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## Long-term outcomes in obstructive sleep apnea

### Clinical Questions

- P (population/problem): In children with obstructive sleep apnea (OSA), who have been treated with adenotonsillectomy (T&A) or continuous positive airway pressure (CPAP)/bilevel positive airway pressure (BiPAP)
- O (outcome) what are the long-term quality of life outcomes, neurocognitive behavior outcomes and clinical outcomes?

**Target Population:** Children with OSA

### Recommendation

It is strongly recommended, for families of children with OSA, that long-term outcomes of treatment with surgery or continuous positive airway pressure be discussed.

#### Quality of life

For children 1 to 17 years of age with OSA, significant statistical improvement in the following parameters has been measured at least 6 months, and as long as 5 years, after T&A or with CPAP treatment:

- sleep disturbance
- sleep breathing and loudness of snoring
- excessive daytime sleepiness
- daytime problems
- physical suffering
- emotional distress
- speech and swallowing difficulties
- caregiver concerns

See Appendix 1 (*Constantin 2007 [4a], Diez-Montiel 2006 [4a], Mitchell 2004b [4a], Flanary 2003 [4a], Marcus 2006 [4b]*).

**Note:** These improvements were found regardless of instrument or inventory used to measure quality of life (*Constantin 2007 [4a], Diez-Montiel 2006 [4a], Mitchell 2004b [4a], Flanary 2003 [4a], Marcus 2006 [4b]*).

#### Neurocognitive behavior

For children 2 to 18 years of age with sleep disordered breathing (SDB) and/or OSA, significant statistical improvement in the following behavioral abnormalities has been measured at least 6 months, and as long as 18 months, after T&A:

- attention deficit
- aggression
- atypicality
- depression
- hyperactivity
- academic difficulties
- daytime sleepiness
- somatization
- behavioral symptoms index (BSI)
- externalizing and internalizing problems
- somnolence

See Appendix 2 (*Ebert 2004 [1b], Chervin 2006 [3a], Mitchell 2006 [4a], Friedman 2003 [4b]*).

**Note 1:** The significance of the improvement may not be seen until 6 to 12 months after surgery but improvement will be maintained at least 18 months (*Mitchell 2006 [4a]*).

**Note 2:** No studies evaluated long-term neurocognitive behavior outcomes in children after treatment with CPAP or BiPAP.

**Note 3:** First-grade children who demonstrated academic difficulties and presented with Sleep Associated Gas Exchange Abnormalities (SAGEA) had an T&A performed, showed significant improvement in their academic performance during the second grade (*Gozal 1998 [2a]*).

### Clinical Parameters

For children 2 to 16 years of age, with CPAP treatment for OSA or treatment with T&A for any reason, significantly statistical improvement in the following clinical parameters has been measured for at least 6 months, and for as long as 12 months:

- AHI
- respiratory parameters
- E/A Ratio, LV diastolic function
- serum IGFBP-3
- Sa<sub>O2</sub> nadir
- weight for height (increase was improvement)
- serum IGF-I
- BMI (increase was improvement)
- mean sleep latency

See Appendix 3 (*Gozal 2008 [2b], Chervin 2006 [3a], Amin 2005 [3b], Selimoglu 2003 [3b], Nieminen 2002 [3b], Marcus 2006 [4b], Stradling 1990 [4b]*).

Recurrence of SDB 12 months post-surgery with increased risk for elevated blood pressure occurs among a significant subset of children regardless of resolution of SDB at 6-weeks post-surgery (*Amin 2008 [3a]*).

**Note:** A prospective study of 40 children with SDB treated with T&A, compared with 30 healthy controls, demonstrated that:

- 50% of children experienced recurrence of SDB at 12 months regardless of 6-week post-surgery resolution rates,
- obesity, velocity of BMI increase, and being African American are independent contributors to recurrent SDB at 12 months post-surgery as demonstrated by multivariable logistic regression, and
- increased blood pressure compared to pre-surgery levels is associated with recurrent SDB 12 months post-surgery ( $P = 0.03$ )

(*Amin 2008 [3a]*).

## **Discussion/summary of evidence**

### Quality of Life

The quality of the evidence for long-term quality of life outcomes is moderate. The findings and areas of improvement were very consistent following treatment with T&A as listed above for all studies (*Constantin 2007 [4a], Diez-Montiel 2006 [4a], Mitchell 2004a [4a], Flanary 2003 [4a], Marcus 2006 [4b]*). One small, well done prospective trial supports treatment with CPAP and improves quality of life, decreases sleepiness, snoring and difficulty breathing at night (*Marcus 2006 [4b]*).

### Neurocognitive Behavior

There is a moderate quality of the body of evidence supporting neurocognitive improvements following T&A and treatment with CPAP. A meta-analysis of 17 studies showed a positive association of the effects of SDB and cognition and behavior (*Ebert 2004 [1b]*). Lower functioning school age children who receive a T&A to correct SAGEA demonstrate improved school grades the following academic year (*Gozal 1998 [2a]*). Following T&A there were improvements in neurocognitive outcomes, such as hyperactivity, attention deficit and neurocognitive performance, even though an array of different assessment tools were used to measure the outcomes in the studies (*Chervin 2006 [3a], Mitchell 2006 [4a], Friedman 2003 [4b]*).

### Clinical Parameters

The quality of the body of evidence for long-term clinical outcomes following T&A and treatment with CPAP is moderate with consistent findings showing improvements such as AHI, Sa<sub>O2</sub> nadir, mean sleep latency and respiratory parameters (*Chervin 2006 [3a], Nieminen 2002 [3b], Marcus 2006 [4b]*).

One small prospective cohort study showed the reversibility, over a 1 year period, of cardiac dysfunction improvement in left ventricle diastolic function with resolution of OSA in children after T&A (*Amin 2005 [3b]*). Multiple studies consistently show weight normalization whereas normalization in height was not consistently found (*Selimoglu 2003 [3b], Nieminen 2002 [3b], Stradling 1990 [4b]*).

## Health Benefits, Side Effects and Risks

In children with OSA about 80% experience successful resolution of their OSA with T&A; therefore, about 20% of children have persistent OSA after T&A (Brietzke 2006 [1b]). Known risk factors for persistent OSA include obesity, neuromuscular disorders, Trisomy 21, and other craniofacial syndromes (Brietzke 2006 [1b]).

CPAP is effective for treating OSA as demonstrated by improvements in AHI, with non-adherence being the main limitation of home treatment. About 75% of patients use the equipment long-term, though an undetermined proportion of these do so for a suboptimal number of hours of sleep (Marcus 2006 [4b]). Many patients and families complain of problems with the CPAP equipment and problems with the masks such as nasal symptoms and skin irritations (Massa 2002 [4a], Marcus 2006 [4b]). Inappropriate mask sizes can lead to reappearance of noisy mouth breathing, disrupted nocturnal sleep and irritable behavior (Guilleminault 1995 [3b], Massa 2002 [4a]). Upper airway infections may require interruption of nasal CPAP treatment for 3 to 4 days because of excessive nasal secretions (Guilleminault 1995 [3b]).

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Note: Full tables of evidence grading system available in separate document:

- Table of Evidence Levels of Individual Studies by Domain, Study Design, & Quality (abbreviated table below)
- Grading a Body of Evidence to Answer a Clinical Question
- Judging the Strength of a Recommendation (abbreviated table below)

**Table of Evidence Levels** (see note above)

<i>Quality level</i>	<i>Definition</i>
1a† or 1b†	Systematic review, meta-analysis, or meta-synthesis of multiple studies
2a or 2b	Best study design for domain
3a or 3b	Fair study design for domain
4a or 4b	Weak study design for domain
5	Other: General review, expert opinion, case report, consensus report, or guideline

†a = good quality study; b = lesser quality study

**Table of Recommendation Strength** (see note above)

<i>Strength</i>	<i>Definition</i>
“Strongly recommended”	There is consensus that benefits clearly outweigh risks and burdens (or visa-versa for negative recommendations).
“Recommended”	There is consensus that benefits are closely balanced with risks and burdens.
No recommendation made	There is lack of consensus to direct development of a recommendation.

**Dimensions:** In determining the strength of a recommendation, the development group makes a considered judgment in a consensus process that incorporates critically appraised evidence, clinical experience, and other dimensions as listed below.

1. Grade of the Body of Evidence (see note above)
2. Safety / Harm
3. Health benefit to patient (*direct benefit*)
4. Burden to patient of adherence to recommendation (*cost, hassle, discomfort, pain, motivation, ability to adhere, time*)
5. Cost-effectiveness to healthcare system (*balance of cost / savings of resources, staff time, and supplies based on published studies or onsite analysis*)
6. Directness (*the extent to which the body of evidence directly answers the clinical question [population/problem, intervention, comparison, outcome]*)
7. Impact on morbidity/mortality or quality of life

**Appendix 1: Quality of life outcome studies following T&A for OSA**

Study Citation	N	Age Range	Inclusion / diagnostic criteria for study participants	Assessment Tool	Outcome Improvement	Significance	Length of Follow up
(Marcus 2006 [4b])	29	2 to 16 years	PSG having at least one of the following: <ul style="list-style-type: none"> <li>AHI <math>\geq 5</math> events / hour</li> <li>Sa<sub>O2</sub> nadir <math>\leq 85\%</math></li> <li>peak end tidal P<sub>CO2</sub> <math>\geq 55</math> mm Hg</li> <li>Sa<sub>O2</sub> <math>&lt; 92\%</math> for 10% TST and end-tidal P<sub>CO2</sub> <math>\geq 50</math> mm Hg for <math>\geq 10\%</math> TST</li> </ul> Plus one of the following: <ul style="list-style-type: none"> <li>snoring and difficulty breathing during sleep</li> <li>failure to thrive</li> <li>pulmonary hypertension</li> <li>excessive daytime sleepiness</li> <li>symptoms of behavioral problems</li> </ul>	Standardized interview	<ul style="list-style-type: none"> <li>sleepiness</li> <li>snoring</li> <li>difficulty breathing at night</li> </ul>	P = 0.03 P < 0.0001 P < 0.0001	6 months
(Constantin 2007 [4a])	86	2 to 17 years	<ul style="list-style-type: none"> <li>more than one event per hour on MDAHI as measured by PSG*</li> </ul>	Conners' Parent Rating Scale-Revised (CPRS-R)	<ul style="list-style-type: none"> <li>daytime breathing</li> <li>sleep breathing</li> <li>loudness of snoring</li> <li>excessiveness of daytime sleepiness</li> </ul>	P < 0.001	3.5 years (42 months)
(Diez-Montiel 2006 [4a])	101	< 14 years	In the judgment of the attending physician all of the following are positive for OSA: <ul style="list-style-type: none"> <li>medical history</li> <li>physical examination findings</li> <li>x-ray, lateral neck</li> <li>2 or more nocturnal pulse oximetry desaturation readings of <math>&lt; 90\%</math></li> </ul>	OSD-6	<ul style="list-style-type: none"> <li>physical suffering</li> <li>sleep disturbance</li> <li>emotional distress</li> <li>caregiver concerns</li> <li>speech &amp; swallowing difficulties</li> <li>activity limitations</li> </ul>	P < 0.001	5 years (61.9 months)
(Mitchell 2004b [4a])	34	3 to 16 years	<ul style="list-style-type: none"> <li>otherwise healthy children</li> <li>RDI <math>&gt; 5</math> as measured by PSG</li> </ul>	OSA-18	<ul style="list-style-type: none"> <li>sleep disturbance</li> <li>physical suffering</li> <li>emotional distress</li> <li>daytime problems</li> <li>caregiver concerns</li> </ul>	P < 0.001	6 months
(Flanary 2003 [4a])	54	1 to 16 years	<ul style="list-style-type: none"> <li>tonsillar size +3 or greater (partially obstructive)</li> <li>history of loud snoring OR experienced a witnessed apnea</li> </ul>	OSA-18 CHQPF-28	<ul style="list-style-type: none"> <li>sleep disturbance</li> <li>physical suffering</li> <li>emotional distress</li> <li>daytime problems</li> <li>caregiver concerns</li> </ul>	P < 0.001	6 months to 12 months

\*this retrospective study included all patients evaluated for OSA; however, not all patients who were positive for OSA had surgery and not all patients who had surgery were positive for OSA

CHQPF-28 = Children's Health Questionnaire Parent Form-28; MDAHI = mixed obstructive apnea/hypopnea index; OSA = obstructive sleep apnea; OSA-18 = 18 item quality of life survey for OSA; OSD-6 = obstructive sleep disorders-6 survey; P<sub>CO2</sub> = partial pressure of carbon dioxide; PSG = polysomnography; RDI = respiratory distress index; Sa<sub>O2</sub> = arterial oxygen saturation; T&A = adenotonsillectomy; TST = total sleep time

**Appendix 2: Neurocognitive and behavioral outcome studies following T&A for OSA**

Study Citation	N	Age Range	Participant Criteria (severity of OSA)	Assessment Tool	Outcome Improvement	Significance	Length of Follow Up
(Ebert 2004 [1b])	17 studies	4 to 14 years			Positive association of the effects of SDB and cognition and behavior		
(Gozal 1998 [2a])	297	7 years	<ul style="list-style-type: none"> <li>• OSAS Questionnaire score of &gt; 5</li> <li>• SAGEA -                             <ul style="list-style-type: none"> <li>◦ More than 2 oxygen desaturation episodes per hour of recording</li> <li>◦ Sustained elevation of transcutaneous carbon dioxide tension of &gt; 8mm of Hg compared with waking values during initial electrode positioning and lasting &gt; 60 % of total recording</li> </ul> </li> <li>• SAGEA identified in 54 lower 10<sup>th</sup> %ile students</li> <li>• 24 underwent T&amp;A</li> </ul>	<ul style="list-style-type: none"> <li>• School Grades</li> </ul>	<ul style="list-style-type: none"> <li>• Overall second year grades increased significantly for those who received T&amp;A vs all other children with SAGEA.</li> </ul>	P < .001	1 year
(Chervin 2006 [3a])	105	5 to 12.9 years	<ul style="list-style-type: none"> <li>• Scheduled for a T&amp;A for any indication</li> </ul>	<ul style="list-style-type: none"> <li>• Conners' Parent Rating Scales-Revised</li> <li>• Child Symptom Inventory</li> <li>• Behavior Hyperactivity Index</li> </ul>	<ul style="list-style-type: none"> <li>• Hyperactive behavior</li> <li>• Attention deficit</li> </ul>	P < .001 P < .001	1 year
(Mitchell 2006 [4a])	23	2 to 18 years	<ul style="list-style-type: none"> <li>• Children referred with an AHI &gt; 5 by PSG.</li> </ul>	<ul style="list-style-type: none"> <li>• Behavioral Assessment System for Children (BASC)</li> </ul>	<ul style="list-style-type: none"> <li>• Most behavioral abnormalities in children with OSAS improve significantly</li> <li>• Improvements maintained long-term</li> </ul>	P < .05	18 months
(Friedman 2003 [4b])	27	5 to 9 year	Children who were otherwise healthy, candidates for T&A because of SDB	OSAS diagnosis based upon history of snoring, difficulty breathing during sleep & apnea witnessed in children with obvious hypertrophied adenoids & tonsils with a respiratory disturbance index (RDI) of at least 1 per hour from PSG. PSG was not performed if the clinical diagnosis of OSAS was obvious	Prior to T&A children with OSAS were significantly lower in K-ABC subsets (p < .02) Six to 10 months after T&A children with OSAS demonstrated significant improvement in neurocognitive performance: <ul style="list-style-type: none"> <li>• Gestalt Closure,</li> <li>• Triangle,</li> <li>• Word Order,</li> <li>• Matrix Analogies,</li> <li>• Sequential Processing Scale,</li> <li>• Simultaneous Processing Scale,</li> <li>• Mental Processing Composite</li> </ul>	P < .001 P < .02 P < .001 P < .02 P < .03 P < .001 P < .001	6 to 10 months

SAGEA = Sleep Associated Gas Exchange Abnormalities; K-ABC = Kaufman Assessment Battery for Children; BASC = Behavioral Assessment System for Children; SDB = sleep disordered breathing; T&A = adenotonsillectomy

**Appendix 3: Clinical outcome studies following T&A or CPAP treatment for OSA**

Study Citation	N	Age Range	Study Population	Inclusion / diagnostic criteria for study participants	Outcome	Significance	Length of Follow up
(Gozal 2008 [2b])	62	3 to 12 years	Prepubertal children evaluated for habitual snoring and diagnosed with moderate to severe OSA	AHI $\geq$ 2 events / hour using the 3-second rule and/or presence of movement arousal	<p><u>Improvements:</u> Non-obese patients</p> <ul style="list-style-type: none"> <li>• LDL</li> <li>• HDL</li> <li>• ApoB</li> <li>• CRP</li> </ul> <p>Obese patients</p> <ul style="list-style-type: none"> <li>• Insulin</li> <li>• TG</li> <li>• Total Chol</li> <li>• LDL</li> <li>• HDL</li> <li>• ApoB</li> <li>• CRP</li> </ul> <p><u>OSA resolution</u></p> <ul style="list-style-type: none"> <li>• Overall 38%</li> <li>• Obese (Ob) 24%</li> <li>• Non-obese (NOB) 60%</li> </ul>	<p>P &lt; 0.0001 P &lt; 0.0001 P &lt; 0.00001 P &lt; 0.0001</p> <p>P &lt; 0.001 P &lt; 0.01 P &lt; 0.01 P &lt; 0.01 P &lt; 0.01 P &lt; 0.001 P &lt; 0.001</p> <p>Between Ob and NOB: P &lt; 0.01</p>	6 to 12 months
(Chervin 2006 [3a])	78	5 to 12.9 years	Children scheduled for T&A for any reason	Not applicable	<p><u>Improvements:</u></p> <ul style="list-style-type: none"> <li>• AHI</li> <li>• mean sleep latency</li> </ul>	<p>P &lt; 0.001 P = 0.001</p>	1 year
(Amin 2008 [3a])	70	7 to 13 years	Children with nightly snoring and hypertrophy of the tonsils and adenoids, and age- and sex-matched healthy children without SDB	PSG: AHI > 1 event / hour	<p><u>Improvement:</u> AHI: all children from baseline</p> <p><u>Recurrence of SDB:</u> AHI: obese children from post-surgery AHI: children with high rate of BMI gain from post-surgery</p> <p><u>Recurrence of elevated BP:</u> associated with subset of children with recurrent SDB at 1 year post-surgery</p>	<p>NA NA NA NA</p>	1 year
(Amin 2005 [3b])	9	8 to 16 years	Otherwise healthy children referred for evaluation of OSA and treated with T&A	PSG: AHI > 1 event / hour	E/A ratio: <u>improvement</u> in LV diastolic function	P = 0.001	1 year
(Selimoglu 2003 [3b])	29	4 to 12 years	Children with obstructive ATH and treated with T&A	ATH score +3 ( $\geq$ 50% obstruction)	<p><u>Improvements:</u></p> <ul style="list-style-type: none"> <li>• weight SD*</li> <li>• height SD</li> <li>• serum IGF-I</li> </ul> <p>*increase was improvement</p>	<p>P &lt; 0.001 P &lt; 0.001 P &lt; 0.001</p>	6 months
(Nieminen 2002 [3b])	19	2.4 to 10.5 years	Children referred for evaluation of OSA and treated with T&A	PSG: AHI $\geq$ 1 event / hour	<p><u>Improvements:</u></p> <ul style="list-style-type: none"> <li>• respiratory parameters</li> <li>• weight for height*</li> <li>• BMI*</li> <li>• peripheral concentrations of IGF-I</li> <li>• peripheral concentrations of IGFBP-3</li> </ul> <p>*increase was improvement</p>	<p>P &lt; 0.001 P = 0.001 P = 0.01 P = 0.002 P &lt; 0.001</p>	6 months

Study Citation	N	Age Range	Study Population	Inclusion / diagnostic criteria for study participants	Outcome	Significance	Length of Follow up
(Marcus 2006 [4b])	29	2 to 16 years	Newly diagnosed children with OSA treated with CPAP or BiPAP	PSG having to meet at least one of the following: <ul style="list-style-type: none"> <li>• AHI <math>\geq</math>5 events / hour</li> <li>• Sa<sub>O2</sub> nadir <math>\leq</math>85%</li> <li>• peak end tidal P<sub>CO2</sub> <math>\geq</math> 55 mm Hg</li> <li>• Sa<sub>O2</sub> &lt; 92% for 10% TST and end-tidal P<sub>CO2</sub> <math>\geq</math> 50 mm Hg for <math>\geq</math> 10 % TST</li> </ul> Plus one of the following: <ul style="list-style-type: none"> <li>• snoring and difficulty breathing during sleep</li> <li>• failure to thrive</li> <li>• pulmonary hypertension</li> <li>• excessive daytime sleepiness</li> <li>• symptoms of behavioral problems</li> </ul>	Improvements: <ul style="list-style-type: none"> <li>• AHI</li> <li>• Sa<sub>O2</sub> nadir</li> </ul>	P = 0.003 P = 0.001	6 months
(Stradling 1990 [4b])	61	2 to 14 years	Children treated with T&A	Described by parents as snorers, recurrent tonsillitis	Improvements: <ul style="list-style-type: none"> <li>• height</li> <li>• weight*</li> <li>• resolution of sleep hypoxemia</li> </ul> *increase was improvement	P < 0.03 P < 0.001 P < 0.0001	6 months

AHI = apnea hypopnea index; ALTE = apparent life-threatening events; ApoB = serum apolipoprotein B; ATH = adenotonsillar hypertrophy; BiPAP = bilevel positive airway pressure; BMI = body mass index; BP = blood pressure; CPAP = continuous positive airway pressure; CRP = serum C-reactive protein; E/A ratio = a measure of left ventricular diastolic function and is the ratio of the velocity of the early wave occurring during early diastolic filling and the velocity of the second wave occurring during atrial contraction; HDL = serum high-density lipoprotein; IGF-I = insulin-like growth factor-I; IGFBP-3 = insulin-like growth factor-binding protein 3; LDL = serum low-density lipoprotein; LV = left ventricular; NA = not available; OSA = obstructive sleep apnea; P<sub>CO2</sub> = partial pressure of carbon dioxide; PSG = polysomnography; Sa<sub>O2</sub> = arterial oxygen saturation; SD = standard deviation; SDB = sleep disordered breathing; T&A = adenotonsillectomy; TG = serum triglycerides; Total chol = total serum cholesterol; TST = total sleep time



## Note

**This Best Evidence Statement addresses only key points of care for the target population; it is not intended to be a comprehensive practice guideline. These recommendations result from review of literature and practices current at the time of their formulation. This Best Evidence Statement does not preclude using care modalities proven efficacious in studies published subsequent to the current revision of this document. This document is not intended to impose standards of care preventing selective variances from the recommendations to meet the specific and unique requirements of individual patients. Adherence to this Statement is voluntary. The clinician in light of the individual circumstances presented by the patient must make the ultimate judgment regarding the priority of any specific procedure.**

**Reviewed by** Clinical Effectiveness