Tonsillectomy for Obstructive Sleep-Disordered Breathing: A Meta-analysis

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CONTEXT: The effectiveness of tonsillectomy or adenotonsillectomy (hereafter, "tonsillectomy") for obstructive sleep-disordered breathing (OSDB) compared with watchful waiting with supportive care is poorly understood.

OBJECTIVE: To compare sleep, cognitive or behavioral, and health outcomes of tonsillectomy versus watchful waiting with supportive care in children with OSDB.

DATA SOURCES: Medline, Embase, and the Cochrane Library.

STUDY SELECTION: Two investigators independently screened studies against predetermined criteria.

DATA EXTRACTION: Two investigators independently extracted key data. Investigators independently assessed study risk of bias and the strength of the evidence of the body of literature. Investigators synthesized data qualitatively and meta-analyzed apnea–hypopnea index (AHI) scores.

RESULTS: We included 11 studies. Relative to watchful waiting, most studies reported better sleep-related outcomes in children who had a tonsillectomy. In 5 studies including children with polysomnography-confirmed OSDB, AHI scores improved more in children receiving tonsillectomy versus surgery. A meta-analysis of 3 studies showed a 4.8-point improvement in the AHI in children who underwent tonsillectomy compared with no surgery. Sleep-related quality of life and negative behaviors (eg, anxiety and emotional lability) also improved more among children who had a tonsillectomy. Changes in executive function were not significantly different. The length of follow-up in studies was generally <12 months.

LIMITATIONS: Few studies fully categorized populations in terms of severity of OSDB; outcome measures were heterogeneous; and the durability of outcomes beyond 12 months is not known.

CONCLUSIONS: Tonsillectomy can produce short-term improvement in sleep outcomes compared with no surgery in children with OSDB. Understanding of longer-term outcomes or effects in subpopulations is lacking.



abstract

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Drs Chinnadurai, Jordan, McPheeters, and Francis and Ms Sathe helped to conceptualize and design the review and helped to draft the initial manuscript; Dr Fonnesbeck helped to conceptualize the review and draft the initial manuscript and conducted the meta-analysis; and all authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Downloaded from by guest on March 9, 2017 PEDIATRICS Volume 139, number 2, February 2017:e20163491 Tonsillectomy or adenotonsillectomy ("tonsillectomy") are commonly performed in the United States and represent >15% of all surgical procedures in children under the age of 15 years.^{1,2} Currently, the most common indication for tonsillectomy is obstructive sleep-disordered breathing (OSDB) (ie, breathing difficulties during sleep, including simple snoring, obstructive sleep apnea [OSA], and upper airway resistance syndrome). OSDB results from obstruction or dynamic collapse of upper airway soft tissue during sleep, which can manifest as snoring, hypopnea, apnea, and restless sleep. Adenotonsillar hypertrophy is the most common contributor to OSDB in children.

OSDB can result in significant quality of life and health consequences. It has been associated with a 5-point decrease in IQ, hypersomnolence, emotional lability, decreased attention, small stature, enuresis, cardiopulmonary morbidity, and missed school.³ Evidence of the relationship is reinforced by the effectiveness of OSDB treatment in improving behavior, attention, quality of life, neurocognitive functioning, enuresis, parasomnias, and restless sleep and reversing of associated cardiovascular sequelae.4,5 Moreover, OSDB occurs at especially high rates in subsets of children with developmental disorders and craniofacial syndromes, including Down syndrome.

As in adults, the gold standard diagnostic test for OSA in children is polysomnography (PSG), which physiologically tests sleep architecture and efficiency. Treatment involves alleviating the inciting upper airway soft tissue obstruction or collapse. One method of primary treatment is continuous positive airway pressure (CPAP). CPAP compliance is highly variable in children.⁶⁻¹⁰ Other approaches include weight loss in overweight children, oral appliances, and allergy TABLE 1 Overview of Studies Addressing Tonsillectomy in Children With OSDB

Characteristic	RCTs	Nonrandomized trial	Prospective Cohort Studies	Retrospective Cohort Studies	Total Literature
Comparison					
Watchful waiting with supportive care	2	1	6	2	11
Frequently reported outcomes					
AHI	2	0	2	2	6
Sleep-related quality of life (OSA-18, M-ESS, PSQ)	1	1	1 ^a	1	4
Executive function, cognitive, or behavioral measures	2	0	1	1	4
Risk of bias					
Low	0	0	0	0	0
Moderate	2	1	2	2	7
High	0	0	4	0	4
Total participants, N	417	64	458	95	1034

^a Reports the T14 Paediatric Throat Disorders Outcome Test.

or antiinflammatory medications. However, because the most common culprit in children is tonsillar hypertrophy-related oropharyngeal obstruction, tonsillectomy is often used to establish an adequate airway.

In this systematic review, we examined the published evidence regarding the effectiveness of tonsillectomy compared with watchful waiting (which includes supportive treatment with medications, such as nasal steroids) for children with OSDB. This review is a component of an Agency for Healthcare Research and Quality-commissioned comparative effectiveness review of tonsillectomy in children conducted by the Vanderbilt Evidence Based Practice Center. The full comparative effectiveness review and review protocol (PROSPERO registry number: CRD42015025600) are available at www.effectivehealthcare. ahrq.gov.

METHODS

Search Strategy and Study Selection

We searched the Medline database via PubMed, Embase, and the Cochrane Library from January 1980 to June 2016 using a combination of controlled vocabulary and key terms related to tonsillectomy and OSDB (eg, tonsillectomy, adenotonsillectomy, and OSA). We also hand-searched the reference lists of included articles and recent reviews addressing tonsillectomy in children to identify potentially relevant articles.

We developed inclusion criteria in consultation with an expert panel of clinicians and researchers (Table 1). We included comparative study designs (eg, randomized controlled trials [RCTs] and prospective or retrospective cohort studies).

Data Extraction and Analysis

One investigator extracted data regarding: study design; descriptions of study populations, intervention, and comparison groups; and baseline and outcome data using a standardized form. A second investigator independently verified the accuracy of the extraction and revised as needed. Principal outcomes of interest included the apnea-hypopnea index (AHI), sleeprelated quality of life (eg, Obstructive Sleep Apnea-18 [OSA-18] and the Pediatric Sleep Questionnaire [PSQ]), cognitive, or behavioral measures. We synthesized studies qualitatively and report descriptive statistics in Table 2. Because only 3 studies were sufficiently homogenous to permit pooling, we used a fixed-effects

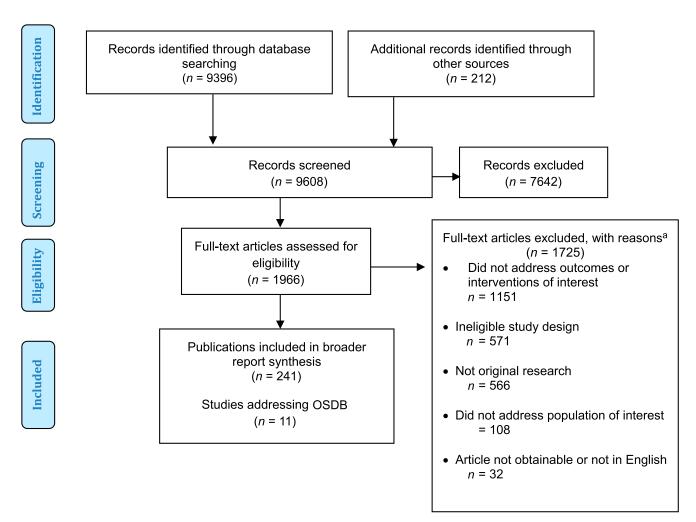


FIGURE 1

Disposition of studies identified for this review. Numbers do not tally as studies could be excluded for multiple reasons.

model to meta-analyze AHI data reported in these studies.

Assessment of Study Risk of Bias and Strength of Evidence

Two investigators independently evaluated the methodologic quality of studies using prespecified questions¹¹ appropriate to each study design to assess the risk of bias of RCTs and observational studies. Senior reviewers resolved discrepancies in the risk-of-bias assessment. We did not include studies with a high risk of bias in our descriptive analyses; however, we did include them in the meta-analysis after we determined that their inclusion did not systematically affect the meta-analysis results. Assessment of the strength of the evidence reflects the confidence that we have in the stability of treatment effects in the face of future research.¹² The degree of confidence that the observed effect of an intervention is unlikely to change (ie, the strength of the evidence) is presented as insufficient, low, moderate, or high. Assessments are based on consideration of 5 domains: study limitations, consistency in direction of the effect, directness in measuring intended outcomes, precision of effect, and reporting bias. We determined the strength of evidence separately for major intervention-outcome pairs using a prespecified approach described in detail in the full review.¹³

RESULTS

Our searches (conducted for the broader systematic review¹³) identified 9608 citations, of which 11 (reported in multiple publications) met inclusion criteria and compared tonsillectomy with watchful waiting (Fig 1).^{14–32} Table 1 outlines study design, risk of bias, and key outcomes reported. As noted, we did not include high-risk-of-bias studies in our qualitative analysis below, but we did include 1 such study²⁷ in a meta-analysis.

OSDB-Related Outcomes

Five studies (reported in multiple publications) evaluated the change in AHI among children with PSG-proven OSDB (Table 2).^{15–23,25,28,29,32} Two studies were RCTs, including the multiple publication Childhood Adenotonsillectomy Trial (CHAT).¹⁵⁻²³ All studies reported improvement in children after tonsillectomy compared with watchful waiting (excluding CPAP); differences in AHI between groups at follow-up were statistically significant in 3 studies.^{16–23,25,29,32} The watchful waiting groups also improved from baseline in 3 studies, but the improvements were greater in the tonsillectomy groups.15-23,25,29 This benefit was consistent across age ranges (1–18 years), although data were most frequently available on children ages 4 to 12 years. The benefits seemed durable, with follow-up ranging from 6 months to 4 years. Where reported, the respiratory disturbance index and oxygen saturation improved significantly after tonsillectomy.^{15,17}

Two retrospective cohort studies also reported results for children with obesity or other conditions.^{25,32} One reported significantly greater improvement in AHI in healthy children with mild OSA undergoing tonsillectomy compared with those not undergoing tonsillectomy.³² In subgroup analyses of obese children and those with comorbidities, such as Down syndrome, there was no significant benefit between groups in surgical and nonsurgical populations. In another study examining a mostly overweight/obese population with PSG-proven OSDB, AHI decreased significantly in children who received tonsillectomy compared with those who did not, but this single study provides inadequate evidence to draw conclusions about the effects of obesity on tonsillectomy effectiveness.²⁵

Three studies reported AHI outcomes that could be combined in a fixed effects meta-analysis (the CHAT RCT^{16-23,29} and 1 prospective²⁵ and 1 retrospective²⁷ cohort study). We estimated an effect size of -4.81 (95% credible interval: -6.5 to -3.1), indicating a reduction (improvement) in AHI of 4.81 points in children receiving tonsillectomy compared with those not undergoing surgery. This change is statistically significant and may be most clinically evident in children with mild or moderate OSDB (ie, AHI scores of 1–10).

Sleep-Related Quality of Life

Four studies (reported in multiple publications)^{15-21,23,25,31} assessed sleep quality outcomes by using several different caregiver-reported quality measures, which limited our ability to compare effectiveness directly across studies. However, outcomes were consistently better in children receiving tonsillectomy (Table 2). One RCT and 1 retrospective cohort used the Clinical Assessment Score-15 (CAS-15),^{15,25} with both reporting significantly greater improvement in sleep quality in scores in the tonsillectomy group compared with watchful waiting. In the 1 study reporting baseline data, scores in the watchful waiting group improved from baseline to the 6-month follow-up (*P* = not reported [NR]).¹⁵ The CHAT RCT used the Modified Epworth Sleepiness Scale (M-ESS) and OSA-18 as a measure of quality of life. Although control group scores improved moderately (P = NR), children that had a tonsillectomy had significantly greater improvements in sleep quality than the nonsurgical group as measured on both scales.^{16–21,23} This RCT also used the PSQ Sleep-related Breathing Disorder scale (PSQ-SRBD), which showed significant improvements in sleep quality after tonsillectomy versus watchful waiting ($P \leq .01$), and small improvements in the control group from baseline (P = NR). In a nonrandomized trial (moderate risk of bias), children with mild OSA (determined by PSG) were self- or caregiver-allocated to tonsillectomy or observation.³¹ At a 4-month follow-up, quality of life assessed using OSA-18 was significantly

improved in children who had surgery (P = .001), but not in the control group. Differences between groups, however, were not significant at the 8-month follow-up visit.

Finally, overall quality of life as measured by the Pediatric Quality of Life Inventory (PedsQL) improved significantly after tonsillectomy, compared with the untreated group in 1 RCT.^{16–21,23,28} Scores improved slightly in the control group from baseline (P = NR). The effects of tonsillectomy on sleep quality in children suffering from OSDB were positive across a number of outcomes and outcome domains. Impaired quality of life was the chief complaint of many parents seeking medical attention for a child with OSDB. Results were consistently positive for tonsillectomy relative to observation in short time frames, with limited data available in the longer term.

Behavioral Outcomes

The CHAT RCT^{16,17,19-23} and 1 prospective²⁸ and 1 retrospective cohort study²⁵ addressed behavioral outcomes (Table 2). All studies had a moderate risk of bias and used different scales to assess outcomes, again limiting our ability to compare effectiveness directly across studies. Two studies used the Child Behavior Checklist (CBC) to measure internalizing (emotionally reactive, anxious/ depressed, somatic complaints, and withdrawn behavior) and externalizing (attention problems and aggressive behavior) behaviors. Scores on the CBC improved from baseline in both groups in 1 cohort study, with no significant group differences.²⁸ In the second study, scores were significantly better in the tonsillectomy group compared with the no tonsillectomy group at follow-up, but baseline measures were not reported.²⁵

CHAT investigators also used the Conners' rating scale to assess behavioral issues, including

Author, Year, Study Type, ROB	Comparison Groups (<i>n</i>)	Baseline Outcomes	Follow-Up AHI Scores Outcomes
Trosman et al, 2016, ³² retrospective cohort, moderate ROB	G1: Tonsillectomy (18)	AHI, mean ± SD	AHI, mean ± SD; 16-mo follow-up (IQR)
	G1a: Tonsillectomy – obese children (8) G1b: Tonsillectomy – syndromic children (6)	G1: 3.5 ± 1.1 G1a: 3.83	G1: 2.69 (1.48 to 3.9)
	G2: WWSC (44) G2a: WWSC – obese children (11)	G1b: 3.08 G2: 3.09 ± 1.1	G1a: 3.08 G1b: 2.03
	G2b: WWSC – syndromic children (9)	G2a: 3.2 G2b: 3.31	G2: 5.18 (2.46 to 7.9) G2a: 3.4 G2b: 2.84 G1 vs G2: P = .03 G1a versus G2a: P = .25
			G1b versus G2b: $P = .36$
larcus et al, 2013, ^{16–23,} ²⁹ RCT, moderate ROB	G1: Tonsillectomy (193)	AHI, events per hour, median (IQR)	AHI, events per hour, change from baseline to 7 mo (IQR
	G2: WWSC (208)	G1: 4.8 (2.7–8.8)	G1: -3.5 (-7.1 to -1.8)
		G2: 4.5 (2.5–8.9) OSA-18 total score	G2: -1.6 (-3.7 to 0.5) G1 versus G2: P < .001
		G1: 53.1 ± 18.3	Effect size: 0.57
		G2: 54.1 ± 18.8	OSA-18 total score, change from baseline
		PSQ	G1: -21 ± 16.5
		$G1: 0.5 \pm 0.2$	G2: -4.5 ± 19.3
		$G2: 0.5 \pm 0.2$	G1 versus G2: $P \le .01$
		M-ESS	Effect size: -0.93
		G1: 7.1 ± 4.7	PSQ, change from baseline
		G2: 7.5 ± 5.2 PedsQL	$G1: -0.3 \pm 0.2$ $G2: -0.0 \pm 0.2$
		G1: 77.3 ± 15.3	G2. -0.0 ± 0.2 G1 versus G2: $P \le .01$
		G2: 76.5 ± 15.7	Effect size: -1.35
		CGI, caregiver	M-ESS, change from baseline
		G1: 52.5 ± 11.6	G1: -2.01 ± 4.7
		G2: 52.6 ± 11.7	G2: 0.28 ± 4.1
		CGI, teacher	G1 versus G2: <i>P</i> < .01
		G1: 56.4 ± 14.4	Effect size: -0.42
		G2: 55.1 ± 12.8	PedsQL, change from baseline to 7 mo
		NEPSY ^a	G1: 5.9 ± 13.6
		G1: 101.5 ± 15.9	$G_{2:} 0.9 \pm 13.3$
		G2: 101.1 ± 15 BRIEF (GEC), caregiver	G1 versus G2: <i>P</i> ≤ .001 Effect size: 0.37
		$G1: 50.1 \pm 11.2$	CGI, caregiver, change from baseline to 7 mo
		G2: 50.1 \pm 11.5	$G_{1:} -2.9 \pm 9.9$
		BRIEF (GEC), teacher	$G2: -0.2 \pm 9.4$
		G1: 57.2 ± 14.1	G1 versus G2: P = .01
		G2: 56.4 ± 11.7	CGI, teacher, change from baseline to 7 mo G1: -4.9 \pm 12.9
			$G2: -1.5 \pm 10.7$
			G1 versus G2: $P = .04$
			NEPSY, ^a change from baseline to 7 mo
			G1: 7.1 ± 13.9 G2: 5.1 ± 13.4
			G2. 0.1 ± 10.4 G1 versus G2: <i>P</i> = NS
			Effect size: 0.15
			BRIEF (GEC), caregiver
			$G_{1:} -3.3 \pm 8.5$
			G2: 0.4 ± 8.8
			G1 versus G2: <i>P</i> < .001
			Effect size: 0.28
			BRIEF (GEC), teacher
			$G_{1:} -3.1 \pm 12.6$
			$G_{2:} -1.0 \pm 11.2$
			G1 versus G2: $P = NS$

TABLE 2 Key OSDB-Related Outcomes in Studies Comparing Tonsillectomy With Watchful Waiting in Children With OSDB

Effect size: 0.18

Author, Year, Study Type, ROB	Comparison Groups (<i>n</i>)	Baseline Outcomes	Follow-Up AHI Scores Outcomes
Biggs et al, 2014, ²⁸ prospective cohort, moderate ROB	G1: Tonsillectomy or nasal steroids (12)	AHI, events per hour	AHI, events per hour (4 y posttonsillectomy)
	G2: WWSC (27)	G1: 9.4 ± 9.9 G2: 1.0 ± 1.2	$G_{1:1.8 \pm 5.2}$ $G_{2:1.7 \pm 6.0}$
		CBC, total problem G1: 64 ± 9 G2: 59 ± 10	G1 versus G2: P = NS CBC, total problem (4 y posttonsillectomy) G1: G1 ± 15
		BRIEF (GEC), caregiver G1: 62 ± 11	G2: 57 ± 12 G1 versus G2: P = NS
		G2: 58 ± 11 WASI full-scale IQ G1:102 ± 13	BRIEF (GEC) caregiver (4 y posttonsillectomy) G1: 58 ± 16 G2: 57 ± 12
		$G_{2:} 106 \pm 14$	G1 versus G2: P < .05 WASI full-scale IQ (4 y posttonsillectomy) G1: 101 ± 12
			G2: 104 ± 15 G1 versus G2: <i>P</i> = NS
Burstein et al, 2013, ²⁵ retrospective cohort, ^b moderate ROB	G1: Tonsillectomy (16)	AHI, median	AHI, median
moderate hob	G2: WWSC (16)	G1: 14.4	G1: 1.1, median change = 10.3
		G2: 9.3 CAS-15	G2: 3.7, median change = 6.5 G1 versus G2, median change: $P = .04$
		G1: NR	CAS-15 $CAS-15$
		G2: NR	G1: 8.9 ± 6.1
		CBC, total problem	G2: 29.4 ± 16.2
		G1: NR	G1 versus G2: <i>P</i> < .001
		G2: NR	CBC total problem (1.66–1.97 y posttonsillectomy) G1: 43.9 G2: 58.9
			G1 versus G2: <i>P</i> < .001
Goldstein et al, 2004, ¹⁵ RCT, moderate ROB	G1: PSG+ plus Tonsillectomy (21) G2: PSG- plus Tonsillectomy (11)	AHI, median G1: 6.2 (median)	AHI, median (6-mo follow-up) G1: 0.9 (median)
NGI, MOUEI ALE NOD	G3: PSG- plus WWSC (9)	G2: 0.5 (median) G3: 0.6 (median)	G2: 0.4 (median) G3: 0
		CAS-15 (median)	G2 versus G3: $P = NS$
		G1: 77	CAS-15 (median)
		G2: 64 G3: 50	G1: 59 G2: 49
		00.00	G3: 8
/olksy et al, 2014, ³¹	Ct. Tanaillastamy (ZO)	0 10 total acons	G2 versus G3: $P = .001$
nonrandomized trial, moderate ROB	G1: Tonsillectomy (30)	OSA-18, total score	OSA-18 total score, 3 mo follow-up
	G2: WWSC (34)	G1: 72.3 ± 20	G1: 33.9 ± 14.6
		G2: 58.5 ± 21.5	G2: 58.2 ± 24.5 G1 versus G2: P = .0001
			OSA-18 total score, 8 mo follow-up
			G1: 33.6 ± 8.6 G2: 45.1 ± 21.9
			G1 versus G2: $P = NS$
Tarasiuk et al, 2004, ²⁴ prospective cohort, moderate ROB	G1: Tonsillectomy (130)	Health care utilization	No. of new admissions, mean ± SE per patient per yea mean

TABLE 2 Continued

Author, Year, Study Type, ROB	Comparison Groups (<i>n</i>)	Baseline Outcomes	Follow-Up AHI Scores Outcomes	
	G2: WWSC (90)	G1 + G2: NR	Year 1	
			G1: 0.15 ± 0.04	
			G2: 0.08 ± 0.03	
			Year 2	
			G1: 0.06 ± 0.02	
			G2: 0.25 ± 0.07	
			No. of emergency department visits, mean \pm SE per	
			patient per year, mean	
			Year 1	
			G1: 0.57 ± 0.09	
			G2: 0.52 ± 0.09	
			Year 2	
			G1: 0.35 ± 0.05	
			G2: 0.37 ± 0.10	
			No. of consultations, mean \pm SE per patient per year,	
			mean	
			Year 1	
			G1: 3.6 ± 0.37	
			G2: 4.4 ± 0.40	
			G1 versus G2: $P = NR$	
			Year 2	
			G1: 1.9 ± 0.26	
			G2: 3.5 ± 0.46	
			G1 versus G2: $P = NR$	

CGI, Connors' Global Index; G, group; GEC, Global Executive Composite; IQR, interquartile range; NA, not applicable; NS, not significant; ROB, risk of bias; WASI, Wechsler Abbreviated Scale of Intelligence; WWSC, watchful waiting with supportive care.

^a NEPSY attention and executive function.

^b Follow-up periods differed in this study: the mean was 1.4 years in the tonsillectomy group and 2.0 years in the no surgery group; *P* = .02.²⁵

emotional lability, and reported improvements (ie, lowering of scores) in both groups, with significantly greater improvements in the tonsillectomy arm compared with the no tonsillectomy arm on both teacher- and parent-reported scales.^{16,17,19-23} In studies reporting baseline data, baseline scores on behavioral measures were not indicative of clinical concern. Although children's behaviors improved in these studies, the clinical significance and magnitude of the improvement is not clear.

Executive Function

One RCT and 1 prospective cohort study used the Developmental Neuropsychological Assessment (NEPSY) to evaluate attention and the Behavior Rating Inventory of Executive Function (BRIEF) to assess behavioral regulation and metacognition (Table 2).^{16,17,19-23,28} In the RCT, scores on the NEPSY improved from baseline in both groups, but group differences were not significant. Global scores on the BRIEF improved significantly among treated children compared with untreated children when evaluated by caregivers.^{16,17,19–23,28} When BRIEF was completed by teachers in a single study, both groups improved, and differences between groups were not significant.^{16,17,19–23}

Cardiopulmonary and Physiologic Outcomes

One RCT reported in multiple publications^{16–23} (moderate risk of bias) addressed outcomes, including cardiometabolic measures. The evidence was insufficient to comment on physiologic parameters, with a single RCT reporting no change in cardiometabolic measures, including insulin, lipids, and C-reactive protein levels.^{16–21,23} Underweight children also showed a significant increase in weight and BMI after tonsillectomy in this RCT. $^{\rm 16-23}$

Use and Other Outcomes

Two cohort studies with moderate risk of bias assessed health care use, defined as clinician contacts or antibiotic prescriptions, and cognitive outcomes (Table 2). A single moderate risk of bias cohort study reported a 33% reduction in gross health care use, including a 60% reduction in hospital admissions in the year after tonsillectomy in children with PSG-proven OSDB. Admissions in the untreated group increased (*P* = NR).²⁴

One cohort study using the Weschler Abbreviated Scale of Intelligence reported a significant improvement in performance IQ at 4-years posttonsillectomy in children who underwent tonsillectomy, but both the tonsillectomy and no surgery groups had declines or no change in

Intervention and Comparator	No./Type of Studies (Total Participants, <i>N</i>)	Key Outcome(s)	SOE Grade	Findings
Tonsillectomy versus no surgery in children with OSDB	Meta-analysis	AHI	Low SOE for greater improvement of AHI with tonsillectomy compared with no surgery	Significant improvement in tonsillectomy versus no surgery groups in 1 RCT and 2 retrospective cohort studies; no significant group differences in 1 RCT and 1 prospective cohort. In 3 studies, children in control arms improved from baseline.
	2 RCT (456) ^{15,17} 1 Prospective cohort (38) ²⁸ 2 Retrospective cohort (94) ^{25,} 32			4.8-point improvement in AHI in tonsillectomy arms in meta-analysis.
	2 RCT (456) ^{15,17} 1 Retrospective cohort (32) ²⁵	Sleep-related quality of life	Moderate SOE for modest improvement in sleep- related quality of life after tonsillectomy versus no surgery	Significant improvements in tonsillectomy versus no tonsillectomy groups on measures of sleep-related quality of life in 2 RCTs and 1 cohort study in the short term.
	1 RCT (397) ¹⁷ 1 Prospective cohort (38) ²⁸ 1 Retrospective cohort (32) ²⁵	Behavioral outcomes	Low SOE for improvements in negative behaviors after tonsillectomy versus no surgery	Significant improvements in tonsillectomy versus no surgery in 1 RCT and 1 retrospective cohort; no significant differences in 1 prospective cohort; differences in measurement time frames across studies (7 mo–4 y) and unclear clinical significance of changes.
	1 Prospective cohort (38) ²⁸	Cognitive changes (IQ)	Insufficient SOE	Insufficient evidence in 1 small study.
	1 RCT (397) ¹⁷ 1 Prospective cohort (38) ²⁸	Executive function	Insufficient SOE	Differences in follow-up time and medium study limitations preclude conclusions.
	1 RCT (397) ¹⁷	Cardiometabolic outcomes	Insufficient SOE	Insufficient evidence in only 1 RCT.
	1 Prospective cohort (220) ²⁴	Health care utilization	Insufficient SOE	Insufficient evidence in only 1 RCT.

TABLE 3 Summary of Evidence in Studies Addressing Effectiveness of Tonsillectomy in Children With OSDB

Non-RCT, nonrandomized trial; SOE, strength of evidence.

full scale IQ and verbal IQ over the same period.²⁸

Strength of the Evidence

Our confidence in these conclusions of greater improvement in AHI and negative behaviors with tonsillectomy versus watchful waiting is low (low strength of evidence). We also found consistently greater improvement in sleep-related quality of life with tonsillectomy versus watchful waiting and have greater confidence in this conclusion (moderate strength of evidence). We could not make conclusions about effects on executive function or IQ (insufficient strength of evidence). Table 3 outlines the strength of evidence findings.

DISCUSSION

Relative to watchful waiting, most studies reported better OSDB

and sleep-related outcomes in tonsillectomized children. The 5 studies that included children whose OSDB was confirmed with PSG found that AHI scores improved more in children receiving a tonsillectomy than in those who did not undergo surgery (significant group differences in 3 studies).15,17,25,27,28 Metaanalysis of 3 studies reporting outcomes that could be combined showed a 4.8-point improvement in AHI in children who underwent tonsillectomy compared with no surgery.^{17,25,27} Sleep-related quality of life and negative behaviors (eg, anxiety and emotional lability) also improved more among children who had a tonsillectomy.^{15,17,25} Changes in executive function were not significantly different between groups.17,28

The literature precludes firmer conclusions because relatively few studies have been published comparing tonsillectomy with a nonsurgical intervention for OSDB. Most studies provided little to no clinical outcome data, focusing instead on intermediate outcomes like the AHI. Patient populations were generally poorly characterized, and little information was available about the use of other treatments before surgery. Most of the evidence addressed short-term effects (<12 months).

Limitations

We included studies published in English only because we identified few non-English studies of relevance in a preliminary scan of non-English literature. We also did not include studies addressing adenoidectomy alone or studies comparing tonsillectomy with adenoidectomy because the choice of procedure is likely driven by the indication for surgery; thus, comparing these approaches would not be appropriate. Given the heterogeneity in anesthetic regimens, surgical techniques, postoperative analgesia and medications, and patient populations themselves, we were limited in our ability to stratify findings or identify potential subgroups that may respond more favorably to tonsillectomy or to supportive care. Long-term effects are limited in the literature base, particularly regarding outcomes that include growth and development, sleep quality outcomes, and behavioral outcomes for children with OSDB. Exploration of the demographics of patient populations more likely to be refractory to initial management strategies is also limited. A particular problem in the literature is a lack of full characterization of the patient population, particularly about clinically documented severity of sleep-disordered breathing. Understanding of "obstructive sleep-disordered breathing" and definitions of "cure" or resolution of symptoms varied from study to study, as did degree of hypertrophy. This heterogeneity makes the generalizability of the findings difficult to assess. The baseline severity of OSDB varied across studies.

Future Research Needs

Despite substantial research, the literature is largely silent on the natural history of OSDB that would provide a basis for the need for tonsillectomy in the long term. Many young patients may outgrow the need for intervention, but more data are needed to describe the potential to outgrow these indications to parents and to describe population factors that may predict resolution.^{20,33,34} Long-term data are needed to enable caregivers to weigh the benefits of surgery versus the reality of managing their child's condition as they wait for it to resolve, although obtaining longer-term data is difficult.

Future studies should take more care to characterize patient populations completely, including severity of OSDB, such that the applicability of findings can be specifically evaluated and potential candidates for surgery or watchful waiting identified. Clear characterization of comorbidities in studies is key for understanding the effects on subpopulations. As we learn more about the deleterious effects of sleep apnea and detection rates increase, more refined and specific treatment algorithms will be in demand. Future research should also address the current gaps in data surrounding treatment of special populations, including young children and children with comorbidities, such as obesity, craniofacial difference, and neuromuscular disease.

Measures commonly used to assess objective improvements in obstructed breathing, such as the AHI, are not patient-centered and may not reflect subjective reports of improvements or worsening of outcomes experienced by patients. Future research exploring the alignment of the AHI with patientreported outcomes, such as quality of life, would help to gauge the effects of tonsillectomy more precisely. Additionally, standardized measures of sleep outcomes are lacking. Finally, relatively little data exist regarding predictable factors contributing to the potential recurrence of symptoms after tonsillectomy for primary management. A better understanding of these factors would allow for more specific patient selection.

CONCLUSIONS

A tonsillectomy can improve sleep outcomes compared with no surgery in children with OSDB; however, modification of these benefits by comorbid and demographic characteristics are poorly characterized. Relative to no intervention, most studies reported better short-term sleep-related outcomes in children with OSDB who had a tonsillectomy. Additional research to define more precisely the population of children most likely to benefit from tonsillectomy compared with supportive care and to refine outcome measures to incorporate patient-focused assessment are key future research needs.

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ABBREVIATIONS

AHI: apnea hypopnea index **BRIEF:** Behavior Rating Inventory of Executive Function CAS-15: Clinical Assessment Score-15 CBC: Child Behavior Checklist CHAT: Childhood Adenotonsillectomy Trial CPAP: continuous positive airway pressure M-ESS: modified Epworth Sleepiness Scale NEPSY: Developmental Neuropsychological Assessment NR: not reported OSA: obstructive sleep apnea OSA-18: Obstructive Sleep Apnea-18 OSDB: obstructive sleep-disordered breathing PSG: polysomnography **PSQ:** Pediatric Sleep Questionnaire PedsQL: Pediatric Quality of Life Inventory RCT: randomized controlled trial The authors of this report are responsible for its content. Statements in the report should not be construed as endorsement by the Agency for Healthcare Research and Quality or the US Department of Health and Human Services.

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REFERENCES

- Boss EF, Marsteller JA, Simon AE. Outpatient tonsillectomy in children: demographic and geographic variation in the United States, 2006. *J Pediatr*. 2012;160(5):814–819
- Cullen KA, Hall MJ, Golosinskiy A. Ambulatory surgery in the United States, 2006. *Natl Health Stat Rep.* 2009;(11):1–25
- Beebe DW. Neurobehavioral morbidity associated with disordered breathing during sleep in children: a comprehensive review. *Sleep.* 2006;29(9):1115–1134
- Teo DT, Mitchell RB. Systematic review of effects of adenotonsillectomy on cardiovascular parameters in children with obstructive sleep apnea. *Otolaryngol Head Neck Surg.* 2013;148(1):21–28
- Walz PC, Schroeder JW Jr. Pediatric polysomnography for sleep-disordered breathing prior to tonsillectomy: a guideline review. *Pediatr Ann.* 2013;42(10):188–194
- Marcus CL, Rosen G, Ward SL, et al. Adherence to and effectiveness of positive airway pressure therapy in children with obstructive sleep apnea. *Pediatrics*. 2006;117(3). Available at: www.pediatrics.org/cgi/content/full/ 117/3/e442
- 7. Prashad PS, Marcus CL, Maggs J, et al. Investigating reasons for

CPAP adherence in adolescents: a qualitative approach. *J Clin Sleep Med.* 2013;9(12):1303–1313

- Ramirez A, Khirani S, Aloui S, et al. Continuous positive airway pressure and noninvasive ventilation adherence in children. *Sleep Med.* 2013;14(12):1290–1294
- 9. Jambhekar SK, Com G, Tang X, et al. Role of a respiratory therapist in improving adherence to positive airway pressure treatment in a pediatric sleep apnea clinic. *Respir Care*. 2013;58(12):2038–2044
- Beecroft J, Zanon S, Lukic D, Hanly P. Oral continuous positive airway pressure for sleep apnea: effectiveness, patient preference, and adherence. *Chest*. 2003;124(6):2200–2208
- Viswanathan M, Ansari MT, Berkman ND, et al. Assessing the risk of bias of individual studies in systematic reviews of health care interventions. In: *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*. Rockville, MD: US Department of Health and Human Services; 2008
- Berkman ND, Lohr KN, Ansari MT, et al. Grading the strength of a body of evidence when assessing health care interventions: an EPC update. *J Clin Epidemiol.* 2015;68(11):1312–1324

- Francis D0, Chinnadurai S, Sathe NA, et al. Tonsillectomy for Obstructive Sleep-Disordered Breathing or Recurrent Throat Infection in Children. Comparative Effectiveness Review No. 183. (Prepared by the Vanderbilt Evidence-based Practice Center under Contract No. 290-2015-00003-I.) AHRQ Publication No. 16-EHC042-EF. Rockville, MD: Agency for Healthcare Research and Quality; 2017.
- Dualibi AP, Pignatari SS, Weckx LL. Nutritional evaluation in surgical treatment of children with hypertrophic tonsils and or adenoids. *Int J Pediatr Otorhinolaryngol.* 2002;66(2):107–113
- Goldstein NA, Pugazhendhi V, Rao SM, et al. Clinical assessment of pediatric obstructive sleep apnea. *Pediatrics*. 2004;114(1):33–43
- Quante M, Wang R, Weng J, et al; Childhood Adenotonsillectomy Trial (CHAT). The effect of adenotonsillectomy for childhood sleep apnea on cardiometabolic measures. *Sleep*. 2015;38(9): 1395–1403
- 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

- Konstantinopoulou S, Gallagher P, Elden L, et al. Complications of adenotonsillectomy for obstructive sleep apnea in school-aged children. *Int J Pediatr Otorhinolaryngol.* 2015;79(2):240–245
- Weinstock TG, Rosen CL, Marcus CL, et al. Predictors of obstructive sleep apnea severity in adenotonsillectomy candidates. *Sleep.* 2014;37(2): 261–269
- Chervin RD, Ellenberg SS, Hou X, et al. Prognosis for spontaneous resolution of obstructive sleep apnea in children. *Chest.* 2015;148(5):1204–1213
- Garetz SL, Mitchell RB, Parker PD, et al. Quality of life and obstructive sleep apnea symptoms after pediatric adenotonsillectomy. *Pediatrics*. 2015;135(2). Available at: www. pediatrics.org/cgi/content/full/135/2/ e477
- Rosen CL, Wang R, Taylor HG, et al. Utility of symptoms to predict treatment outcomes in obstructive sleep apnea syndrome. *Pediatrics*. 2015;135(3). Available at: www. pediatrics.org/cgi/content/full/135/3/ e662
- Katz ES, Moore RH, Rosen CL, et al. Growth after adenotonsillectomy for obstructive sleep apnea: an RCT. *Pediatrics*. 2014;134(2):282–289

- Tarasiuk A, Simon T, Tal A, Reuveni H. Adenotonsillectomy in children with obstructive sleep apnea syndrome reduces health care utilization. *Pediatrics*. 2004;113(2):351–356
- Burstein DH, Jackson A, Weedon J, Graw-Panzer KD, Fahmy S, Goldstein NA. Adenotonsillectomy for sleep-disordered breathing in a predominantly obese pediatric population. *Int J Pediatr Otorhinolaryngol.* 2013;77 (4):525–529
- Fernandes AA, Alcântara TA, D'Avila DV, D'Avila JS. Study of weight and height development in children after adenotonsillectomy. *Rev Bras Otorrinolaringol (Engl Ed)*. 2008;74(3):391–394
- Ben-Israel N, Zigel Y, Tal A, Segev Y, Tarasiuk A. Adenotonsillectomy improves slow-wave activity in children with obstructive sleep apnoea. *Eur Respir J.* 2011;37(5):1144–1150
- Biggs SN, Vlahandonis A, Anderson V, et al. Long-term changes in neurocognition and behavior following treatment of sleep disordered breathing in school-aged children. *Sleep.* 2014;37(1):77–84
- Paruthi S, Rosen CL, Wang R, et al. End-tidal carbon dioxide measurement during pediatric polysomnography: signal quality, association with

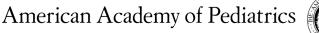
apnea severity, and prediction of neurobehavioral outcomes. *Sleep.* 2015;38(11):1719–1726

- Thong G, Davies K, Murphy E, Keogh I. Significant improvements in quality of life following paediatric tonsillectomy: a prospective cohort study [published online ahead of print January 18, 2016]. *Ir J Med Sci.* doi:10.1007/ s11845-016-1398-6
- Volsky PG, Woughter MA, Beydoun HA, Derkay CS, Baldassari CM. Adenotonsillectomy vs observation for management of mild obstructive sleep apnea in children. *Otolaryngol Head Neck Surg.* 2014;150(1): 126–132
- Trosman SJ, Eleff DJ, Krishna J, Anne S. Polysomnography results in pediatric patients with mild obstructive sleep apnea: adenotonsillectomy vs. watchful waiting. *Int J Pediatr Otorhinolaryngol.* 2016;83:25–30
- 33. Fox R, Temple M, Owens D, Short A, Tomkinson A. Does tonsillectomy lead to improved outcomes over and above the effect of time? A longitudinal study. *J Laryngol Otol.* 2008;122(11):1197–1200
- 34. Fox R, Tomkinson A, Myers P. Morbidity in patients waiting for tonsillectomy in Cardiff: a cross-sectional study. *J Laryngol Otol.* 2006;120(3):214–218

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