to baseline OSAS severity, race, and weight. Furthermore, linear regression models were used to assess associations between change in QoL or symptoms and change in PSG measures (log transformed to approximate normal distribution). In this last regression model, data from the 2 treatment arms were combined. This technique was used because OSAS resolution, defined as AHI <2 and OAI <1 at follow-up, was observed in a large proportion of subjects in both treatment arms (46% of WWSC subjects and 79% of eAT subjects). Sensitivity analyses were conducted, however, stratified by treatment arm. A total of 24 children (16 in the WWSC arm and 8 in the eAT arm) were not treated per protocol. Exploratory analyses performed for the original CHAT publication did not yield appreciable changes in results when those subjects were excluded from the analyses. Cohen's d effect size was calculated as (mean change difference)/(pooled SD). Statistical analyses were performed by using SAS version 9.3 (SAS Institute, Inc, Cary, NC) with α cutoff of ≤0.01.

RESULTS

No significant baseline differences in demographic characteristics, QoL, or symptom survey total scores were seen between treatment arms. There was a significant difference in the emotional function domain of the parent PedsQL with a higher score seen in the eAT arm (Tables 1 and 2).

Generic Health-Related QoL (PedsQL)

The PedsQL parent-reported total score improved significantly more in

TABLE 1 Demographic Characteristics of the Study Population at Baseline

Characteristic	eAT Arm (*n* = 227)	WWSC Arm (*n* = 226)
Age, mean ± SD, y	6.5 ± 1.4	6.6 ± 1.4
Male sex	118 (52.0)	101 (44.7)
Race		
African American	123 (54.2)	126 (55.8)
White	81 (35.7)	74 (32.7)
Other	23 (10.1)	26 (11.5)
Hispanic ethnicity	21 (9.3)	16 (7.2)
Maternal education		
Less than high school	22 (9.7)	20 (8.8)
High school diploma/GED or higher	200 (88.5)	205 (90.3)
Not sure/missing	4 (1.77)	2 (0.88)
Income		
<$30 000	91 (40.3)	92 (40.5)
≥$30 000	100 (44.3)	107 (47.1)
Missing	35 (15.5)	28 (12.3)
Height *z* score	0.6 ± 1.0	0.7 ± 1.0
Weight *z* score	1.0 ± 1.2	1.0 ± 1.3
Weight class		
Overweight or obese (BMI >85th percentile)	106 (46.7)	107 (47.4)
Obese (BMI >95th percentile)	76 (33.5)	74 (32.7)
Site		
Philadelphia	72 (31.7)	75 (33.2)
Cincinnati	40 (17.6)	39 (17.3)
Cleveland	60 (26.4)	64 (28.3)
St Louis	30 (13.2)	30 (13.3)
New York	9 (4.0)	7 (3.1)
Boston	16 (7.0)	11 (4.9)
AHI	6.9 ± 0.4	6.7 ± 0.4
ODI	7.3 ± 0.5	7.0 ± 0.5

No differences between arms were detected (all $P > .05$). Data are presented as mean ± SD or *n* (%). GED, General Educational Development.

TABLE 2 QoL and Symptom Measures According to Treatment Arm at Baseline

Outcome	eAT Baseline	WWSC Baseline	P^a	P^b
PedsQL (parent) total	77.9 ± 15.4	76.7 ± 15.5	.33	.30
PedsQL (parent) emotional function	78.2 ± 18.6	73.3 ± 19.6	<.01	<.01
PedsQL (parent) physical function	80.3 ± 20.3	83.1 ± 18.3	.12	.19
PedsQL (parent) school function	74.4 ± 19.6	73.2 ± 20.1	.44	.49
PedsQL (parent) social function	84.2 ± 19.0	81.9 ± 19.3	.17	.17
PedsQL (child) total	68.3 ± 16.1	67.6 ± 14.8	.59	.49
PedsQL (child) emotional function	66.0 ± 23.2	64.5 ± 23.5	.46	.36
PedsQL (child) physical function	73.3 ± 18.2	73.5 ± 17.0	.91	.90
PedsQL (child) school function	63.1 ± 21.7	65.4 ± 19.4	.23	.26
PedsQL (child) social function	68.3 ± 24.8	64.0 ± 24.2	.05	.06
OSA-18 total	53.1 ± 18.3	54.1 ± 18.8	.55	.36
OSA-18 sleep disturbance	3.8 ± 1.4	3.8 ± 1.5	.76	.96
OSA-18 emotional distress	2.4 ± 1.5	2.6 ± 1.8	.20	.18
OSA-18 physical suffering	2.7 ± 1.4	2.7 ± 1.3	.61	.91
OSA-18 daytime problems	2.8 ± 1.4	2.9 ± 1.5	.42	.37
OSA-18 caregiver concerns	2.8 ± 1.5	3.0 ± 1.5	.22	.18
PSQ-SRBD total	0.5 ± 0.2	0.5 ± 0.2	.47	.49
PSQL snoring subscale	0.8 ± 0.3	0.8 ± 0.3	.85	.66
PSQL sleepiness subscale	0.4 ± 0.3	0.5 ± 0.3	.49	.52
PSQL behavior subscale	0.4 ± 0.3	0.5 ± 0.3	.34	.43
SLSC total (mESS)	7.1 ± 4.7	7.5 ± 5.2	.23	.25

Data are presented as mean ± SD.

[a] Adjusting for stratified variables only: site, race (African American versus non–African American), age (5–7 vs 8–10 years old), and overweight (≥85th vs <85th BMI percentile).

[b] Adjusting for site, race (African American versus non–African American), age (continuous), obese, gender, maternal education (less than high school, high school or higher, or missing/not sure), income (>$30 000, ≤$30 000, or missing), and baseline log AHI.

the eAT group compared with the WWSC group (5.9 ± 13.6 points vs 0.95 ± 13.3 points [$P < .01$], yielding an effect size of 0.37) (Table 3). Significance did not alter with adjustment for site, continuous age, race, socioeconomic status, or obesity status. This difference was driven by highly significant differences for the school (academic performance) and physical function domains. The change scores for the emotional function domain also differed between arms after adjusting for baseline differences ($P < .01$). Changes in the social function (peer interaction) domain were not significantly different between the arms. No significant differences in change scores between treatment groups in the PedsQL total score or the 4 domains were noted in the surveys answered directly by the children.

Disease-Specific Health-Related QoL (OSA-18)

Total OSA-18 scores in the eAT group improved more than in the WWSC group by –21.4 ± 16.5 vs –4.5 ± 19.3, producing a large effect size of –0.93 ($P < .01$) (Table 3). Significant differences in the change scores between the 2 arms were seen in all of the individual domains of the OSA-18, including sleep disturbance, daytime problems, physical suffering, caregiver concerns, and emotional distress (all $P \leq .01$).

TABLE 3 Change Scores in QoL and Symptom Measures by Treatment Arm

Outcome	eAT		WWSC		Effect Size[a]	P^b	P^c
	Baseline	Change	Baseline	Change			
PedsQL (parent) total	77.9 ± 15.4	5.9 ± 13.6	76.7 ± 15.5	0.9 ± 13.3	0.37	<.01	<.01
PedsQL (parent) emotional function	78.2 ± 18.6	4.9 ± 16.7	73.3 ± 19.6	2.1 ± 18.1	0.16	.12	<.01
PedsQL (parent) physical function	80.3 ± 20.3	7.4 ± 19.9	83.1 ± 18.3	−0.7 ± 18.2	0.42	<.01	<.01
PedsQL (parent) school function	74.4 ± 19.6	7.4 ± 18.1	73.2 ± 20.1	0.2 ± 19.7	0.38	<.01	<.01
PedsQL (parent) social function	84.2 ± 19.0	3.2 ± 19.6	81.9 ± 19.3	2.9 ± 17.2	0.02	>.99	.56
PedsQL (child) total	68.3 ± 16.1	3.4 ± 17.3	67.6 ± 14.8	3.3 ± 16.9	0.01	.92	.43
PedsQL (child) emotional function	66.0 ± 23.2	3.9 ± 28.9	64.5 ± 23.5	2.2 ± 29.5	0.06	.55	.07
PedsQL (child) physical function	73.3 ± 18.2	3.0 ± 20.3	73.5 ± 17.0	2.0 ± 22.3	0.05	.63	.38
PedsQL (child) school function	63.1 ± 21.7	4.3 ± 23.9	65.4 ± 19.4	3.5 ± 22.5	0.03	.70	.89
PedsQL (child) social function	68.3 ± 24.8	2.8 ± 26.1	64.0 ± 24.2	7.0 ± 26.2	−0.16	.12	.63
OSA-18 total	53.1 ± 18.3	−21 ± 16.5	54.1 ± 18.8	−4.5 ± 19.3	−0.93	<.01	<.01
OSA-18 sleep disturbance	3.8 ± 1.4	−2.2 ± 1.3	3.8 ± 1.5	−0.5 ± 1.6	−1.14	<.01	<.01
OSA-18 emotional distress	2.4 ± 1.5	2.1 ± 1.5	2.6 ± 1.8	2.6 ± 1.6	−0.30	<.01	.01
OSA-18 physical suffering	2.7 ± 1.4	−0.9 ± 1.3	2.7 ± 1.3	−0.1± 1.5	−0.60	<.01	<.01
OSA-18 daytime problems	2.8 ± 1.4	−1.0 ± 1.3	2.9 ± 1.5	−0.1 ± 1.5	−0.68	<.01	<.01
OSA-18 caregiver concerns	2.8 ± 1.5	−1.2 ± 1.4	3.0 ± 1.5	−0.4 ± 1.6	−0.51	<.01	<.01
PSQ-SRBD total	0.5 ± 0.2	−0.3 ± 0.2	0.5 ± 0.2	−0.0 ± 0.2	−1.35	<.01	<.01
PSQL snoring subscale	0.8 ± 0.3	−0.7 ± 0.3	0.8 ± 0.3	−0.1 ± 0.4	−1.55	<.01	<.01
PSQL sleepiness subscale	0.4 ± 0.3	−0.3 ± 0.4	0.5 ± 0.3	−0.0 ± 0.4	−0.65	<.01	<.01
PSQL behavior subscale	0.4 ± 0.3	−0.1 ± 0.3	0.5 ± 0.3	−0.0 ± 0.3	−0.34	<.01	<.01
SLSC total (mESS)	7.1 ± 4.7	−2.0 ± 4.2	7.5 ± 5.2	−0.3 ± 4.1	−0.42	<.01	<.01

[a] Cohen's d.

[b] Adjusting stratified variables only: site, race (African American versus non–African American), age (5–7 vs 8–10 years old), and overweight (≥85th vs <85th BMI percentile).

[c] Adjusting for site, race (African American versus non–African American), age (continuous), obese, gender, maternal education (less than high school, high school or higher, or missing/not sure), income (>$30 000, ≤$30 000, or missing), baseline AHI quartile, and baseline outcome variable.

Symptom Questionnaires (PSQ SRBD and mESS Scores)

For the Sleep-Related Breathing Scale of the Pediatric Sleep Questionnaire (PSQ-SRBD), a –0.28 ± 0.2 point change in the eAT group and –0.03 ± 0.2 change in the WWSC group produced a large effect size of –1.35 ($P < .01$) for the differences between arms (Table 3). Moreover, significant differences in the change scores between treatment arms were seen for the behavior, sleepiness, and snoring subscales (all $P < .01$). Improved sleepiness was corroborated by significant improvement in the mESS score in the eAT group of –2.01 ± 4.7 compared with 0.28 ± 4.1 in the WWSC arm, with a moderate effect size of –0.42 ($P < .01$).

Change score differences between the treatment arms for the QoL and symptom survey total scores are summarized in Fig 1.

Assessment of Effect Modification by Race and Baseline Weight and OSAS Severity

Weight did not influence the associations between treatment arm and QoL or symptoms (Table 4, all $P > .05$). Interaction terms for race were not significant for models for the majority of QoL and symptom outcomes. In contrast, effect modification by race was observed for the association between intervention group and both the PSQ-SRBD total score and behavior subscale, even after adjustment for measures of socioeconomic status (Table 5). Specifically, smaller relative improvements associated with AT were reported by caregivers of African-American children compared with non–African-American children for those 2 symptom measures ($P = .01$ and $<.01$, respectively, for the relevant interaction terms). These differences persisted in analyses restricted to the 76 African-American children and 81 non–African-American children in the eAT arm whose OSAS resolved by PSG (P values for the fully adjusted models all $<.01$, data not shown).

Baseline OSAS severity (AHI or ODI quartiles) also did not influence the association between treatment arm and QoL or symptoms (all $P > .01$, data not shown).

Association of QoL and OSAS Symptoms With PSG Measures

In general, improvements in OSAS severity measured by using PSG explained only a small portion of the variance in the QoL and symptom change scores. Change in AHI correlated, albeit weakly, with change in mESS (partial $r^2 = 0.03$, $P < .01$), OSA-18 (partial $r^2 = 0.07$, $P < .01$), PSQ SRBD scale (partial $r^2 = 0.14$, $P < .01$), PSQ snoring subscale (partial $r^2 = 0.17$, $P < .01$), and PSQ sleepiness subscale (partial $r^2 = 0.03$, $P < .01$) (Table 6). Small but significant associations were also seen between change in ODI and OSA-18 total score (partial $r^2 = 0.05$, $P < .01$), PSQ SRBD scale (partial $r^2 = 0.09$, $P < .01$), PSQ snoring subscale (partial $r^2 = 0.09$, $P < .01$), and PSQ sleepiness subscale (partial $r^2 = 0.02$, $P < .01$) (Table 7). In contrast, changes in AHI and ODI were not significantly associated with changes in generic health-related QoL.

DISCUSSION

This large, randomized controlled trial of children with OSAS found that key symptoms and QoL improved

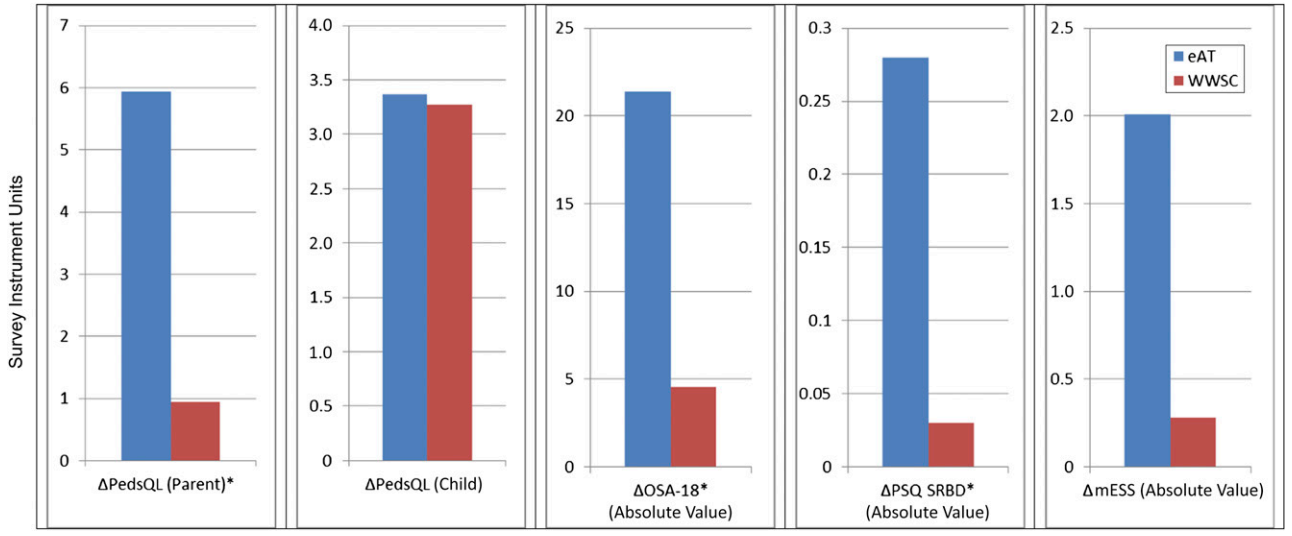

FIGURE 1

Summary of differences in QoL and OSAS symptom score changes in the eAT and WWSC arms. Absolute values were used when change scores were negative to facilitate comparisons of effect magnitude. *$P < .01$ for difference between arms, adjusted for site, race, age, obese (<95 or >95 BMI percentile), gender, maternal education (less than high school, high school or higher, or missing), income (>$30 000, ≤$30 000, or missing), log baseline AHI, and baseline outcome variable.

TABLE 4 Effect Modification on Change: Weight Category (Normal Versus Overweight Versus Obese)

Outcome	eAT			WWSC			P^a	P^b
	Normal	Overweight	Obese	Normal	Overweight	Obese		
Peds QL (parent) total	5.54 ± 1.33	1.91 ± 1.61	4.09 ± 2.31	−0.00 ± 1.24	−2.58 ± 1.56	−0.63 ± 2.33	.99	.91
Peds QL (child) total	5.11 ± 1.73	0.86 ± 2.06	5.22 ± 2.94	4.64 ± 1.65	−0.14 ± 2.06	1.27 ± 3.03	.89	.74
OSA-18 total	−21.23 ± 1.77	−18.57 ± 2.14	−18.70 ± 3.19	−4.19 ± 1.68	−2.33 ± 2.08	−1.14 ± 3.11	.79	.96
PSQ-SRBD total	−0.28 ± 0.02	−0.24 ± 0.02	−0.24 ± 0.03	−0.03 ± 0.02	−0.00 ± 0.02	−0.01 ± 0.03	.92	.76
PSQL snoring subscale	−0.65 ± 0.03	−0.59 ± 0.04	−0.59 ± 0.06	−0.11 ± 0.03	−0.05 ± 0.04	−0.08 ± 0.06	.89	.92
PSQL sleepiness subscale	−0.28 ± 0.03	−0.26 ± 0.04	−0.28 ± 0.06	−0.04 ± 0.03	−0.02 ± 0.04	0.08 ± 0.06	.32	.36
PSQL behavior subscale	−0.12 ± 0.03	−0.12 ± 0.04	−0.04 ± 0.05	0.02 ± 0.03	−0.03 ± 0.04	−0.06 ± 0.05	.10	.13
SLSC total (mESS)	−2.37 ± 0.41	−1.14 ± 0.50	−2.77 ± 0.72	−0.20 ± 0.39	−0.41 ± 0.48	0.13 ± 0.72	.12	.09

Data are presented as mean ± SD; marginal means adjusting for variables included in *P* value 1.

[a] *P* value for interaction term adjusting stratified variables only: site, race (African American versus non–African American), and age (5–7 vs 8–10 years old).

[b] *P* value for interaction term adjusting for site, race (African American versus non–African American), age (continuous), gender, maternal education (less than high school, high school or higher, or missing/not sure), income (>$30 000, ≤$30 000, and missing), baseline log AHI, and baseline outcome variable.

substantially more after eAT than WWSC. Benefits from eAT were evident in generic and disease-specific health-related QoL (as measured by using the PedsQL and OSA-18) and in OSAS symptoms (as reflected by using the PSQ SRBD scale and the mESS). Moderate to large improvements were observed for most QoL and symptom measurements, including the parent-completed PedsQL (total score, school, emotional, and physical function domains), OSA-18 (total and all 5 domains), mESS, and the PSQ SRBD (total score and snoring, sleepiness, and inattentive/behavioral subscales). Improvement in OSAS severity measured by using PSG variables explained only a small proportion of the improvements seen in OSAS symptoms and QoL. These observations have important clinical implications for the many children with OSAS who are evaluated for AT. The findings are of particular relevance, given the growing interest from patients, payers, and providers that QoL and symptom outcomes be highlighted in the management of chronic health conditions.

Clinically, many factors are considered when making a decision to perform surgery or to judge the success of surgical interventions. Previous studies measuring success rates for AT in children with OSAS have often focused somewhat narrowly on normalization of PSG parameters, with reports of surgical success rates ranging from 27% to 83%; lower cure rates are typically reported in obese children.[19,28–31] This emphasis on PSG measures of disease resolution may be partially due to assumptions that PSG severity parallels severity of the symptoms seen with OSAS. This concept is not well supported by the current literature for either neurobehavioral morbidity or QoL.[19,26] Previous studies of children with OSAS have shown no association between baseline OSA-18 scores and severity of OSAS on PSG.[32] Moreover, studies have failed to demonstrate clear correlation between extent of PSG improvements after AT and improvement in QoL.[33,34] In CHAT, we observed correlations between changes in AHI or ODI and changes in QoL and symptom severity measures. However, PSG improvements explained only a small portion of the variance for the change scores (partial r^2 ranging from <0.01 to 0.17). Thus, both previous literature and current data indicate that using PSG results as the sole metric for effectiveness of AT in pediatric OSAS may neglect other benefits that are important to children and their families.

TABLE 5 Effect Modification on Change: Race (African American Versus Non–African American)

Outcome	eAT		WWSC		P^a	P^b
	African American	Non–African American	African American	Non–African American		
Peds QL (parent) total	3.18 ± 2.07	7.44 ± 1.82	−0.12 ± 2.47	2.12 ± 2.22	.57	.77
Peds QL (child) total	4.55 ± 2.50	0.85 ± 2.17	3.09 ± 3.03	2.44 ± 2.65	.48	.26
OSA-18 total	−17.85 ± 2.84	−22.51 ± 2.51	−10.71 ± 3.36	−5.07 ± 3.03	.04	.09
PSQ-SRBD total	−0.23 ± 0.03	−0.32 ± 0.02	−0.10 ± 0.03	−0.07 ± 0.03	.01	.01
PSQL Snoring sub-scale	−0.67 ± 0.05	−0.68 ± 0.05	−0.23 ± 0.06	−0.25 ± 0.06	.91	.79
PSQL Sleepiness sub-scale	−0.13 ± 0.06	−0.29 ± 0.05	−0.07 ± 0.07	−0.02 ± 0.06	.03	.26
PSQL Behavior sub-scale	−0.01 ± 0.04	−0.18 ± 0.04	−0.06 ± 0.05	−0.03 ± 0.05	<.01	<.01
SLSC total (mESS)	−1.67 ± 0.60	−2.57 ± 0.53	−0.90 ± 0.72	−0.91 ± 0.65	.40	.32

Data are presented as mean ± SD; marginal means adjusting for variables included in *P* value 1.

[a] *P* value for the effect modification adjusting for stratified variables only: site, age (5–7 vs 8–10 years old), and overweight (≥85th vs <85th BMI percentile).

[b] *P* value for the effect modification adjusting for site, age (continuous), obese (<95 vs ≥95 BMI percentile), gender, maternal education (less than high school, high school or higher, or missing/not sure), income (>$30 000, ≤$30 000, or missing), baseline log AHI, and baseline outcome variable.

TABLE 6 Association Between QoL and Symptom Change Scores and PSG Change Scores (Log AHI)

Outcome	P^a			P^b		
	Log AHI Change β(SE)	Partial R^2	Log AHI Change *P*	Log AHI Change β(SE)	Partial R^2	Log AHI Change *P*
Peds QL (parent) total	−0.66 (0.42)	<0.01	0.12	−0.75 (0.38)	<0.01	0.05
Peds QL (child) total	0.60 (0.54)	<0.01	0.27	−0.07 (0.48)	<0.01	0.88
OSA-18 total	3.32 (0.60)	0.07	<0.01	3.49 (0.55)	0.07	<0.01
PSQ-SRBD total	0.05 (0.01)	0.14	<0.01	0.05 (0.01)	0.13	<0.01
PSQL Snoring subscale	0.12 (0.01)	0.17	<0.01	0.12 (0.01)	0.17	<0.01
PSQL Sleepiness subscale	0.04 (0.01)	0.03	<0.01	0.05 (0.01)	0.04	<0.01
PSQL Behavior subscale	0.01 (0.01)	<0.01	0.34	0.02 (0.01)	<0.01	0.04
SLSC total (mESS)	0.47 (0.13)	0.03	<0.01	0.51 (0.12)	0.04	<0.01

[a] *P* value for change in log AHI adjusting stratified variables only: site, race (African American versus non–African American), age (5–7 vs 8–10 years old), and overweight (≥85th vs < 85th BMI percentile).

[b] *P* value for change in log AHI adjusting for site, race (African American versus non–African American), age (continuous), obese (<95 vs ≥95 BMI percentile), gender, maternal education (less than high school, high school or higher, or missing/not sure), income (>$30 000, ≤$30 000, or missing), baseline log AHI, and baseline outcome variable.

The large proportion of our subjects who were overweight or obese allowed for subgroup analysis of QoL and symptoms. Increased likelihood of persistent OSAS after AT in obese children has been well documented, including a meta-analysis of 23 studies.[28,30] Obesity has also been associated with decreased QoL in children.[35] Improvement in QoL after AT for OSAS in the obese population has, however, been reported. A study of children with OSAS and BMI >95% showed improvement in OSA-18 general and domain scores despite lack of resolution of OSAS in the majority of subjects.[31] In the present analysis, although only obese children considered to be candidates for AT were included, obesity did not influence the relative changes in QoL or OSAS symptom severity with each intervention. These findings are supported by a study of QoL in children with severe obesity which showed that of 7 obesity-related comorbidities, only OSAS was associated with significant decreases in QoL.[35] The improved QoL and symptom outcomes seen in obese children support a clinically beneficial effect of surgery relative to watchful waiting for children in this group for whom treatment controversies exist.

OSAS has also been shown to be more common in African-American children.[36] More than one-half (55%) of the CHAT study participants were African American, which enabled evaluation for effect modification of race on the changes in QoL and symptoms between treatment arms. A significant effect modification of treatment by race was seen when comparing African-American versus non−African-American study participants for the PSQ SRBD total score and behavior subscale. Specifically, caregivers of American-African children in the eAT arm reported less improvement in children's behavior than did caregivers of non−African-American children. These differences persisted after adjustment for socioeconomic status and in an analysis restricted to children in whom OSAS resolved by PSG. In conjunction with the lack of improvement noted by the child-completed PedsQL survey, however, it must be considered that differing caregiver expectations about the beneficial effects of surgery or what constitutes problematic behavior may have influenced responses.

In the present study, none of the child-reported PedsQL measurements differed significantly between the 2 treatment groups. Previous studies have shown an ability of the child PedsQL to detect significant differences in the summary and

TABLE 7 Association Between QoL and Symptom Change Scores and PSG Change Scores (log ODI)

Outcome	P^a			P^b		
	Log ODI Change β(SE)	Partial R^2	Log ODI Change P	Log ODI Change β(SE)	Partial R^2	Log ODI Change P
Peds QL (parent) total	−0.66 (0.49)	<0.01	0.18	−0.66 (0.45)	<0.01	0.14
Peds QL (child) total	0.20 (0.62)	<0.01	0.75	−0.26 (0.56)	<0.01	0.65
OSA-18 total	3.14 (0.71)	0.05	<0.01	2.87 (0.66)	0.04	<0.01
PSQ-SRBD total	0.05 (0.01)	0.09	<0.01	0.05 (0.01)	0.08	<0.01
PSQL Snoring subscale	0.10 (0.02)	0.09	<0.01	0.10 (0.01)	0.09	<0.01
PSQL Sleepiness subscale	0.04 (0.01)	0.02	<0.01	0.04 (0.01)	0.02	<0.01
PSQL Behavior subscale	0.02 (0.01)	<0.01	0.12	0.02 (0.01)	0.01	0.02
SLSC total (mESS)	0.32 (0.15)	0.01	0.04	0.42 (0.14)	0.02	<0.01

[a] *P* value for change in log ODI adjusting stratified variables only: site, race (African American versus non–African American), age (5–7 vs 8–10 years old), and overweight (≥85th vs < 85th BMI percentile).

[b] *P* value for change in log ODI adjusting for site, race (African American versus non–African American), age (continuous), obese (<95 vs ≥95 BMI percentile), gender, maternal education (less than high school, high school or higher, missing/not sure), income (>$30 000, ≤$30 000, or missing), baseline log AHI, and baseline outcome variable.

domain scores between healthy children and children with a variety of chronic diseases.[37] However, OSAS was not specifically evaluated. Conceivably, children have difficulty recognizing their own sleepiness, irritability, or decreased concentration or do not consider those symptoms as problematic as the pain or physical limitations experienced with other chronic diseases. An alternate explanation is that the improvements reported by caregivers represent a desire to justify surgical interventions.

The major strengths of this study of health-related QoL and OSAS symptoms in pediatric patients undergoing AT for OSAS were a large, diverse sample recruited from multiple pediatric centers and use of a randomized design with a control group and highly rigorous and standardized measurement approaches. The study addressed patient-reported outcomes, which are increasingly recognized as important to patients and other stakeholders in health care. However, it should be noted that measures of QoL are inherently subjective, and in the setting of a surgical trial with an inability to blind participants, it is possible that the larger improvements in QoL and symptom measurements seen in the eAT arm could reflect a surgical placebo effect or variability of caregivers in assessing symptoms. However, the significant (albeit small) correlation with PSG improvement provides support for treatment-associated effects. An additional shortcoming was the limited follow-up period of 7 months.

CONCLUSIONS

This large, multisite, prospective, randomized controlled study of AT for PSG-documented pediatric OSAS found that key parent-reported measures of QoL and symptoms, or "patient- centered outcomes," improved substantially and significantly more in children treated with surgical AT than in children treated with WWSC. Improvements in QoL and OSAS symptoms were associated with improvement in PSG indicators of disease severity; however, only a small proportion of the observed QoL and symptomatic improvement was explained by PSG improvement. This study strongly supports the consideration of metrics beyond those reflected by PSG parameters when evaluating the value of AT in children with symptomatic OSAS.

ACKNOWLEDGMENTS

CHAT gratefully acknowledges the superb support of the CHAT research staff: Jean Arnold, Mary Ellen Carroll, Mary Anne Cornaglia, Beth Ann Compton, Casey Critchlow, Judith Emancipator, Melissa Fernando, Theresa Friederich, Amanda Goodman, Xiaoling Hou, Elise Hodges, Laurie Karamessinis, Kim Lacy, Megan McDougall, Daniel Mobley, Michelle Nicholson, Angela Orlando, Deborah L. Ruzicka, Gauri Sathe, Nancy Scott, Susan Surovec, Omarya Vega, Xingmei Wang, and Catherine Williams. The authors also appreciate the generous participation of the families enrolled in the study. They are grateful for the helpful guidance during the study of the CHAT Data and Safety Monitoring Board: Lynn Taussig, MD (Chair); Thomas Anders, MD; Julie Buring, ScD; Karina Davidson, PhD; Estelle Gauda, MD; Steven Piantadosi, MD, PhD; Bennett Shaywitz, MD; Benjamin Wilfond, MD; Tucker Woodson, MD; and Robert Zeiger, MD.

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

FINANCIAL DISCLOSURE: Dr Rosen has consulted for Natus and Advance-Medical and is a consultant for Jazz Pharmaceuticals. Dr Chervin has received research grants from the National Institutes of Health, Fox Foundation, and the University of Michigan. He has received support for an educational program from Philips Respironics and Fisher Paykel. He serves on boards of directors for the American Academy of Sleep Medicine, the American Sleep Medicine Foundation, the American Board of Sleep Medicine, Associated Professional Sleep Societies, and the International Pediatric Sleep Association. He has consulted for Proctor and Gamble, Zansors, and MC3. He serves as a section editor for UpToDate and a book editor for Cambridge University Press, and he serves as a volunteer on the advisory board of not-for-profit Sweet Dreamzzz. Dr Chervin is also named in patents, patents pending, and copyrighted material related to sleep disorder diagnosis and assessment and owned by the University of Michigan. This copyrighted material includes the Pediatric Sleep Questionnaire Sleep-Related Breathing Disorders questionnaire used in the research reported here and currently available online for license and use free of charge (http://inventions.umich.edu/technologies/3773/sleep-related-breathing-disorder-scale-srbd-scale-from-pediatric-sleep-questionnaire-to-identify-symptoms-of-obstructive-sleep-apnea-in-children). Dr Marcus reports research support from Phillips Respironics and Ventus, unrelated to the current study. Ms Parker is currently employed by SAS. Dr Redline reports that Brigham Women's Hospital received grant support from ResMed Foundation and equipment for research (not for the present study) from ResMed Inc and Philips Respironics, and equipment for CHAT from Novametrix. The other authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: For CHAT (Childhood Adenotonsillectomy Trial): Boston Children's Hospital, Harvard University, Boston, Massachusetts (Eliot Katz, MD; Janice Ware, PhD; Dwight Jones, MD); Brigham and Women's Hospital and Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, Massachusetts (Susan Redline, MD, MPH; Rui Wang, PhD); Cardinal Glennon Children's Hospital, Saint Louis University, St Louis, Missouri (Ron Mitchell, MD; Shalini Paruthi, MD; Karen Snyder, MS); University of Pennsylvania/Children's Hospital of Philadelphia, Pennsylvania (Carole Marcus, MBBCh; Nina H. Thomas, PhD; Lisa Elden, MD); Cincinnati Children's

Medical Center, University of Cincinnati, Cincinnati, Ohio (Raouf Amin, MD; Dean Beebe, PhD; Paul Willging, MD); Montefiore Children's Hospital, Albert Einstein College of Medicine, Yeshiva University, Bronx, New York (Raanan Arens, MD; Hiren Muzumdar, MD; Shelby Harris, PsyD CBSM); Rainbow Babies and Children's Hospital, University Hospitals Case Medical Center, Case Western Reserve University School of Medicine, Cleveland, Ohio (Carol Rosen, MD; H. Gerry Taylor, PhD; Robert Sprecher, MD; James Arnold, MD); University of Kentucky, Louisville, Kentucky (David Gozal, MD); University of Michigan, Ann Arbor, Michigan (Ronald Chervin, MD; Susan Garetz, MD, Bruno Giordani, PhD; Tim Hoban, MD); University of Pennsylvania, Philadelphia, Pennsylvania (Susan Ellenberg, PhD; Reneé H. Moore, PhD; Kim Lacy, RN, BSN). Grant support received from the National Institutes of Health (HL083075, HL083129, UL1 RR024134, and UL1 RR024989). Funded by the National Institutes of Health (NIH).

POTENTIAL CONFLICT OF INTEREST: Dr Rosen has consulted for Natus and Advance-Medical and is a consultant for Jazz Pharmaceuticals. Dr Chervin has received research grants from the National Institutes of Health, the Fox Foundation, and the University of Michigan. He has received support for an educational program from Philips Respironics and Fisher Paykel. He serves on boards of directors for the American Academy of Sleep Medicine, the American Sleep Medicine Foundation, the American Board of Sleep Medicine, Associated Professional Sleep Societies, and the International Pediatric Sleep Association. He has consulted for Proctor and Gamble, Zansors, and MC3. He serves as a section editor for UpToDate and a book editor for Cambridge University Press, and he serves as a volunteer on the advisory board of not-for-profit Sweet Dreamzzz. Dr Chervin is also named in patents, patents pending, and copyrighted material related to sleep disorder diagnosis and assessment and owned by the University of Michigan. This copyrighted material includes the Pediatric Sleep Questionnaire Sleep-Related Breathing Disorders questionnaire used in the research now reported and currently available online for license and use free of charge (http://inventions.umich.edu/technologies/3773/sleep-related-breathing-disorder-scale-srbd-scale-from-pediatric-sleep-questionnaire-to-identify-symptoms-of-obstructive-sleep-apnea-in-children). Dr Marcus reports research support from Phillips Respironics and Ventus, unrelated to the current study. Ms Parker is currently employed by SAS. Dr Redline reports that Brigham Women's Hospital received grant support from ResMed Foundation and equipment for research (not for the present study) from ResMed Inc and Philips Respironics, and equipment for CHAT from Novametrix. The other authors have indicated they have no potential conflicts of interest to disclose.

REFERENCES

1. Brunetti L, Rana S, Lospalluti ML, et al. Prevalence of obstructive sleep apnea syndrome in a cohort of 1,207 children of southern Italy. *Chest*. 2001;120(6):1930–1935
2. Gislason T, Benediktsdóttir B. Snoring, apneic episodes, and nocturnal hypoxemia among children 6 months to 6 years old. An epidemiologic study of lower limit of prevalence. *Chest*. 1995;107(4):963–966
3. Marcus CL, Greene MG, Carroll JL. Blood pressure in children with obstructive sleep apnea. *Am J Respir Crit Care Med*. 1998;157(4 pt 1):1098–1103
4. Amin R, Somers VK, McConnell K, et al. Activity-adjusted 24-hour ambulatory blood pressure and cardiac remodeling in children with sleep disordered breathing. *Hypertension*. 2008;51(1):84–91
5. Ali NJ, Pitson D, Stradling JR. Sleep disordered breathing: effects of adenotonsillectomy on behaviour and psychological functioning. *Eur J Pediatr*. 1996;155(1):56–62
6. Blunden S, Lushington K, Kennedy D, Martin J, Dawson D. Behavior and neurocognitive performance in children aged 5-10 years who snore compared to controls. *J Clin Exp Neuropsychol*. 2000;22(5):554–568
7. Gottlieb DJ, Vezina RM, Chase C, et al. Symptoms of sleep-disordered breathing in 5-year-old children are associated with sleepiness and problem behaviors. *Pediatrics*. 2003;112(4):870–877
8. Kaemingk KL, Pasvogel AE, Goodwin JL, et al. Learning in children and sleep disordered breathing: findings of the Tucson Children's Assessment of Sleep Apnea (tuCASA) prospective cohort study. *J Int Neuropsychol Soc*. 2003;9(7):1016–1026
9. O'Brien LM, Mervis CB, Holbrook CR, et al. Neurobehavioral implications of habitual snoring in children. *Pediatrics*. 2004;114(1):44–49
10. Baldassari CM, Mitchell RB, Schubert C, Rudnick EF. Pediatric obstructive sleep apnea and quality of life: a meta-analysis. *Otolaryngol Head Neck Surg*. 2008;138(3):265–273
11. Georgalas C, Tolley N, Kanagalingam J. Measuring quality of life in children with adenotonsillar disease with the Child Health Questionnaire: a first U.K. study. *Laryngoscope*. 2004;114(10):1849–1855
12. Stewart MG, Friedman EM, Sulek M, et al. Quality of life and health status in pediatric tonsil and adenoid disease. *Arch Otolaryngol Head Neck Surg*. 2000;126(1):45–48
13. Rosen CL, Palermo TM, Larkin EK, Redline S. Health-related quality of life and sleep-disordered breathing in children. *Sleep*. 2002;25(6):657–666
14. Goldstein NA, Fatima M, Campbell TF, Rosenfeld RM. Child behavior and quality of life before and after tonsillectomy and adenoidectomy. *Arch Otolaryngol Head Neck Surg*. 2002;128(7):770–775
15. De Serres LM, Derkay C, Sie K, et al. Impact of adenotonsillectomy on quality of life in children with obstructive sleep disorders. *Arch Otolaryngol Head Neck Surg*. 2002;128(5):489–496
16. Mitchell RB, Kelly J, Call E, Yao N. Long-term changes in quality of life after surgery for pediatric obstructive sleep apnea. *Arch Otolaryngol Head Neck Surg*. 2004;130(4):409–412
17. Mitchell RB, Kelly J, Call E, Yao N. Quality of life after adenotonsillectomy for obstructive sleep apnea in children. *Arch Otolaryngol Head Neck Surg*. 2004;130(2):190–194
18. Flanary VA. Long-term effect of adenotonsillectomy on quality of life in pediatric patients. *Laryngoscope*. 2003;113(10):1639–1644
19. Marcus CL, Moore RH, Rosen CL, et al; Childhood Adenotonsillectomy Trial (CHAT). A randomized trial of adenotonsillectomy for childhood sleep apnea. *N Engl J Med*. 2013;368(25):2366–2376
20. Redline S, Amin R, Beebe D, et al. The Childhood Adenotonsillectomy Trial (CHAT): rationale, design, and challenges of a randomized controlled trial evaluating a standard surgical procedure in a pediatric population. *Sleep*. 2011;34(11):1509–1517

21. Centers for Disease Control and Prevention. Clinical growth charts. Available at: www.cdc.gov/growthcharts/clinical_charts.htm. Accessed November 20, 2014
22. Varni JW, Seid M, Kurtin PS. PedsQL 4.0: reliability and validity of the Pediatric Quality of Life Inventory version 4.0 generic core scales in healthy and patient populations. *Med Care*. 2001; 39(8):800–812
23. Franco RA Jr, Rosenfeld RM, Rao M. First place—resident clinical science award 1999. Quality of life for children with obstructive sleep apnea. *Otolaryngol Head Neck Surg*. 2000;123(1 pt 1):9–16
24. Bannink N, Maliepaard M, Raat H, Joosten KF, Mathijssen IM. Reliability and validity of the obstructive sleep apnea-18 survey in healthy children and children with syndromic craniosynostosis. *J Dev Behav Pediatr*. 2011;32(1):27–33
25. Chervin RD, Hedger K, Dillon JE, Pituch KJ. Pediatric sleep questionnaire (PSQ): validity and reliability of scales for sleep-disordered breathing, snoring, sleepiness, and behavioral problems. *Sleep Med*. 2000;1(1):21–32
26. Chervin RD, Ruzicka DL, Giordani BJ, et al. Sleep-disordered breathing, behavior, and cognition in children before and after adenotonsillectomy. *Pediatrics*. 2006;117(4). Available at: www.pediatrics.org/cgi/content/full/117/4/e769
27. Melendres MC, Lutz JM, Rubin ED, Marcus CL. Daytime sleepiness and hyperactivity in children with suspected sleep-disordered breathing. *Pediatrics*. 2004;114(3):768–775
28. Bhattacharjee R, Kheirandish-Gozal L, Spruyt K, et al. Adenotonsillectomy outcomes in treatment of obstructive sleep apnea in children: a multicenter retrospective study. *Am J Respir Crit Care Med*. 2010;182(5):676–683
29. Brietzke SE, Gallagher D. The effectiveness of tonsillectomy and adenoidectomy in the treatment of pediatric obstructive sleep apnea/hypopnea syndrome: a meta-analysis. *Otolaryngol Head Neck Surg*. 2006; 134(6):979–984
30. Friedman M, Wilson M, Lin HC, Chang HW. Updated systematic review of tonsillectomy and adenoidectomy for treatment of pediatric obstructive sleep apnea/hypopnea syndrome. *Otolaryngol Head Neck Surg*. 2009; 140(6):800–808
31. Mitchell RB, Kelly J. Adenotonsillectomy for obstructive sleep apnea in obese children. *Otolaryngol Head Neck Surg*. 2004;131(1):104–108
32. Tran KD, Nguyen CD, Weedon J, Goldstein NA. Child behavior and quality of life in pediatric obstructive sleep apnea. *Arch Otolaryngol Head Neck Surg*. 2005; 131(1):52–57
33. Stewart MG, Glaze DG, Friedman EM, Smith EO, Bautista M. Quality of life and sleep study findings after adenotonsillectomy in children with obstructive sleep apnea. *Arch Otolaryngol Head Neck Surg*. 2005; 131(4):308–314
34. Mitchell RB, Kelly J. Outcome of adenotonsillectomy for severe obstructive sleep apnea in children. *Int J Pediatr Otorhinolaryngol*. 2004;68(11): 1375–1379
35. Schwimmer JB, Burwinkle TM, Varni JW. Health-related quality of life of severely obese children and adolescents. *JAMA*. 2003;289(14):1813–1819
36. Rosen CL, Larkin EK, Kirchner HL, 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(4): 383–389
37. Varni JW, Limbers CA, Burwinkle TM. Impaired health-related quality of life in children and adolescents with chronic conditions: a comparative analysis of 10 disease clusters and 33 disease categories/severities utilizing the PedsQL 4.0 Generic Core Scales. *Health Qual Life Outcomes*. 2007;5:43