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AHA SCIENTIFIC STATEMENT

Sleep-Disordered Breathing and Cardiovascular Disease in Children and Adolescents

A Scientific Statement From the American Heart Association

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ABSTRACT: Obstructive sleep apnea (OSA) is a known risk factor for cardiovascular disease in adults. It is associated with incident systemic hypertension, arrhythmia, stroke, coronary artery disease, and heart failure. OSA is common in children and adolescents, but there has been less focus on OSA as a primary risk factor for cardiovascular disease in children and adolescents. This scientific statement summarizes what is known regarding the impact of sleep-disordered breathing and, in particular, OSA on the cardiovascular health of children and adolescents. This statement highlights what is known regarding the impact of OSA on the risk for hypertension, arrhythmia, abnormal ventricular morphology, impaired ventricular contractility, and elevated right heart pressure among children and adolescents. This scientific statement also summarizes current best practices for the diagnosis and evaluation of cardiovascular disease–related complications of OSA in children and adolescents with sleep apnea and highlights potential future research in the area of sleep-disordered breathing and cardiovascular health during childhood and adolescence.

Key Words: AHA Scientific Statements ■ arrhythmia ■ cardiovascular disease ■ left ventricular hypertrophy ■ obstructive sleep apnea ■ pediatric ■ sleep-disordered breathing ■ systemic hypertension

Obstructive sleep apnea (OSA) is associated with cardiovascular disease (CVD) in adults.[1-3] Cross-sectional and longitudinal studies have demonstrated a relationship between OSA and systemic hypertension, arrhythmia, coronary artery disease, stroke, and all-cause CVD-related morbidity and mortality.[1,4–10] Fewer studies have demonstrated a relationship between OSA and cardiovascular health among children and adolescents.[11] OSA results in disrupted sleep. Shorter sleep duration[12] has been linked to a greater odds of hypertension in some but not all studies,[11] and OSA as diagnosed via polysomnography testing has been associated with a greater prevalence of left ventricular hypertrophy (LVH) in children and adolescents.[13] Associations between OSA and CVD risk factors, such as hypertension, arrhythmia, ventricular remodeling, and right heart hypertension in children and adolescents deserve further attention and are the focus of this scientific statement. Associations between OSA and cognitive and behavioral disorders, such as attention deficit hyperactivity disorder, are beyond the scope of this statement and have been well described in other published reviews.[14-17] This statement briefly discusses approved treatments for OSA, as a detailed review of therapeutic options can be found elsewhere.[16,18]

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CLINICAL PRESENTATION OF SLEEP-DISORDERED BREATHING AND OSA: SYMPTOMS AND SIGNS IN CHILDREN AND ADOLESCENTS

Sleep-disordered breathing (SDB) is a spectrum of conditions that includes primary snoring, upper airway resistance syndrome, obstructive hypoventilation, and OSA (Figure 1).[19] The clinical presentation of OSA in children and adolescents can vary by age and includes symptoms and signs of upper airway obstruction. Habitual snoring (≥3 nights/wk), labored breathing during sleep, gasps/snorting noises, sleeping in a seated position or with the neck hyperextended, headaches on awakening, and daytime sleepiness may all be associated with the presence of OSA in children and adolescents.[16] In certain populations, these manifestations are not present, so maintenance of a high degree of clinical suspicion is recommended to detect OSA.[16,20] Reliance on physical examination findings, such as tonsillar size, may not correlate well with the degree of airway obstruction (Figure 2).[16,21] Other grading systems for assessing pharyngeal anatomy, such as the Mallampati score and the Friedman palate position, have also not been shown to correlate well with severity of airway obstruction.[16]

DIAGNOSTIC EVALUATION OF SDB AND OSA SYNDROME

Diagnosis

According to the American Academy of Otolaryngology–Head and Neck Surgery (AAO–HNS), polysomnography is the gold standard for diagnosing sleep-disordered breathing in children, including OSA.[23] Polysomnography is recommended before tonsillectomy in children with SDB who have conditions that increase their risk for complications of surgery, such as obesity, Down syndrome,[23,24] craniofacial abnormalities (eg, Pierre-Robin sequence and cleft palate),[23,25,26] neuromuscular disorders (eg, muscular dystrophy), sickle cell disease (SCD), or mucopolysaccharidoses.[23] Children with Down syndrome have adenotonsillar hypertrophy, midface and mandibular hypoplasia, relative macroglossia, glossoptosis, generalized muscular hypotonia, and obesity, increasing their risk for airway obstruction. Younger children with syndromes resulting in craniofacial malformations are at a particularly high risk for OSA.[27] Polysomnographic criteria for diagnosing OSA include (1) ≥1 obstructive events (obstructive or mixed apnea or obstructive hypopnea) per hour of sleep or (2) obstructive hypoventilation (eg, end-tidal CO_2 >50 mm Hg for >25% of the tested sleep time) coupled with snoring, paradoxical chest and abdominal wall movement, or flattening of the nasal airway waveform.[28] SDB includes primary snoring, upper airway resistance syndrome, obstructive hypoventilation, and OSA syndrome,[28] but, excluding primary snoring, OSA is the most common.[2]

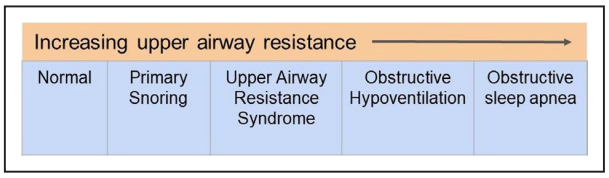

Figure 1. Sleep-disordered breathing.
Obstructive sleep apnea syndrome.[19] Adapted from Carroll.[19] Copyright 2003, with permission from Elsevier.

Childhood OSA, as in adults, is predominantly a rapid eye movement (REM)–related disease, with more frequent and longer apneas and greater desaturation during REM versus non-REM sleep.[29] Although REM sleep typically occurs during the latter portion of the sleep cycle and apnea is more common during REM sleep, apnea severity worsens over the course of the night, independent of REM sleep.[29] An important distinction between childhood OSA and adult OSA is that children with OSA syndrome demonstrate lower apnea-hypopnea index (AHI) compared with adult-OSA syndrome, despite similar severity in oxygen desaturation and clinical presentation.[30]

In adults, OSA has significant effects on sleep architecture.[31] Adults with severe OSA have a lower percentage of slow-wave sleep. They also have higher percentages of the lighter stages of sleep (N1 and N2). Overall, the arousal index and respiratory-related arousal index increase with higher OSA severity in adults.[31] This high arousal index is reflected in increased sleep fragmentation; increased sleep fragmentation is correlated with increases in sleepiness measures and decreases in measures of cognitive function. In contrast, children with OSA have been shown to have less cortical arousal after respiratory disturbances.[29,32,33] This higher arousal threshold in response to OSA in children and adolescents may result in less sleep fragmentation.[32]

The diagnosis of OSA is based on a combination of clinical and polysomnographic criteria. The evaluation of a child with suspected OSA begins with a thorough history and physical examination. OSA can cause both nighttime and daytime symptoms, and children and adolescents should be assessed for both. Physical examination includes an assessment of growth and detailed examination of the upper airway, including the nose and oropharynx for signs of adenotonsillar hypertrophy.[16]

History and physical examination, however, have low sensitivity and specificity for diagnosing OSA

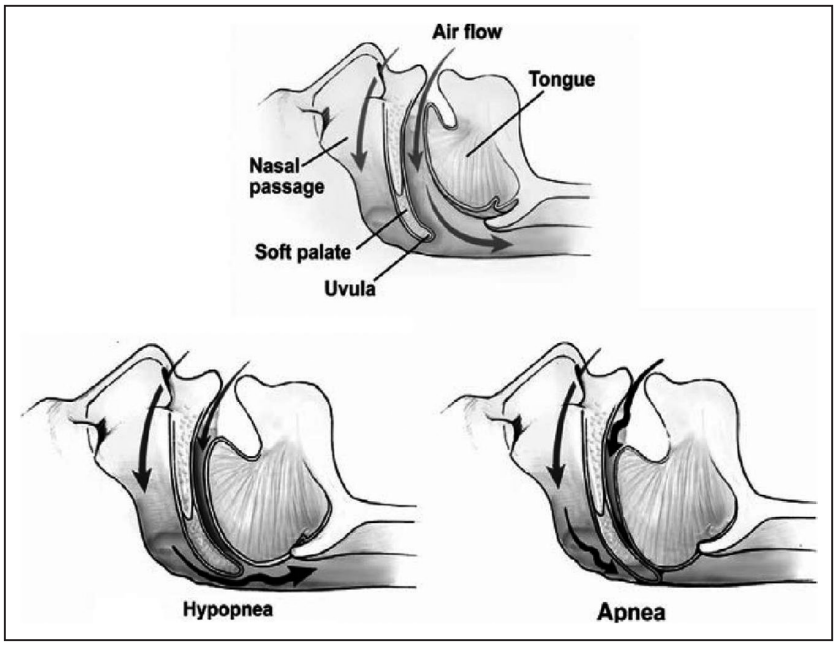

Figure 2. Partial and complete airway obstruction resulting in hypopnea and apnea, respectively.
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and cannot be used to reliably distinguish a primary snorer from one with OSA[18] or for making a diagnosis of OSA[23,34] or the severity of OSA.[35] Clinical assessment of tonsillar size (Brodsky score) is a weak predictor of the presence or severity of OSA.[16] Overnight polysomnographic testing is considered the gold standard for diagnosing OSA by the American Thoracic Society, the American Academy of Pediatrics (AAP),[18] and the American Academy of Sleep Medicine,[16,18] while the AAO–HNS recommends polysomnography only for suspected OSA in children with obesity, Down syndrome, craniofacial abnormalities, neuromuscular disorders, SCD, or mucopolysaccharidoses.[23] In children without these conditions and in whom the need for surgery is uncertain, or where there is discordance between the physical examination and the reported severity, the AAO–HNS also advocates for polysomnography before tonsillectomy. Studies have shown that a single-night polysomnography is adequate for diagnosis, as there is very little night-to-night variability.[36]

Metrics provided by polysomnography for the diagnosis of OSA include the AHI. The AHI is the number of apneas, hypopneas, and mixed apneas per hour of sleep (Table).[21,22] The respiratory disturbance index includes respiratory effort–related arousals in addition to the AHI. In pediatric laboratories that do not score respiratory effort–related arousals, the AHI is similar to the respiratory disturbance index. An AHI of >1 event/h is considered statistically abnormal in children.[28,34,36] Pediatric OSA can be categorized as mild (AHI of 1–4 events/h), moderate (5–9 events/h), or severe (≥10 events/h).[36] Other variables that are considered when attempting to classify OSA severity include gas exchange abnormalities and the degree of sleep fragmentation.

Severity assessment based on the polysomnogram enables the clinician to stratify surgical risk, predict morbidity, plan for postoperative management, and determine the likelihood of persistent disease. However, in areas where sleep laboratories with pediatric expertise are not available, alternative tests may need to be considered.[18] These alternative tests have weaker positive and negative predictive values when compared with polysomnography. They include daytime nap polysomnography, nocturnal oximetry, and nocturnal video recording.[18] However, polysomnography is currently the only test that can reliably distinguish primary snoring from OSA.[18] Home sleep apnea tests are now part of the clinical practice guideline for diagnosing OSA in adults,[38] but the use of home sleep apnea tests is not recommended for diagnosing OSA in children.[39] Because most home sleep apnea tests do not include end-tidal CO_2 and electroencephalographic monitoring, their use may lead to an underestimation of the presence and severity of OSA because of an inability to assess hypoventilation and arousals.

Additional measures used for diagnosing OSA in children and adolescents include questionnaires validated to assess signs and symptoms associated with OSA. These questionnaires are useful as screening but not as diagnostic tools and may be best suited for research purposes. An example is the Sleep-Related Breathing Disorder scale from the well-validated Pediatric Sleep Questionnaire.[40] The Sleep-Related Breathing Disorder

Table 1. Definition of Terms

Term	Definition
Apnea	Repetitive interruption of ventilation during sleep caused by collapse of the pharyngeal airway. Cessation of airflow >2 breaths in duration for children and adolescents and >10 s for adults
AHI	Frequency of apneas and hypopneas per hour of sleep; measure of OSA severity
Arousal	Abrupt change in EEG frequency lasting at least 3 s with at least 10 s of stable sleep preceding the change, with concurrent increase in chin EMG for at least 1 s during REM sleep
Hypopnea	Reduction in airflow signal amplitude of at least 30%, in the presence of chest/abdominal wall motion, associated with oxygen desaturation of hemoglobin ≥3% or with an arousal
Hypoventilation	P_{CO_2} >50 ppm
NREM sleep	NREM or quiet sleep
Obstructive hypoventilation	Gas exchange abnormalities without discrete obstructive apneas
OSA	Prolonged upper airway obstruction and intermittent complete obstructions leading to disruptions in normal ventilation during sleep
Polysomnography	Multichannel electrophysiologic recording that captures respiratory activity, EEG, EMG, and EOG recordings
Primary snoring	Snoring is a respiratory sound generated in the upper airway during sleep. Primary snoring is snoring that is not associated with apneas or gas exchange abnormalities.
REM sleep	REM or active sleep; associated with skeletal muscle atonia, rapid movements of the eyes, and dreaming
Sleep efficiency	Defined as the proportion of time spent asleep while in bed (or during recording time in a sleep study)
SDB	Defined by the degree of upper airway resistance, presence of sleep arousals, abnormalities in gas exchange, and apnea; includes primary snoring, upper airway resistance syndrome, obstructive hypoventilation, and OSA syndrome
Upper airway resistance syndrome	Increased upper airway resistance sufficient to degrade sleep quality; causes increased work of breathing leading to frequent arousals; no associated gas exchange abnormalities

AHI indicates apnea-hypopnea index; EEG, electroencephalographic; EMG, electromyogram/electromyographic; EOG, electrooculographic; NREM, nonrapid eye movement; OSA, obstructive sleep apnea; REM, rapid eye movement; and SDB, sleep-disordered breathing.

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scale has been shown to have a sensitivity of 81% and a specificity of 87% for polysomnography-defined OSA.[41] It is effective as a screen to identify children at high versus low risk for OSA.[42-46] Another validated questionnaire used in the evaluation of sleepiness, but not OSA, in children and adolescents is the Epworth Sleepiness Scale for Children and Adolescents (ESS-CHAD). The ESS-CHAD is a reliable and an internally valid measure of daytime sleepiness in adolescents 12 to 18 years of age.[47]

Children undergoing evaluation for OSA should also be screened for conditions that may reflect associated morbidity, including those affecting the cardiovascular system such as hypertension and metabolic syndrome (MetS).[48] An assessment of the central nervous system and screening for comorbid behavioral disorders is also recommended.[16]

Because snoring or other nonubiquitous OSA symptoms are often used to identify subjects eligible for pediatric polysomnography, underestimation of OSA prevalence may occur, especially if there is a failure to recognize symptoms of OSA by parents or if clinical signs are absent. Finally, complete laboratory-based polysomnography remains a resource-intensive procedure, and therefore the sample sizes of children studied with polysomnography are relatively small.[49] In conclusion, diagnosing OSA in children and adolescents requires a high index of suspicion and, although the diagnosis may be made on the basis of clinical findings, polysomnography is considered to be the gold standard by the American Thoracic Society, AAP, and American Academy of Sleep Medicine, and AAO–HNS. However, according to the AAO–HNS, the premise for the need for polysomnography before tonsillectomy and adenoidectomy in children 2 to 18 years of age is if the indication for surgery is SDB, and the child has conditions that increase risk for complications from surgery, such as obesity, Down syndrome, craniofacial abnormalities, neuromuscular disorders, SCD, or mucopolysaccharidoses.

Epidemiology

OSA is common among children and adolescents. It disrupts the normal restorative properties of sleep, thereby negatively impacting the emotional, metabolic, immunologic, and cardiovascular health of children and adolescents.[50] Approximately 1% to nearly 6% of all children and adolescents have OSA.[16,18]

The prevalence of OSA peaks between 2 and 8 years of age, corresponding to a peak prevalence of adenotonsillar hypertrophy.[20] Variations in estimated prevalence of OSA are likely attributable to differences in definition,[18] as well as differences in reliance on clinical versus polysomnographic criteria for diagnosing OSA. The criteria within studies used to define OSA vary and thus impact reported prevalence, as does the age of the children studied and their comorbid conditions.[16,18,49]

Risk Factors

There have been several pathophysiologic mechanisms proposed to explain the presence of OSA in

affected children and adolescents, including the size of the pediatric airway, which is dependent on craniofacial and soft tissue structures; increases in upper airway resistance, including narrowing/retropositioning of the maxilla/mandible; adenotonsillar hypertrophy; and the stability of the upper airway based on neuromuscular activation, arousal threshold, and ventilatory control.[51] A detailed description of the these various proposed pathophysiologic mechanisms is beyond the scope of this statement and can be found elsewhere.[51] Knowledge of the primary sites of anatomic obstruction in OSA facilitates a greater understanding of the potential risk factors for OSA in children and adolescents.

The primary sites of anatomic obstruction among persons with OSA are at the levels of the nasal, palatal, and hypopharyngeal airway. Persons with increased risk for collapse of the upper airway because of anatomic and neuromuscular disease are at particularly high risk. Thus, risk factors contributing to the presence of OSA in children and adolescents have been determined to be obesity, particularly among children <6 years of age, where younger age (<6 years) and body mass index (BMI) *Z*-score >1.036 is associated with a 6.5 times greater odds of OSA compared with older age and BMI *Z*-score >1.036[52]; upper and lower airway disease[53]; hypotonia; parental history of adenotonsillar hyperplasia[54]; craniofacial malformations[34]; neuromuscular disorders; and allergic rhinitis.[16,55] Because of the relationship between craniofacial malformations and OSA, the prevalence of OSA among children and adolescents with clinical syndromes such as Apert, Crouzon, and Pfeiffer syndrome is very high. It is estimated that OSA is prevalent in roughly 60% of children with Apert and Crouzon syndromes and in 46% of children with Pfeiffer syndrome.[56] Marked mandibular hypoplasia is a risk factor for airway obstruction as occurs in cases of Pierre Robin sequence (eg, triad of micrognathia, glossoptosis, and upper airway obstruction),[26] Treacher Collins,[57] Nager,[58] and Stickler syndromes.[58] The reported prevalence of OSA in children with Pierre Robin sequence is 46% to 85%, but advancing age in this group may result in improvements in the degree of OSA during the first year of life as the mandible grows, thus allowing for more conservative management.[26] OSA also occurs among 8.5% of youth with unrepaired and repaired cleft palate.[59] Approximately 14.7% of children with isolated cleft lip/palate have OSA. Children with cleft lip/palate have abnormal craniofacial structure and anatomic changes to the nose, nasopharynx, oropharynx, and palate that contribute to airway obstruction.[60] Neuromuscular disorders, including cerebral palsy, Duchenne muscular dystrophy,[61] and myotonic muscular dystrophy, are associated with poor muscle tone and consequent airway collapse contributing to the risk for OSA. All people with DMD will eventually develop SDB attributable to progressive decline in neuromuscular function.[62] Complex abnormalities such as achondroplasia and epilepsy have also been associated with OSA. People with achondroplasia have a reported prevalence of OSA of 20% to 32% that is thought to be at least partially related to the presence of midface hypoplasia.[63] It is unclear if seizures increase the risk for OSA or if OSA increases the risk for refractory seizures, but a relationship has been demonstrated.[64] Physical findings of overweight status, tonsillar hypertrophy, micrognathia, retrognathia, and high arched palate contribute to further airway narrowing and are associated with an increased risk for OSA.[18] Premature birth (<36 weeks' gestation) has also been identified as a risk factor for OSA. Children who were delivered preterm may be at increased risk for SDB, partly because of exposures within the perinatal environment influencing the development of respiratory control or upper airway size. However, the risk of apnea appears to decrease with increasing postgestational age.[65] Some studies, but not all, have identified male sex as a risk factor for OSA.[65]

There are limited data to support that children with congenital heart disease (CHD) may be at greater risk for SDB and OSA. A small (n=14) prospective case-control study estimated that SDB was prevalent in roughly 11 of the 14 infants with CHD. Investigators reported a higher AHI among infants with acyanotic and cyanotic CHD (2.4 and 2.5, respectively) versus among infants without CHD (AHI, 0.7).[66] A small, uncontrolled, observation study of 15 infants with single-ventricle physiology found that 14 of the 15 had an AHI >1/h.[67] A larger, retrospective study of 461 778 children with CHD included in the administrative Kids' Inpatient Database between 1997 and 2012 found that 4839 had SDB, with 14% meeting criteria for OSA. However, only central apnea (4% of the infants) and not OSA was associated with increased mortality, while OSA and central apnea were associated with longer hospital stay and increased total charges when compared with infants without SDB.[68]

Social constructs (eg, race) and economic factors may be associated with both the prevalence of OSA and access to care.[69] Black American race has been reported as a risk factor for OSA (odds ratio [OR], 5.0; 95% CI, 1.8–14.0).[53,65] According to data from the Cleveland Children's Sleep and Health Study that categorized the sleep, breathing, and general health of 907 children 8 to 11 years of age using questionnaires and in-home overnight sleep study data, Black American race, even when adjusting for preterm birth (<36 weeks) and BMI, was shown to be a significant risk factor for OSA (OR, 4.9; 95% CI, 1.7–17.8),[65] but mechanisms mediating this relationship require further determination,[70] as degree of adenotonsillar

hypertrophy and socioeconomic factors may be potential confounders.[71] In fact, a cross-sectional study by Wang et al[72] found that the relationship between Black American race and OSA prevalence and severity in children is no longer significant after controlling for neighborhood socioeconomic variables such as poverty rate and percentage of single-female–headed households. These results highlight that neighborhood socioeconomic factors likely explain perceived racial differences in OSA prevalence and severity among children. Historically, studies have been insufficiently powered to determine whether other races are at greater risk for OSA.[65] The impact of potential confounders such as daily stressors, racial/social inequality and racism, housing inequities, environmental pollutants, and sleep duration on reported prevalence among this population have yet to be determined and deserves further attention.[70] It is difficult to make wide assumptions regarding the relationship between race or ethnicity and sleep quality; further data are needed to verify and explain this reported relationship. Furthermore, differences in treatment strategy deserve further attention as it has been shown that Black American children are less likely to undergo adenotonsillectomy independent of socioeconomic status.[69]

Children and adolescents with allergic rhinitis are at risk for airway obstruction, particularly youth with allergic rhinitis and adenotonsillar hypertrophy.[73] Allergic rhinitis is common, affecting roughly 10% to 40% of all persons.[73] Adenotonsillar hypertrophy is present in largely 90% of children and adolescents with allergic rhinitis, contributing to the relationship between allergic rhinitis and OSA.[73] Inflammatory factors and chemical mediators released in children and adolescents with allergic rhinitis may play an important role, contributing to the presence of OSA. A recent meta-analysis of data from 44 studies from across the world assessed the relationship between allergic rhinitis and OSA. The mean age of children studied was 7.7±3 years. Among children, the prevalence of OSA was 45.2%.[73] Perioperative administration of albuterol in a randomized clinical controlled trial among children and adolescents at the time of adenotonsillectomy has been shown to reduce rates of airway obstruction, decrease airway inflammation, and lead to more favorable outcome at the time of tonsillectomy.[74]

Finally, SCD is a reported risk factor for OSA.[23] In fact, it has been reported that SCD is an independent risk factor for OSA with a reported prevalence that is higher than that among Black American children without SCD.[75]

Risk factors for OSA may vary with age.[76] Forty-nine percent of 5- to 9-year-old candidates for tonsillectomy who were randomly assigned to no intervention had resolution of polysomnographic evidence of OSA beginning at 7 months after diagnosis.[77] A single longitudinal study found that the only risk factor for OSA that persisted from middle childhood (8–11 years of age) into adolescence (16–19 years of age) was obesity.[76] Habitual snoring, living in an underresourced neighborhood, premature birth, obesity, and Black American race were risk factors for OSA between 8 and 11 years of age, but only obesity was associated with a greater incidence of OSA in middle childhood and in adolescence. Other risk factors for OSA by cross-sectional analysis in youth (16–19 years of age), when adjusted for obesity status, included male sex (adjusted OR, 10.63; 95% CI, 2.45–46.16), history of tonsillectomy (adjusted OR, 3.37; 95% CI, 1.18–9.62) or adenoidectomy (adjusted OR, 4.81; 95% CI, 1.96–11.85) and obesity in middle childhood.[76]

Data suggest that although it is important to be aware of risk factors for OSA in childhood, obesity is the main risk factor, and families and health care professionals should be counseled regarding this relationship.

As in adults, the presence of increased inflammation, among children with obesity, may explain the relationship between obesity and OSA.[78] An initial cross-sectional analysis of data from the Penn State Child Cohort study revealed that increases in inflammatory markers (eg, elevated C-reactive protein) mediate an association between visceral adiposity and OSA in adolescents.[79] A follow-up longitudinal study evaluating the relationship between serum C-reactive protein and OSA in children suggests that among obese male children, elevations in serum C-reactive protein precede the development of OSA.[80] However, even among youth without obesity, management of inflammation (eg, initiation of steroid, leukotriene inhibitors) may help to alleviate the severity of symptoms of OSA by reducing inflammation.[81] Adenotonsillectomy has also been shown to reduce levels of inflammation in children treated for OSA.[82]

CARDIOVASCULAR COMPLICATIONS OF SDB AND OSA

Inadequate sleep duration of <5 hours per night in children and adolescents has been linked to an increased risk of hypertension and is also associated with an increased prevalence of obesity.[50,83] Mild degrees of OSA (eg, AHI as low as 2 events/h) have been associated with unfavorable changes in the cardiometabolic health of youth.[84] Given that ≈30% to 60% of obese youth have OSA[84] and obesity is associated with hypertension in youth,[85] the question of whether OSA alone versus the comorbidity of obesity drives elevations in blood pressure (BP)

among children and adolescents with OSA remains to be determined.[83] Children with OSA are at greater risk for autonomic dysfunction, endothelial dysfunction, and ventricular remodeling.[46,86,87,88] OSA during childhood has also recently been shown to be an independent predictor of hypertension during adulthood.[89] However, 2 meta-analyses and a series of studies have reported opposing conclusions regarding the impact of OSA on BP.[90,91] Nevertheless, it is important to consider the potential role of OSA on risk for hypertension in children, given that hypertension is a primary risk factor for CVD that tracks from childhood into adulthood.[92,93]

OSA and Systemic Hypertension in Children and Adolescents

Hypertension is independently associated with SDB among adults in a dose-dependent manner with estimated OR of 2.89 (95% CI, 1.46–5.64) among adults with severe OSA (eg, AHI ≥15.0 events/h) according to in-office manual BP assessments.[94] However, given that OSA-associated hypertension is largely nocturnal, ambulatory BP monitoring may be a more accurate modality for diagnosing hypertension among adults with OSA.[95]

Among children and adolescents, a potential relationship between hypertension and OSA was first reported in 1976.[96] The relationship between BP and OSA is complex, regulated by activation of peripheral (eg, located within the carotid body) and central chemoreceptors (eg, located within the ventrolateral medullary surface of the brain stem) in response to hypoxia and increased CO_2 retention.[97] In response to the hypoxia and hypercapnia that occur secondary to airway obstruction, there is an increase in sympathetic nerve activation.[97] Hypoxia also stimulates the peripheral chemoreceptors, resulting in systemic vasoconstriction.[98] The result is elevation in systemic BP during episodes of apnea.[99] BP is also influenced by autonomic variability in children and adolescents. It has been proposed that the early stages of abnormal BP control may present with autonomic dysfunction in the form of increased sympathetic activity and decreased vagal tone, a change that is more likely to occur as children age.[100] Increased sympathetic activity during periods of apnea may contribute to the development of hypertension among children with OSA, but correlation between AHI and measured serum catecholamine levels is weak: noradrenaline: AHI r=0.36; adrenaline: AHI r=0.31.[101] In a large community sample, (eg, TuCASA [Tucson Children's Assessment of Sleep Apnea] study), elevations in systolic blood pressure (SBP) among children and adolescents with OSA were considered to be secondary to increased sympathetic vascular reactivity.[87,88,102]

Obesity and Systemic Hypertension in Children and Adolescents With OSA

It has been proposed that obesity, a condition known to be associated with higher BP, may explain the relationship between OSA and hypertension,[72,102,103] especially given the rising prevalence of childhood obesity.[83] Longitudinal studies, including data from the TuCASA study, suggest that independent of age or ethnicity (Hispanic compared with White), decreased sleep time and increased obesity are associated with increased BP among children 6 to 13 years of age.[12] The effects of OSA severity on BP may also be age dependent. Younger children 10 to 11 years of age with more severe OSA may have BP dysregulation, while older children develop higher sustained elevation in BP.[104] It is possible that obesity is a confounder for daytime elevations in BP that can be determined via in-office BP measurement, while nocturnal hypertension is less dependent on obesity status and more dependent on OSA severity.

Systemic Hypertension: Ambulatory BP Assessment

An AHI ≥5 events/h has been shown to be an independent risk factor for elevated SBP and diastolic blood pressure (DBP), even after adjusting for confounding factors such as increased BMI.[105] In a study by Li et al, among children 6 to 13 years of age, OSA was associated with nocturnal hypertension with an OR of 5.0 (95% CI, 2.0–12.7) for sleep SBP and an OR of 3.5 (95% CI, 1.5–8.1) for sleep DBP, respectively, compared with healthy controls.[106] In this same study and in a study published by Amin et al, however, there was no significant identified correlation between elevated daytime BP and OSA in children once analyses were adjusted for BMI.[104,106] Amin et al found that although there was greater BP variability, daytime BP was not higher.[104] In a separate cohort study of 96 children with reported snoring and high AHI (AHI >5 events/h) versus low AHI (AHI ≤5 events/h), BP recordings using ambulatory BP monitoring devices found that children with high AHI had higher wake SBP, sleep SBP, and sleep DBP. Children with higher wake SBP were more likely to be obese, while high sleep SBP and DBP were independent of obesity status. Increased oxygen desaturation index was a major contributor to the development of elevated sleep DBP.[72]

A normal response in BP during sleep is for the BP to drop by >10%, known as "nocturnal dipping." Children and adolescents with OSA have a limited (<10%) dip in BP while asleep (eg, less nocturnal dipping), consistent with abnormal BP regulation.[104] Children and adolescents with more severe OSA, as defined by an AHI >5 events/h, compared with children and adolescents with primary snoring, have less nocturnal SBP

dipping. Nocturnal dipping was 7.6% among children and adolescents with AHI >5 events/h versus 11.5% among children and adolescents with primary snoring (P<0.01).[105]

Manual and In-Office BP Assessment

According to data from the TuCASA study, elevated daytime SBP is associated with OSA (OR, 4.57; 95% CI, 1.21–17.3), while elevation in DBP is associated both with OSA (OR, 4.75; 95% CI, 1.22–18.5) and with obesity (OR, 4.57; 95% CI, 1.36–15.4).[102] In a study of 23 children and adolescents with adenotonsillar hyperplasia, SBP and DBP during REM sleep tended to correlate with AHI[107] such that higher SBP and DBP was associated with higher AHI. Elevations in daytime SBP and DBP among children with OSA may be dependent on obesity status.[102]

Despite observational and cohort study data, a large meta-analysis did not identify a relationship between SBP, DBP, and OSA in children and adolescents,[91] likely attributable to study heterogeneity. However, an updated meta-analysis revealed that OSA was associated with 3-to-1 greater odds of hypertension in children.[90] Additional studies demonstrate that the more severe the OSA, the more likely a child is to have high BP.[108]

Among normal-weight children, a relationship between OSA severity and SBP has also been observed. Normal-weight children and adolescents with AHI >5 events/h, have been shown to have higher BP compared with children and adolescents with an AHI of ≤1 event/h.[108] Similarly, among normal-weight children, there is an observed increase in sleeping SBP at baseline by OSA severity.[109] In conclusion, children with OSA appear to have higher BP than controls during both sleep and wake times, and BP levels increase with increasing severity of OSA.[106]

Cardiomyopathy and LVH

OSA is a major contributor to increased morbidity and mortality associated with CVD. The relationship between OSA and increased CVD risk is likely secondary to the proposed impact of OSA on ventricular mass.[110,111] Pathologic increase in left ventricular (LV) mass (eg, LVH) has been shown to be an independent risk factor for CVD that develops not only in response to the presence of comorbidities such as obesity and hypertension, but that may occur secondary to hypoxia, myocardial injury, and impaired nocturnal dipping (eg, normal decrease in BP while sleeping), occurring among persons with OSA, independent of hypertension. A cross-sectional study[112] evaluating the effect of OSA on LV mass in overweight/obese adolescents determined that children with OSA are more likely to have LVH (85.7% versus 59.4%; P=0.047). Furthermore, this same study determined that OSA was associated with 4 times greater odds of LVH (95% CI, 1.15–14.65; P=0.030) even after adjusting for age, sex, race, and BMI z-score. The odds of LVH among adolescents with severe OSA (AHI >10 events/h) were even greater. The described study demonstrated a 14:1 greater odds of LVH among youth with more severe OSA (95% CI, 1.14–172.64; P=0.039).[112] Amin et al[13] reported a similar result, finding that OSA was associated with at least an 11-fold increase in the risk for LVH in children (P<0.05), an association that was not demonstrated among children and adolescents with only primary snoring.

Among children and adolescents with known cardiomyopathy, OSA may result in worse cardiovascular-related outcome. In a prospective study of children and adolescents with cardiomyopathy, more than half of the children snored, and 48% had OSA. This study found that the median LV end diastolic volume index was significantly higher in children with OSA than in children without OSA (72.4 versus 54.0 mL/m^2; P=0.03).[113]

Right ventricular dimensions may also be negatively impacted by the presence of OSA. An AHI of >10 events/h is significantly associated with right ventricular (RV) dimension above the 95th percentile (OR, 6.7; 95% CI, 1.4–32; P<0.05).[13] Decreased RV systolic function, as measured by echocardiogram, has been reported among persons with OSA,[114,115] especially in the presence of complex disorders such as Down syndrome, Duchenne muscular dystrophy, and mucopolysaccharidoses.[16,116,117]

Treatment of OSA may result in improved LV wall thickness[118] and RV and LV systolic function.[114] Small cohort studies have demonstrated improved LV function and RV function in children and adolescents with moderate to severe OSA after adenotonsillectomy.[114,119] However, more research is needed to better elucidate the relationships between OSA and RV and LV structure, size, and function, as not all studies have consistently demonstrated a relationship between OSA and cardiac remodeling.[120]

Arrhythmia and OSA

In adults, OSA is associated with arrhythmia in at least 50% of patients.[21] Arrhythmias including atrial tachyarrhythmias (eg, atrial fibrillation),[121] ventricular tachyarrhythmias, bradyarrhythmias, prolongation of the QT interval,[122] and sudden cardiac arrest have been reported.[2,21,123] Adults with OSA are at particularly high risk for nocturnal arrhythmia according to

data from the DREAM (Determining Risk of Vascular Events by Apnea Monitoring) study. Even after adjusting for increased BMI, sex, and additional CVD risk factors (eg, angina, coronary artery disease, myocardial infarction, congestive heart failure, pacemaker, and history of coronary artery bypass grafting), the risk of nocturnal arrhythmia among people with OSA increased by 10% for every 10-unit increase in AHI (OR, 1.10; 95% CI, 1.04–1.15; *P*=0.0005).[124] Ventricular arrhythmias are more likely to occur during periods of apnea, but the mechanism mediating this response is uncertain.[21] The risk for bradycardia is thought to be attributable to the dive reflex that occurs after prolonged apnea and hypoxia.[21] Atrioventricular block and asystole have also been reported. Treatment of bradyarrhythmias under these circumstances includes treatment of OSA.[21]

OSA in adults has also been associated with poor response to antiarrhythmic medication use.[125] P-wave dispersion, the difference between maximum and minimum P-wave duration, as measured by ECG, is increased among adults with more severe OSA,[126] where P-wave dispersion reflects prolongation of intra- and interatrial conduction times in the remodeled atrium prone to atrial arrhythmia, including atrial fibrillation.[127,128] Among children and adolescents, there has been very little published regarding the relationship between OSA and arrhythmia. It has been proposed that hypoxemia, hypercapnia, changes in intrathoracic pressure, arousal, and sleep deprivation associated with OSA result in sympathetic activation, left atrial enlargement, and systemic inflammation, leading to an increased risk for arrhythmia.[123] QT dispersion may also be a precursor of ventricular arrhythmia among people with OSA.[129] In a study of 44 children 1 to 12 years of age with OSA, P-wave dispersion was most pronounced among youth with more severe OSA versus mild OSA or unaffected controls.[130] Higher QT dispersion, defined as the difference between the maximum and minimum QT interval, has also been associated with increased risk for ventricular arrhythmia and has been reported among children with more severe OSA.[129] Autonomic regulation of heart rate may be affected by OSA, such that higher heart rate variability has been investigated as a potential marker of more severe OSA. A small retrospective cohort of children with OSA (1993–1995) identified enhanced beat-to-beat (R-to-R) interval variation at lower heart rates and reduced variation at higher heart rates.[131,132] More recent studies have demonstrated that heart rate variability among youth with OSA may not vary with polysomnography-defined OSA severity.[133]

Obesity and MetS

Seventeen percent of children and adolescents have obesity, while 2% to 6% have severe obesity.[134,135] Numerous studies have demonstrated a linear relationship between sleep duration and BMI. A recently published meta-analysis has shown that for each fewer hour of sleep, the risk of overweight/obesity increases[136] and that children with shorter-than-recommended sleep duration have a 1.58 pooled odds for overweight/obesity (pooled OR, 1.58; 95% CI, 1.26–198, *P*<0.05) while children with shortest sleep duration have a 1.92 pooled odds for overweight/obesity.[137] OSA has also been associated with impaired glucose homeostasis.[107]

OSA severity may be improved with multidisciplinary weight reduction intervention.[138] Increased sleep duration may facilitate weight loss via increases in serum leptin levels (a hormone predominantly made by adipose cells and enterocytes in the small intestine that helps to regulate energy balance by inhibiting hunger).[139]

MetS is a strong risk factor for CVD and is associated with higher serum insulin levels, triglyceride levels, elevated BP, and lower high-density lipoprotein cholesterol levels. Severely obese children and adolescents are not only at risk for MetS, but have elevated AHI levels, lower nadir Sao_2, and other markers of more severe OSA.[84] The association between MetS and OSA in children is not limited to children with severe OSA, but MetS is also present in children with mild OSA (AHI ≥2 events/h). Evidence to support a relationship between MetS and OSA in children and adolescents is further compounded by findings that continuous positive airway pressure (CPAP), a treatment for OSA, appears to result in significant lowering of the serum triglyceride and low-density lipoprotein cholesterol levels and in improved high-density lipoprotein cholesterol levels.[140] Greater desaturation time (time during sleep when O_2 saturations are <90%) is associated with higher glycated hemoglobin values, even if these values are within the normal range.[107] Finally, OSA negatively impacts glycemic control in children with diabetes mellitus, just as it does in adults.[141] Treatment of OSA with adenotonsillectomy may lead to improved markers of MetS in youth, including insulin resistance, fasting glucose, serum triglyceride, and high-density lipoprotein cholesterol in the short term.[142] There may be no immediate change in inflammatory (C-reactive protein, circulating intercellular adhesion molecule-1) and metabolic marker (eg, insulin level) levels or in BP.[142] Obesity status may be the primary mediator of the relationship between OSA and insulin resistance.[48]

PULMONARY HYPERTENSION, COR PULMONALE, AND SDB

Hypoxia is an important influencer of pulmonary vasomotor tone and is a potent pulmonary vasoconstrictor. A relationship between hypertrophied tonsils and adenoids, upper airway obstruction causing hypoxia, pulmonary hypertension, and cor pulmonale was first proposed in 1965.[143,144] Current pediatric pulmonary hypertension guidelines recommend that if primary causes of pulmonary hypertension, such as lung disease and CHD, are ruled out, children and adolescents should undergo a sleep study.[145]

However, additional evidence suggests that the presence of pulmonary hypertension and the development of cor pulmonale may be less common in children and adolescents with OSA and, if present, secondary to other comorbid conditions.[16,146] A retrospective study of 2020 pediatric patients diagnosed with OSA in the San Antonio Military Health System found that the prevalence of pulmonary hypertension was low among children and adolescents with OSA (eg, 1.8%). This study also found that none of the patients with pulmonary hypertension had severe OSA and that all of the children with pulmonary hypertension had comorbid cardiac conditions.[146]

However, if a child develops sleep-dependent airway obstruction, early recognition and appropriate treatment with improved respiratory control leads to improved ventilation and elimination of asphyxia during sleep and thus a lower risk for pulmonary hypertension and cor pulmonale.[116] The presence of cor pulmonale once developed can be reversed by surgical removal of obstructing airway tissue.[117] In conclusion, although the deleterious effects of recurrent upper airway obstruction on pulmonary circulation may be physiologically intuitive, only a small number of studies have reported an association between OSA and pulmonary hypertension in children and adolescents.[16,115,147] The presence of pulmonary hypertension among children and adolescents with OSA may be more related to the severity and duration of hypoxia, the presence of hypercapnia, and the presence of acidosis rather than the absolute presence of airway obstruction leading to direct pulmonary vasoconstriction.[116,117] Additional studies are necessary to improve our understanding of how pulmonary circulatory pressures may be impacted by upper airway obstruction and whether there truly exists a causal link between OSA and pulmonary hypertension among children and adolescents. However, the greater risk is that of CVD and MetS among children with OSA.

TREATMENT AND OUTCOMES: INADEQUATE SLEEP DURATION, SDB, AND OSA

A detailed description of the treatment of OSA in youth is beyond the scope of this scientific statement, and at present there are no universally accepted criteria for initiation of treatment. Options for treatment of inadequate sleep duration, poor sleep efficiency, and OSA include behavioral, medical, and surgical intervention. Later school start times can improve sleep duration in adolescents,[148] and the AAP recommends that middle and high schools start after 8:30 AM.[149] Whether later school start times will result in improved cardiometabolic health in children is an area for future study.

Sleep habits that improve sleep quality and duration include consistent bedtime and wake times. Consistent and earlier bedtimes among younger children lead to decreased sleep onset latency and increased sleep duration, in both longitudinal and interventional studies.[150] Several small randomized controlled trials have shown that it is possible to improve sleep routines and sleep duration in children[151-153] and in adolescents[139,154,155,156] using educational interventions, phone- or text-based coaching, the provision of beds and bedding if children and adolescents lack adequate bedding. Two randomized controlled trials demonstrated that not only are such interventions associated with improved sleep hygiene but have also been associated with reductions in adiposity.[139,152] No randomized trials to date, however, have assessed the impact of such therapies on cardiovascular risk factors other than adiposity.

Over the past decade, treatment of OSA has been formalized with the recommendations encapsulated within the clinical guidelines of 3 societies: the AAP, the American Academy of Sleep Medicine, and the AAO–HNS.[18,38,50] The AAP, American Academy of Sleep Medicine, and AAO–HNS generally agree on adenotonsillectomy as the first line of treatment of upper airway obstruction, with multiple studies indicating relief of upper airway obstruction as measured by polysomnography as well as symptoms.[18] Watchful waiting is also suggested as a potential option for children with mild disease. The only randomized controlled trial comparing early adenotonsillectomy to watchful waiting in children 5 to 10 years of age, the CHAT (Childhood Adenotonsillectomy Trial), study found that surgery is superior in the domains of behavioral, quality-of-life, and symptom score outcomes.[77]

Today, symptoms of OSA are the principal indication for almost 500 000 children undergoing adenotonsillectomy in the United States. Otolaryngologists perform the procedure commonly in outpatient settings, and a recovery period of a few days is anticipated. The

most common serious complication related to the procedure is bleeding, which may occur immediately or in a delayed fashion in up to 5% of all children. The severity of OSA may predict the incidence of perioperative respiratory adverse events, which could be minimized by the administration of preoperative albuterol and the appropriate titration of perioperative anesthetic protocols.[157]

For children who are not candidates for adenotonsillectomy, CPAP therapy has been used and has been shown to be effective,[77] but adherence to recommended use remains a major barrier. For children, milder forms of OSA are usually not treated. The mechanism of CPAP-related benefit is related to the elimination of obstructive events by pneumatic stenting of the airway. Although CPAP has been shown to be efficacious and well tolerated in other studies, the principal limitation associated with its use has been compliance. Hawkins et al[158] showed that continuous adherence to CPAP therapy is suboptimal, although female sex and developmental delay are associated with better adherence. Although behavioral interventions may promote adherence, future investigations should focus on other pathways that could potentially improve adherence.

In children with persistent symptoms after adenotonsillectomy or when CPAP is considered as primary modality of treatment, surgical procedures to improve the upper airway may be of benefit. Investigations should focus on identification of the site of obstruction. A simple nasal examination aided by nasal endoscopy may identify a deviated septum, the correction of which may improve nasal airflow and facilitate better use of CPAP masks. Assessment of craniofacial anatomy may also provide surgical options such as distraction osteogenesis for mandibular retrognathia and maxillomandibular advancement to improve the airway at the level of the palate and tongue. Lingual tonsillectomy, tongue base reduction, and laryngeal procedures such as supraglottoplasty address anatomic obstruction at the level of the tongue base and the larynx. In children in whom the severity of obstruction has progressed to cardiopulmonary complications, or when other forms of treatment have failed, a tracheostomy may provide benefit.

Impact of Treatment of OSA on Cardiovascular Health

Adenotonsillectomy is highly effective from a procedural perspective; however, there is currently limited high-quality evidence of an improved cardiovascular profile after adenotonsillectomy.[114,142,159,160,161] Cardiovascular parameters improved by adenotonsillectomy include improvements in ventricular function,[114] BP,[160] and pulmonary artery pressure.[161] In a systematic review,[161] the majority of the 14 articles included in the study reported an improvement in cardiovascular parameters and OSA symptoms after surgery. The authors showed that 3 studies reported improvement in BP, 6 reported improvement in mean pulmonary artery pressure, 7 reported improvement in echocardiographic findings, and 1 reported a decrease in pulse rate and pulse rate variability after adenotonsillectomy. After adenotonsillectomy, 44 youth who underwent repeat polysomnography were found to have significantly lower overall DBP load (proportion of elevated readings) despite a significant increase in BMI.[162] However, adenotonsillectomy may have very little impact on ambulatory BP control in children and adolescents 4 to 16 years of age with OSA who have normal preoperative BP.[162-164] Obese children and adolescents may also be less likely to experience an improvement in BP with treatment of OSA if there is persistent airway obstruction.[18,165-167] Improvements in LV mass and wall thickness were not demonstrated in response to adenotonsillectomy.[159]

Children who undergo adenotonsillectomy may have symptoms of attention deficit hyperactivity disorder and daytime sleepiness, which respond well to surgery[168]; however, the lack of significant differences in the majority of outcomes in the long term between groups of children who undergo surgery and those who are managed conservatively may suggest the need to investigate better outcome measures to assess response to treatment. Furthermore, a consistent relationship between baseline symptoms and objective measures of upper airway obstruction such as AHI and oxygen desaturation index has not been observed, complicating the assessment for surgical candidacy of children who are evaluated with symptoms of OSA. Weight loss in obese or overweight children as an intervention for relief of airway obstruction has been shown to be procedurally effective, although concerns regarding compliance and long-term effectiveness have prevented its mainstream implementation. Children with comorbid conditions who are considered to be high risk on the basis of preoperative assessment for general anesthesia may be recommended alternate treatments. The use of intranasal corticosteroids with or without systemic anti-inflammatory agents may be considered suitable as first-line treatment for children with mild OSA in whom tonsillectomy is contraindicated. Intranasal corticosteroids may be more effective in younger, nonobese children. Nasal fluticasone or budesonide has been shown to reduce both the frequency and severity of obstructive events, specifically when the severity of OSA is mild to moderate on the basis of polysomnography assessments. In others, a combination therapy that includes oral leukotriene receptor antagonists may be efficacious, although they are generally deemed to be inferior in outcomes related to symptom relief.[169]

ANESTHESIA RISK AND PERIOPERATIVE CONSIDERATIONS IN SDB AND OSA

Children and adolescents with severe OSA require careful preoperative assessment and meticulous intra- and postoperative management.[20,23] Anesthetic agents should be carefully considered when managing children and adolescents with OSA, and attempts should be made to reduce opioid-associated respiratory depression.[20,23] Given that they are at risk for severe airway obstruction, including hypoxemia and hypercapnia, during and after surgery,[20] it is recommended that children with severe OSA, either clinically determined or if AHI >10 events/h, and children <3 years of age with significant comorbidities (eg, failure to thrive, obesity, cardiac involvement such as RV hypertrophy, trisomy 21, history of prematurity, craniofacial abnormalities, neuromuscular diseases, chronic lung disease, and SCD), be hospitalized for at least 23 hours after surgery.[170] Identification of children and adolescents with severe OSA requiring adenotonsillectomy and who are at greatest risk for adenotonsillectomy-related complications is particularly important.

In conclusion, OSA is common among children and adolescents. Children with severe OSA and children <3 years of age with significant comorbidities are at greater risk for severe and potentially life-threatening airway obstruction with anesthetic administration and immediately after surgery. Hospitalization for high-risk patients for the first 23 hours immediately after surgery is indicated.

Future Studies

To better understand the long-term CVD-related risk associated with the presence of OSA in childhood, additional well-designed longitudinal studies incorporating ambulatory blood pressure monitoring data and measures of metabolic disease (eg, lipid profile, glucose, and glycated hemoglobin levels) are needed over time. Also important are studies evaluating the relationship between OSA and noninvasive markers of CVD, including carotid intima media thickness and pulse wave velocity.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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†Significant.

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REFERENCES

1. Gottlieb DJ, Yenokyan G, Newman AB, O'Connor GT, Punjabi NM, Quan SF, Redline S, Resnick HE, Tong EK, Diener-West M, et al. Prospective study of obstructive sleep apnea and incident coronary heart disease and heart failure: the Sleep Heart Health Study. *Circulation*. 2010;122:352–360. doi: 10.1161/CIRCULATIONAHA.109.901801
2. Sarkar P, Mukherjee S, Chai-Coetzer CL, McEvoy RD. The epidemiology of obstructive sleep apnoea and cardiovascular disease. *J Thorac Dis*. 2018;10:S4189–S4200. doi: 10.21037/jtd.2018.12.56
3. Porto F, Sakamoto YS, Salles C. Association between obstructive sleep apnea and myocardial infarction: a systematic review. *Arq Bras Cardiol*. 2017;108:361–369. doi: 10.5935/abc.20170031
4. Postrzech-Adamczyk K, Nahorecki A, Zatońska K, Lawson J, Wołyniec M, Skomro R, Szuba A. Prevalence and risk of obstructive sleep apnea and arterial hypertension in the adult population in Poland: an observational subset of the international Prospective Urban Rural Epidemiology (PURE) study. *Adv Exp Med Biol*. 2019;1222:37–42. doi: 10.1007/5584_2019_419
5. Bacci MR, Emboz JNM, Alves B, Veiga GLD, Murad N, Meneghini A, Chagas ACP, Fonseca FLA. Obstructive sleep apnea syndrome and sleep quality in hypertensive patients. *Rev Assoc Med Bras (1992)*. 2017;63:1055–1060. doi: 10.1590/1806-9282.63.12.1055
6. Correa CM, Gismondi RA, Cunha AR, Neves MF, Oigman W. Twenty-four hour blood pressure in obese patients with moderate-to-severe obstructive sleep apnea. *Arq Bras Cardiol*. 2017;109:313–320. doi: 10.5935/abc.20170130
7. Borsini E, Blanco M, Bosio M, Schrappe M, Ernst G, Nosetto D, Gaggioli N, Salvado A, Manuale O, Schiavone M. Prevalence of sleep apnea and cardiovascular risk factors in patients with hypertension in a day hospital model. *Clin Exp Hypertens*. 2018;40:231–237. doi: 10.1080/10641963.2017.1356841
8. Platek AE, Szymanski FM, Filipiak KJ, Dudzik-Plocica A, Krzowski B, Karpinski G. Stratification of cardiovascular risk in patients with atrial fibrillation and obstructive sleep apnea-validity of the 2MACE score. *Sleep Breath*. 2017;21:601–606. doi: 10.1007/s11325-017-1469-6
9. Wang X, Fan JY, Zhang Y, Nie SP, Wei YX. Association of obstructive sleep apnea with cardiovascular outcomes after percutaneous coronary intervention: a systematic review and meta-analysis. *Medicine (Baltimore)*. 2018;97:e0621. doi: 10.1097/MD.0000000000010621
10. Wang L, Cai A, Zhang J, Zhong QI, Wang R, Chen J, Zhou Y. Association of obstructive sleep apnea plus hypertension and prevalent cardiovascular diseases: a cross-sectional study. *Medicine (Baltimore)*. 2016;95:e4691. doi: 10.1097/MD.0000000000004691
11. Chaput J-P, Gray CE, Poitras VJ, Carson V, Gruber R, Olds T, Weiss SK, Connor Gorber S, Kho ME, Sampson M, et al. Systematic review of the relationships between sleep duration and health indicators in school-aged children and youth. *Appl Physiol Nutr Metab*. 2016;41:S266–S282. doi: 10.1139/apnm-2015-0627
12. Archbold KH, Vasquez MM, Goodwin JL, Quan SF. Effects of sleep patterns and obesity on increases in blood pressure in a 5-year period: report from the Tucson Children's Assessment of Sleep Apnea Study. *J Pediatr*. 2012;161:26–30. doi: 10.1016/j.jpeds.2011.12.034
13. Amin RS, Kimball TR, Bean JA, Jeffries JL, Willging JP, Cotton RT, Witt SA, Glascock BJ, Daniels SR. Left ventricular hypertrophy and abnormal ventricular geometry in children and adolescents with obstructive sleep apnea. *Am J Respir Crit Care Med*. 2002;165:1395–1399. doi: 10.1164/rccm.2105118
14. Perfect MM, Archbold K, Goodwin JL, Levine-Donnerstein D, Quan SF. Risk of behavioral and adaptive functioning difficulties in youth with previous and current sleep disordered breathing. *Sleep*. 2013;36:517–525b. doi: 10.5665/sleep.2536
15. Sedky K, Bennett DS, Carvalho KS. Attention deficit hyperactivity disorder and sleep disordered breathing in pediatric populations: a meta-analysis. *Sleep Med Rev*. 2014;18:349–356. doi: 10.1016/j.smrv.2013.12.003
16. Kaditis AG, Alonso Alvarez ML, Boudewyns AN, Alexopoulos EI, Ersu R, Joosten K, Larramona H, Miano S, Narang I, Trang HA, et al. Obstructive sleep disordered breathing in 2- to 18-year-old children: diagnosis and management. *Eur Respir J*. 2016;47:69–94. doi: 10.1183/13993003.00385-2015
17. Beebe DW. Neurobehavioral morbidity associated with disordered breathing during sleep in children: a comprehensive review. *Sleep*. 2006;29:1115–1134. doi: 10.1093/sleep/29.9.1115
18. Marcus CL, Brooks LJ, Ward SD, Draper KA, Gozal D, Halbower AC, Jones J, Lehmann C, Schechter MS, Sheldon S, et al. Diagnosis

and management of childhood obstructive sleep apnea syndrome. *Pediatrics*. 2012;130:e714–e755. doi: 10.1542/peds.2012-1672
19. Carroll JL. Obstructive sleep-disordered breathing in children: new controversies, new directions. *Clin Chest Med*. 2003;24:261–282. doi: 10.1016/S0272-5231(03)00024-8
20. Patino M, Sadhasivam S, Mahmoud M. Obstructive sleep apnoea in children: perioperative considerations. *Br J Anaesth*. 2013;111(suppl 1):i83–i95. doi: 10.1093/bja/aet371
21. Somers VK, White DP, Amin R, Abraham WT, Costa F, Culebras A, Daniels S, Floras JS, Hunt CE, Olson LJ, et al. Sleep apnea and cardiovascular disease: an American Heart Association/American College of Cardiology Foundation scientific statement from the American Heart Association Council for High Blood Pressure Research Professional Education Committee, Council on Clinical Cardiology, Stroke Council, and Council on Cardiovascular Nursing. *Circulation*. 2008;118:1080–1111. doi: 10.1161/CIRCULATIONAHA.107.189420
22. Hahn PYS, Virend K. Sleep apnea and hypertension. In: Lip GYH, Hall JE, Hahn PY, Somers VK, eds. *Comprehensive Hypertension*. St. Louis: Mosby; 2007:201–207.
23. Roland PS, Rosenfeld RM, Brooks LJ, Friedman NR, Jones J, Kim TW, Kuhar S, Mitchell RB, Seidman MD, Sheldon SH, et al. Clinical practice guideline: polysomnography for sleep-disordered breathing prior to tonsillectomy in children. *Otolaryngol Head Neck Surg*. 2011;145:S1–S15. doi: 10.1177/0194599811409837
24. American Academy of Pediatrics. Health supervision for children with Down syndrome. *Pediatrics*. 2001;107:442–449.
25. Fernandes MBL, Salgueiro A, Bighetti EJB, Trindade-Suedam IK, Trindade IEK. Symptoms of obstructive sleep apnea, nasal obstruction, and enuresis in children with nonsyndromic cleft lip and palate: a prevalence study. *Cleft Palate Craniofac J*. 2019;56:307–313. doi: 10.1177/1055665618776074
26. Ehsan Z, Kurian C, Weaver KN, Pan BS, Huang G, Hossain MM, Simakajornboon N. Longitudinal sleep outcomes in neonates with Pierre Robin sequence treated conservatively. *J Clin Sleep Med*. 2019;15:477–482. doi: 10.5664/jcsm.7680
27. Qubty WF, Mrelashvili A, Kotagal S, Lloyd RM. Comorbidities in infants with obstructive sleep apnea. *J Clin Sleep Med*. 2014;10:1213–1216. doi: 10.5664/jcsm.4204
28. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. *Chest*. 2014;146:1387–1394. doi: 10.1378/chest.14-0970
29. Goh DY, Galster P, Marcus CL. Sleep architecture and respiratory disturbances in children with obstructive sleep apnea. *Am J Respir Crit Care Med*. 2000;162:682–686. doi: 10.1164/ajrccm.162.2.9908058
30. Yamadera W, Chiba S, Itoh H, Ozone M, Takahashi T, Sasaki M, Ushijima S, Moriyama H. Sleep architectures of obstructive sleep apnea syndrome in the young child. *Psychiatry Clin Neurosci*. 2000;54:330–331. doi: 10.1046/j.1440-1819.2000.00700.x
31. Shahveisi K, Jalali A, Moloudi MR, Moradi S, Maroufi A, Khazaie H. Sleep architecture in patients with primary snoring and obstructive sleep apnea. *Basic Clin Neurosci*. 2018;9:147–156. doi: 10.29252/nirp.bcn.9.2.147
32. McNamara F, Issa FG, Sullivan CE. Arousal pattern following central and obstructive breathing abnormalities in infants and children. *J Appl Physiol (1985)*. 1996;81:2651–2657. doi: 10.1152/jappl.1996.81.6.2651
33. Walter LM, Nixon GM, Davey MJ, O'Driscoll DM, Trinder J, Horne RS. Sleep disturbance in pre-school children with obstructive sleep apnoea syndrome. *Sleep Med*. 2011;12:880–886. doi: 10.1016/j.sleep.2011.07.007
34. Beck SE, Marcus CL. Pediatric polysomnography. *Sleep Med Clin*. 2009;4:393–406. doi: 10.1016/j.jsmc.2009.04.007
35. Mitchell RB, Garetz S, Moore RH, Rosen CL, Marcus CL, Katz ES, Arens R, Chervin RD, Paruthi S, Amin R, et al. The use of clinical parameters to predict obstructive sleep apnea syndrome severity in children: the Childhood Adenotonsillectomy (CHAT) study randomized clinical trial. *JAMA Otolaryngol Head Neck Surg*. 2015;141:130–136. doi: 10.1001/jamaoto.2014.3049
36. Katz ES, Greene MG, Carson KA, Galster P, Loughlin GM, Carroll J, Marcus CL. Night-to-night variability of polysomnography in children with suspected obstructive sleep apnea. *J Pediatr*. 2002;140:589–594. doi: 10.1067/mpd.2002.123290
37. Bradley TD, Floras JS. Sleep apnea and heart failure: part I: obstructive sleep apnea. *Circulation*. 2003;107:1671–1678. doi: 10.1161/01.CIR.0000061757.12581.15
38. Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, Harrod CG. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med*. 2017;13:479–504. doi: 10.5664/jcsm.6506
39. Kirk V, Baughn J, D'Andrea L, Friedman N, Galion A, Garetz S, Hassan F, Wrede J, Harrod CG, Malhotra RK. American Academy of Sleep Medicine position paper for the use of a home sleep apnea test for the diagnosis of OSA in children. *J Clin Sleep Med*. 2017;13:1199–1203. doi: 10.5664/jcsm.6772
40. 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;1:21–32. doi: 10.1016/s1389-9457(99)00009-x
41. Chervin RD, Weatherly RA, Garetz SL, Ruzicka DL, Giordani BJ, Hodges EK, Dillon JE, Guire KE. Pediatric sleep questionnaire: prediction of sleep apnea and outcomes. *Arch Otolaryngol Head Neck Surg*. 2007;133:216–222. doi: 10.1001/archotol.133.3.216
42. Øverland B, Berdal H, Akre H. Obstructive sleep apnea in 2–6 year old children referred for adenotonsillectomy. *Eur Arch Otorhinolaryngol*. 2019;276:2097–2104. doi: 10.1007/s00405-019-05362-3
43. Burghard M, Brożek-Mądry E, Krzeski A. Sleep disordered breathing in children—diagnostic questionnaires, comparative analysis. *Int J Pediatr Otorhinolaryngol*. 2019;120:108–111. doi: 10.1016/j.ijporl.2019.02.008
44. Spruyt K, Gozal D. Pediatric sleep questionnaires as diagnostic or epidemiological tools: a review of currently available instruments. *Sleep Med Rev*. 2011;15:19–32. doi: 10.1016/j.smrv.2010.07.005
45. Raman VT, Splaingard M, Tumin D, Rice J, Jatana KR, Tobias JD. Utility of screening questionnaire, obesity, neck circumference, and sleep polysomnography to predict sleep-disordered breathing in children and adolescents. *Paediatr Anaesth*. 2016;26:655–664. doi: 10.1111/pan.12911
46. DelRosso LM. Epidemiology and diagnosis of pediatric obstructive sleep apnea. *Curr Probl Pediatr Adolesc Health Care*. 2016;46:2–6. doi: 10.1016/j.cppeds.2015.10.009
47. Janssen KC, Phillipson S, O'Connor J, Johns MW. Validation of the Epworth Sleepiness Scale for children and adolescents using Rasch analysis. *Sleep Med*. 2017;33:30–35. doi: 10.1016/j.sleep.2017.01.014
48. Kaditis AG, Alexopoulos EI, Damani E, Karadonta I, Kostadima E, Tsolakidou A, Gourgoulianis K, Syrogiannopoulos GA. Obstructive sleep-disordered breathing and fasting insulin levels in nonobese children. *Pediatr Pulmonol*. 2005;40:515–523. doi: 10.1002/ppul.20306
49. Lumeng JC, Chervin RD. Epidemiology of pediatric obstructive sleep apnea. *Proc Am Thorac Soc*. 2008;5:242–252. doi: 10.1513/pats.200708-135MG
50. Paruthi S, Brooks LJ, D'Ambrosio C, Hall WA, Kotagal S, Lloyd RM, Malow BA, Maski K, Nichols C, Quan SF, et al. Consensus statement of the American Academy of Sleep Medicine on the recommended amount of sleep for healthy children: methodology and discussion. *J Clin Sleep Med*. 2016;12:1549–1561. doi: 10.5664/jcsm.6288
51. Katz ES, D'Ambrosio CM. Pathophysiology of pediatric obstructive sleep apnea. *Proc Am Thorac Soc*. 2008;5:253–262. doi: 10.1513/pats.200707-111MG
52. Kaditis AG, Alexopoulos EI, Hatzi F, Karadonta I, Chaidas K, Gourgoulianis K, Zintzaras E, Syrogiannopoulos GA. Adiposity in relation to age as predictor of severity of sleep apnea in children with snoring. *Sleep Breath*. 2008;12:25–31. doi: 10.1007/s11325-007-0132-z
53. Redline S, Tishler PV, Schluchter M, Aylor J, Clark K, Graham G. Risk factors for sleep-disordered breathing in children. Associations with obesity, race, and respiratory problems. *Am J Respir Crit Care Med*. 1999;159:1527–1532. doi: 10.1164/ajrccm.159.5.9809079
54. Alexopoulos EI, Charitos G, Malakasioti G, Varlami V, Gourgoulianis K, Zintzaras E, Kaditis AG. Parental history of adenotonsillectomy is associated with obstructive sleep apnea severity in children with snoring. *J Pediatr*. 2014;164:1352–1357. doi: 10.1016/j.jpeds.2014.01.021
55. Bixler EO, Vgontzas AN, Lin H-M, Liao D, Calhoun S, Vela-Bueno A, Fedok F, Vlasic V, Graff G. Sleep disordered breathing in children in a general population sample: prevalence and risk factors. *Sleep*. 2009;32:731–736. doi: 10.1093/sleep/32.6.731
56. Inverso G, Brustowicz KA, Katz E, Padwa BL. The prevalence of obstructive sleep apnea in symptomatic patients with syndromic craniosynostosis. *Int J Oral Maxillofac Surg*. 2016;45:167–169. doi: 10.1016/j.ijom.2015.10.003

57. Akre H, Øverland B, Åsten P, Skogedal N, Heimdal K. Obstructive sleep apnea in Treacher Collins syndrome. *Eur Arch Otorhinolaryngol*. 2012;269:331–337. doi: 10.1007/s00405-011-1649-0
58. Cielo CM, Marcus CL. Obstructive sleep apnoea in children with craniofacial syndromes. *Paediatr Respir Rev*. 2015;16:189–196.
59. Robison JG, Otteson TD. Increased prevalence of obstructive sleep apnea in patients with cleft palate. *Arch Otolaryngol Head Neck Surg*. 2011;137:269–274. doi: 10.1001/archoto.2011.8
60. Silvestre J, Tahiri Y, Paliga JT, Taylor JA. Screening for obstructive sleep apnea in children with syndromic cleft lip and/or palate. *J Plast Reconstr Aesthet Surg*. 2014;67:1475–1480. doi: 10.1016/j.bjps.2014.07.026
61. Wagner MH, Berry RB. Disturbed sleep in a patient with Duchenne muscular dystrophy. *J Clin Sleep Med*. 2008;4:173–175. doi: 10.5664/jcsm.27134
62. ElMallah M, Bailey E, Trivedi M, Kremer T, Rhein LM. Pediatric obstructive sleep apnea in high-risk populations: clinical implications. *Pediatr Ann*. 2017;46:e336–e339. doi: 10.3928/19382359-20170815-01
63. Afsharpaiman S, Sillence DO, Sheikhvatan M, Ault JE, Waters K. Respiratory events and obstructive sleep apnea in children with achondroplasia: investigation and treatment outcomes. *Sleep Breath*. 2011;15:755–761. doi: 10.1007/s11325-010-0432-6
64. Malow BA, Levy K, Maturen K, Bowes R. Obstructive sleep apnea is common in medically refractory epilepsy patients. *Neurology*. 2000;55:1002–1007. doi: 10.1212/WNL.55.7.1002
65. Rosen CL, Larkin EK, Kirchner HL, Emancipator JL, Bivins SF, Surovec SA, Martin RJ, Redline S. Prevalence and risk factors for sleep-disordered breathing in 8- to 11-year-old children: association with race and prematurity. *J Pediatr*. 2003;142:383–389. doi: 10.1067/mpd.2003.28
66. Ykeda DS, Lorenzi-Filho G, Lopes AA, Alves RS. Sleep in infants with congenital heart disease. *Clinics (Sao Paulo)*. 2009;64:1205–1210. doi: 10.1590/S1807-59322009001200011
67. Stamm RW, Henry BM, Sawnani H, Simakajornboon N, Rulong G, Ollberding NJ, Hanke SP, Dye TJ, Cooper DS. Clinically asymptomatic sleep-disordered breathing in infants with single-ventricle physiology. *J Pediatr*. 2020;218:92–97. doi: 10.1016/j.jpeds.2019.11.005
68. Combs D, Skrepnek G, Seckeler MD, Barber BJ, Morgan WJ, Parthasarathy S. Sleep-disordered breathing is associated with increased mortality in hospitalized infants with congenital heart disease. *J Clin Sleep Med*. 2018;14:1551–1558. doi: 10.5664/jcsm.7334
69. Boss EF, Smith DF, Ishman SL. Racial/ethnic and socioeconomic disparities in the diagnosis and treatment of sleep-disordered breathing in children. *Int J Pediatr Otorhinolaryngol*. 2011;75:299–307. doi: 10.1016/j.ijporl.2010.11.006
70. Kingsbury JH, Buxton OM, Emmons KM, Redline S. Sleep and its relationship to racial and ethnic disparities in cardiovascular disease. *Curr Cardiovasc Risk Rep*. 2013;7:387–394. doi: 10.1007/s12170-013-0330-0
71. Goldstein NA, Abramowitz T, Weedon J, Koliskor B, Turner S, Taioli E. Racial/ethnic differences in the prevalence of snoring and sleep disordered breathing in young children. *J Clin Sleep Med*. 2011;7:163–171. doi: 10.5664/jcsm.28104
72. Wang R, Dong Y, Weng J, Kontos EZ, Chervin RD, Rosen CL, Marcus CL, Redline S. Associations among neighborhood, race, and sleep apnea severity in children. A six-city analysis. *Ann Am Thorac Soc*. 2017;14:76–84. doi: 10.1513/AnnalsATS.201609-662OC
73. Cao Y, Wu S, Zhang L, Yang Y, Cao S, Li Q. Association of allergic rhinitis with obstructive sleep apnea: a meta-analysis. *Medicine (Baltimore)*. 2018;97:e13783. doi: 10.1097/MD.0000000000013783
74. von Ungern-Sternberg BS, Sommerfield D, Slevin L, Drake-Brockman TFE, Zhang G, Hall GL. Effect of albuterol premedication vs placebo on the occurrence of respiratory adverse events in children undergoing tonsillectomies: the REACT randomized clinical trial. *JAMA Pediatr*. 2019;173:527–533. doi: 10.1001/jamapediatrics.2019.0788
75. Rosen CL, Debaun MR, Strunk RC, Redline S, Seicean S, Craven DI, Gavlak JCD, Wilkey O, Inusa B, Roberts I, et al. Obstructive sleep apnea and sickle cell anemia. *Pediatrics*. 2014;134:273–281. doi: 10.1542/peds.2013-4223
76. Spilsbury JC, Storfer-Isser A, Rosen CL, Redline S. Remission and incidence of obstructive sleep apnea from middle childhood to late adolescence. *Sleep*. 2015;38:23–29. doi: 10.5665/sleep.4318
77. Marcus CL, Moore RH, Rosen CL, Giordani B, Garetz SL, Taylor HG, Mitchell RB, Amin R, Katz ES, Arens R, et al. A randomized trial of adenotonsillectomy for childhood sleep apnea. *N Engl J Med*. 2013;368:2366–2376. doi: 10.1056/NEJMoa1215881
78. Nadeem R, Molnar J, Madbouly EM, Nida M, Aggarwal S, Sajid H, Naseem J, Loomba R. Serum inflammatory markers in obstructive sleep apnea: a meta-analysis. *J Clin Sleep Med*. 2013;9:1003–1012. doi: 10.5664/jcsm.3070
79. Tsaoussoglou M, Bixler EO, Calhoun S, Chrousos GP, Sauder K, Vgontzas AN. Sleep-disordered breathing in obese children is associated with prevalent excessive daytime sleepiness, inflammation, and metabolic abnormalities. *J Clin Endocrinol Metab*. 2010;95:143–150. doi: 10.1210/jc.2009-0435
80. Gaines J, Vgontzas AN, Fernandez-Mendoza J, He F, Calhoun SL, Liao D, Bixler EO. Increased inflammation from childhood to adolescence predicts sleep apnea in boys: a preliminary study. *Brain Behav Immun*. 2017;64:259–265. doi: 10.1016/j.bbi.2017.04.011
81. Kheirandish-Gozal L, Bandla HP, Gozal D. Montelukast for children with obstructive sleep apnea: results of a double-blind, randomized, placebo-controlled trial. *Ann Am Thorac Soc*. 2016;13:1736–1741. doi: 10.1513/AnnalsATS.201606-432OC
82. Ingram DG, Matthews CK. Effect of adenotonsillectomy on C-reactive protein levels in children with obstructive sleep apnea: a meta-analysis. *Sleep Med*. 2013;14:172–176. doi: 10.1016/j.sleep.2012.11.011
83. Khan MA, Mathur K, Barraza G, Sin S, Yang CJ, Arens R, Sutton N, Mahgerefteh J. The relationship of hypertension with obesity and obstructive sleep apnea in adolescents. *Pediatr Pulmonol*. 2020;55:1020–1027. doi: 10.1002/ppul.24693
84. Roche J, Corgosinho FC, Dâmaso AR, Isacco L, Miguet M, Fillon A, Guyon A, Moreira GA, Pradella-Hallinan M, Tufik S, et al. Sleep-disordered breathing in adolescents with obesity: when does it start to affect cardiometabolic health? *Nutr Metab Cardiovasc Dis*. 2020;30:683–693. doi: 10.1016/j.numecd.2019.12.003
85. Sorof JM, Lai D, Turner J, Poffenbarger T, Portman RJ. Overweight, ethnicity, and the prevalence of hypertension in school-aged children. *Pediatrics*. 2004;113:475–482. doi: 10.1542/peds.113.3.475
86. Bhattacharjee R, Kheirandish-Gozal L, Pillar G, Gozal D. Cardiovascular complications of obstructive sleep apnea syndrome: evidence from children. *Prog Cardiovasc Dis*. 2009;51:416–433. doi: 10.1016/j.pcad.2008.03.002
87. O'Brien LM, Gozal D. Autonomic dysfunction in children with sleep-disordered breathing. *Sleep*. 2005;28:747–752. doi: 10.1093/sleep/28.6.747
88. Baharav A, Kotagal S, Rubin BK, Pratt J, Akselrod S. Autonomic cardiovascular control in children with obstructive sleep apnea. *Clin Auton Res*. 1999;9:345–351. doi: 10.1007/BF02318382
89. Chan KC, Au CT, Hui LL, Wing YK, Li AM. Childhood osa is an independent determinant of blood pressure in adulthood: longitudinal follow-up study. *Thorax*. 2020;75:422–431. doi: 10.1136/thoraxjnl-2019-213692
90. Kwok KL, Ng DK, Chan CH. Cardiovascular changes in children with snoring and obstructive sleep apnoea. *Ann Acad Med Singapore*. 2008;37:715–721.
91. Zintzaras E, Kaditis AG. Sleep-disordered breathing and blood pressure in children: a meta-analysis. *Arch Pediatr Adolesc Med*. 2007;161:172–178. doi: 10.1001/archpedi.161.2.172
92. Chen X, Wang Y. Tracking of blood pressure from childhood to adulthood: a systematic review and meta-regression analysis. *Circulation*. 2008;117:3171–3180. doi: 10.1161/CIRCULATIONAHA.107.730366
93. Theodore RF, Broadbent J, Nagin D, Ambler A, Hogan S, Ramrakha S, Cutfield W, Williams MJA, Harrington H, Moffitt TE, et al. Childhood to early-midlife systolic blood pressure trajectories: early-life predictors, effect modifiers, and adult cardiovascular outcomes. *Hypertension*. 2015;66:1108–1115. doi: 10.1161/HYPERTENSIONAHA.115.05831
94. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med*. 2000;342:1378–1384. doi: 10.1056/NEJM200005113421901
95. Baguet J-P, Boutin I, Barone-Rochette G, Levy P, Tamisier R, Pierre H, Boggetto-Graham L, Pépin J-L. Hypertension diagnosis in obstructive sleep apnea: self or 24-hour ambulatory blood pressure monitoring? *Int J Cardiol*. 2013;167:2346–2347. doi: 10.1016/j.ijcard.2012.11.037
96. Guilleminault C, Eldridge FL, Simmons FB, Dement WC. Sleep apnea in eight children. *Pediatrics*. 1976;58:23–30.
97. Somers VK, Mark AL, Zavala DC, Abboud FM. Contrasting effects of hypoxia and hypercapnia on ventilation and sympathetic activity

in humans. *J Appl Physiol (1985)*. 1989;67:2101–2106. doi: 10.1152/jappl.1989.67.5.2101
98. Fidone SJ, Gonzalez C. Initiation and control of chemoreceptor activity in the carotid body. In: Fishman AP, Cherniack NS, Widdicombe JG, Geiger SR, eds. *Handbook of Physiology. Section 3: The Respiratory System. Vol II. Control of Breathing*. Bethesda, MD: American Physiological Society; 1986:247–312.
99. Garpestad E, Katayama H, Parker JA, Ringler J, Lilly J, Yasuda T, Moore RH, Strauss HW, Weiss JW. Stroke volume and cardiac output decrease at termination of obstructive apneas. *J Appl Physiol (1985)*. 1992;73:1743–1748. doi: 10.1152/jappl.1992.73.5.1743
100. Abhishekh HA, Nisarga P, Kisan R, Meghana A, Chandran S, Trichur R, Sathyaprabha TN. Influence of age and gender on autonomic regulation of heart. *J Clin Monit Comput*. 2013;27:259–264. doi: 10.1007/s10877-012-9424-3
101. O'Driscoll DM, Horne RSC, Davey MJ, Hope SA, Anderson V, Trinder J, Walker AM, Nixon GM. Increased sympathetic activity in children with obstructive sleep apnea: cardiovascular implications. *Sleep Med*. 2011;12:483–488. doi: 10.1016/j.sleep.2010.09.015
102. Enright PL, Goodwin JL, Sherrill DL, Quan JR, Quan SF. Blood pressure elevation associated with sleep-related breathing disorder in a community sample of White and Hispanic children: the Tucson Children's Assessment of Sleep Apnea Study. *Arch Pediatr Adolesc Med*. 2003;157:901–904. doi: 10.1001/archpedi.157.9.901
103. Reade EP, Whaley C, Lin JJ, McKenney DW, Lee D, Perkin R. Hypopnea in pediatric patients with obesity hypertension. *Pediatr Nephrol*. 2004;19:1014–1020. doi: 10.1007/s00467-004-1513-1
104. Amin RS, Carroll JL, Jeffries JL, Grone C, Bean JA, Chini B, Bokulic R, Daniels SR. Twenty-four-hour ambulatory blood pressure in children with sleep-disordered breathing. *Am J Respir Crit Care Med*. 2004;169:950–956. doi: 10.1164/rccm.200309-1305OC
105. Bixler EO, Vgontzas AN, Lin H-M, Liao D, Calhoun S, Fedok F, Vlasic V, Graff G. Blood pressure associated with sleep-disordered breathing in a population sample of children. *Hypertension*. 2008;52:841–846. doi: 10.1161/HYPERTENSIONAHA.108.116756
106. Li AM, Au CT, Sung RYT, Ho C, Ng PC, Fok TF, Wing YK. Ambulatory blood pressure in children with obstructive sleep apnoea: a community based study. *Thorax*. 2008;63:803–809. doi: 10.1136/thx.2007.091132
107. Kohyama J, Hasegawa T, Ohinata JS. Glucose metabolism in sleep disordered breathing. *Arch Dis Child*. 2003;88:89. doi: 10.1136/adc.88.1.89
108. Hinkle J, Connolly HV, Adams HR, Lande MB. Severe obstructive sleep apnea in children with elevated blood pressure. *J Am Soc Hypertens*. 2018;12:204–210. doi: 10.1016/j.jash.2017.12.010
109. Li AM, Au CT, Ng C, Lam HS, Ho CKW, Wing YK. A 4-year prospective follow-up study of childhood OSA and its association with BP. *Chest*. 2014;145:1255–1263. doi: 10.1378/chest.13-1333
110. Levy D, Larson MG, Vasan RS, Kannel WB, Ho KK. The progression from hypertension to congestive heart failure. *JAMA*. 1996;275:1557–1562. doi: 10.1001/jama.1996.03530440037034
111. Hill JA, Olson EN. Cardiac plasticity. *N Engl J Med*. 2008;358:1370–1380. doi: 10.1056/NEJMra072139
112. Hanlon CE, Binka E, Garofano JS, Sterni LM, Brady TM. The association of obstructive sleep apnea and left ventricular hypertrophy in obese and overweight children with history of elevated blood pressure. *J Clin Hypertens (Greenwich)*. 2019;21:984–990. doi: 10.1111/jch.13605
113. Al-Saleh S, Kantor PF, Chadha NK, Tirado Y, James AL, Narang I. Sleep-disordered breathing in children with cardiomyopathy. *Ann Am Thorac Soc*. 2014;11:770–776. doi: 10.1513/AnnalsATS.201309-325OC
114. Cincin A, Sakalli E, Bakirci EM, Dizman R. Relationship between obstructive sleep apnea-specific symptoms and cardiac function before and after adenotonsillectomy in children with adenotonsillar hypertrophy. *Int J Pediatr Otorhinolaryngol*. 2014;78:1281–1287. doi: 10.1016/j.ijporl.2014.05.011
115. Tugcu A, Guzel D, Yildirimturk O, Aytekin S. Evaluation of right ventricular systolic and diastolic function in patients with newly diagnosed obstructive sleep apnea syndrome without hypertension. *Cardiology*. 2009;113:184–192. doi: 10.1159/000193146
116. Hunt CE, Brouillette RT. Abnormalities of breathing control and airway maintenance in infants and children as a cause of cor pulmonale. *Pediatr Cardiol*. 1982;3:249–256. doi: 10.1007/BF02240461
117. Levin DL, Muster AJ, Pachman LM, Wessel HU, Paul MH, Koshaba J. Cor pulmonale secondary to upper airway obstruction. cardiac catheterization, immunologic, and psychometric evaluation in nine patients. *Chest*. 1975;68:166–171. doi: 10.1378/chest.68.2.166
118. Corral J, Mogollon MV, Sánchez-Quiroga M-Á, Gómez de Terreros J, Romero A, Caballero C, Teran-Santos J, Alonso-Álvarez ML, Gómez-García T, González M, et al. Echocardiographic changes with noninvasive ventilation and CPAP in obesity hypoventilation syndrome. *Thorax*. 2018;73:361–368. doi: 10.1136/thoraxjnl-2017-210642
119. Mu H, Liu J, Gong K, Li D, Zhang J. Quantitative tissue velocity imaging evaluation of ventricular function in obstructive sleep apnoea-hypopnoea syndrome in children. *Clin Exp Pharmacol Physiol*. 2015;42:602–608. doi: 10.1111/1440-1681.12408
120. Revenaugh PC, Chmielewski LJ, Edwards T, Krishna J, Krakovitz P, Anne S. Utility of preoperative cardiac evaluation in pediatric patients undergoing surgery for obstructive sleep apnea. *Arch Otolaryngol Head Neck Surg*. 2011;137:1269–1275. doi: 10.1001/archoto.2011.208
121. Gami AS, Hodge DO, Herges RM, Olson EJ, Nykodym J, Kara T, Somers VK. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. *J Am Coll Cardiol*. 2007;49:565–571. doi: 10.1016/j.jacc.2006.08.060
122. Shamsuzzaman AS, Somers VK, Knilans TK, Ackerman MJ, Wang Y, Amin RS. Obstructive sleep apnea in patients with congenital long QT syndrome: implications for increased risk of sudden cardiac death. *Sleep*. 2015;38:1113–1119. doi: 10.5665/sleep.4824
123. Di Fusco SA, Pignalberi C, Santini L, Colivicchi F, Santini M. Arrhythmias and sleep apnea: physiopathologic link and clinical implications. *J Interv Card Electrophysiol*. 2020;57:387–397. doi: 10.1007/s10840-020-00707-z
124. Selim BJ, Koo BB, Qin LI, Jeon S, Won C, Redeker NS, Lampert RJ, Concato JP, Bravata DM, Ferguson J, et al. The association between nocturnal cardiac arrhythmias and sleep-disordered breathing: the DREAM study. *J Clin Sleep Med*. 2016;12:829–837. doi: 10.5664/jcsm.5880
125. Monahan K, Brewster J, Wang LI, Parvez B, Goyal S, Roden DM, Darbar D. Relation of the severity of obstructive sleep apnea in response to anti-arrhythmic drugs in patients with atrial fibrillation or atrial flutter. *Am J Cardiol*. 2012;110:369–372. doi: 10.1016/j.amjcard.2012.03.037
126. Çiçek D, Lakadamyali H, Gökay S, Sapmaz I, Muderrisoglu H. Effect of obstructive sleep apnea on heart rate, heart rate recovery and QTc and P-wave dispersion in newly diagnosed untreated patients. *Am J Med Sci*. 2012;344:180–185. doi: 10.1097/MAJ.0b013e318239a67f
127. Pérez-Riera AR, de Abreu LC, Barbosa-Barros R, Grindler J, Fernandes-Cardoso A, Baranchuk A. P-wave dispersion: an update. *Indian Pacing Electrophysiol J*. 2016;16:126–133. doi: 10.1016/j.ipej.2016.10.002
128. Okutucu S, Aytemir K, Oto A. P-wave dispersion: what we know till now? *JRSM Cardiovasc Dis*. 2016;5:2048004016639443. doi: 10.1177/2048004016639443
129. Khositseth A, Nantarakchaikul P, Kuptanon T, Preutthipan A. QT dispersion in childhood obstructive sleep apnoea syndrome. *Cardiol Young*. 2011;21:130–135. doi: 10.1017/S1047951110001514
130. Kraikriangsri C, Khositseth A, Kuptanon T. P-wave dispersion as a simple tool for screening childhood obstructive sleep apnea syndrome. *Sleep Med*. 2019;54:159–163. doi: 10.1016/j.sleep.2018.09.032
131. Aljadeff G, Gozal D, Schechtman VL, Burrell B, Harper RM, Ward SL. Heart rate variability in children with obstructive sleep apnea. *Sleep*. 1997;20:151–157. doi: 10.1093/sleep/20.2.151
132. Muzumdar HV, Sin S, Nikova M, Gates G, Kim D, Arens R. Changes in heart rate variability after adenotonsillectomy in children with obstructive sleep apnea. *Chest*. 2011;139:1050–1059. doi: 10.1378/chest.10-1555
133. Isaiah A, Bertoni D, Pereira KD, Diaz-Abad M, Mitchell RB, Das G. Treatment-related changes in heart rate variability in children with sleep apnea. *Otolaryngol Head Neck Surg*. 2020;162:737–745. doi: 10.1177/0194599820907882
134. Ogden CL, Carroll MD, Fakhouri TH, Hales CM, Fryar CD, Li X, Freedman DS. Prevalence of obesity among youths by household income and education level of head of household—United States 2011–2014. *MMWR Morb Mortal Wkly Rep*. 2018;67:186–189. doi: 10.15585/mmwr.mm6706a3
135. Kelly AS, Barlow SE, Rao G, Inge TH, Hayman LL, Steinberger J, Urbina EM, Ewing LJ, Daniels SR. Severe obesity in children and

adolescents: identification, associated health risks, and treatment approaches: a scientific statement from the American Heart Association. *Circulation*. 2013;128:1689–1712. doi: 10.1161/CIR.0b013e3182a5cfb3
136. Fatima Y, Doi SA, Mamun AA. Longitudinal impact of sleep on overweight and obesity in children and adolescents: a systematic review and bias-adjusted meta-analysis. *Obes Rev*. 2015;16(2):137–149. doi: 10.1111/obr.12245
137. Chen X, Beydoun MA, Wang Y. Is sleep duration associated with childhood obesity? A systematic review and meta-analysis. *Obesity (Silver Spring)*. 2008;16:265–274. doi: 10.1038/oby.2007.63
138. Roche J, Isacco L, Masurier J, Pereira B, Mougin F, Chaput J-P, Thivel D. Are obstructive sleep apnea and sleep improved in response to multidisciplinary weight loss interventions in youth with obesity? A systematic review and meta-analysis. *Int J Obes (Lond)*. 2020;44:753–770. doi: 10.1038/s41366-019-0497-7
139. Hart CN, Carskadon MA, Considine RV, Fava JL, Lawton J, Raynor HA, Jelalian E, Owens J, Wing R. Changes in children's sleep duration on food intake, weight, and leptin. *Pediatrics*. 2013;132:e1473–e1480. doi: 10.1542/peds.2013-1274
140. Nadeem R, Singh M, Nida M, Waheed I, Khan A, Ahmed S, Naseem J, Champeau D. Effect of obstructive sleep apnea hypopnea syndrome on lipid profile: a meta-regression analysis. *J Clin Sleep Med*. 2014;10:475–489. doi: 10.5664/jcsm.3690
141. Koren D, O'Sullivan KL, Mokhlesi B. Metabolic and glycemic sequelae of sleep disturbances in children and adults. *Curr Diab Rep*. 2015;15:562. doi: 10.1007/s11892-014-0562-5
142. Apostolidou MT, Alexopoulos EI, Damani E, Liakos N, Chaidas K, Boultadakis E, Apostolidis T, Gourgoulianis K, Kaditis AG. Absence of blood pressure, metabolic, and inflammatory marker changes after adenotonsillectomy for sleep apnea in Greek children. *Pediatr Pulmonol*. 2008;43:550–560. doi: 10.1002/ppul.20808
143. Forster CS. 50 years ago in the Journal of Pediatrics: hypoventilation and cor pulmonale due to chronic upper airway obstruction. *J Pediatr*. 2015;167:285. doi: 10.1016/j.jpeds.2015.02.032
144. Menashe VD, Farrehi C, Miller M. Hypoventilation and cor pulmonale due to chronic upper airway obstruction. *J Pediatr*. 1965;67:198. doi: 10.1016/S0022-3476(65)80242-6
145. Abman SH, Hansmann G, Archer SL, Ivy DD, Adatia I, Chung WK, Hanna BD, Rosenzweig EB, Raj JU, Cornfield D, et al. Pediatric pulmonary hypertension: guidelines from the American Heart Association and American Thoracic Society. *Circulation*. 2015;132:2037–2099. doi: 10.1161/CIR.0000000000000329
146. Burns AT, Hansen SL, Turner ZS, Aden JK, Black AB, Hsu DP. Prevalence of pulmonary hypertension in pediatric patients with obstructive sleep apnea and a cardiology evaluation: a retrospective analysis. *J Clin Sleep Med*. 2019;15:1081–1087. doi: 10.5664/jcsm.7794
147. Ingram DG, Singh AV, Ehsan Z, Birnbaum BF. Obstructive sleep apnea and pulmonary hypertension in children. *Paediatr Respir Rev*. 2017;23:33–39. doi: 10.1016/j.prrv.2017.01.001
148. Nahmod NG, Lee S, Buxton OM, Chang AM, Hale L. High school start times after 8:30 AM are associated with later wake times and longer time in bed among teens in a national urban cohort study. *Sleep Health*. 2017;3:444–450. doi: 10.1016/j.sleh.2017.09.004
149. Adolescent Sleep Working Group, Committee on Adolescence and Council on School Health. School start times for adolescents. *Pediatrics*. 2014;134:642–649.
150. Mindell JA, Sedmak R, Boyle JT, Butler R, Williamson AA. Sleep well!: a pilot study of an education campaign to improve sleep of socioeconomically disadvantaged children. *J Clin Sleep Med*. 2016;12:1593–1599. doi: 10.5664/jcsm.6338
151. Mindell JA, Williamson AA. Benefits of a bedtime routine in young children: sleep, development, and beyond. *Sleep Med Rev*. 2018;40:93–108. doi: 10.1016/j.smrv.2017.10.007
152. Haines J, McDonald J, O'Brien A, Sherry B, Bottino CJ, Schmidt ME, Taveras EM. Healthy habits, happy homes: randomized trial to improve household routines for obesity prevention among preschool-aged children. *JAMA Pediatr*. 2013;167:1072–1079. doi: 10.1001/jamapediatrics.2013.2356
153. Yoong SL, Grady A, Stacey F, Polimeni M, Clayton O, Jones J, Nathan N, Wyse R, Wolfenden L. A pilot randomized controlled trial examining the impact of a sleep intervention targeting home routines on young children's (3–6 years) physical activity. *Pediatr Obes*. 2019;14:e12481. doi: 10.1111/ijpo.12481
154. Wing YK, Chan NY, Man Yu MW, Lam SP, Zhang J, Li SX, Kong APS, Li AM. A school-based sleep education program for adolescents: a cluster randomized trial. *Pediatrics*. 2015;135:e635–e643. doi: 10.1542/peds.2014-2419
155. Kloss JD, Nash CO, Walsh CM, Culnan E, Horsey S, Sexton-Radek K. A "sleep 101" program for college students improves sleep hygiene knowledge and reduces maladaptive beliefs about sleep. *Behav Med*. 2016;42:48–56. doi: 10.1080/08964289.2014.969186
156. Kaplan KA, Mashash M, Williams R, Batchelder H, Starr-Glass L, Zeitzer JM. Effect of light flashes vs sham therapy during sleep with adjunct cognitive behavioral therapy on sleep quality among adolescents: a randomized clinical trial. *JAMA Netw Open*. 2019;2:e1911944. doi: 10.1001/jamanetworkopen.2019.11944
157. Katz SL, Monsour A, Barrowman N, Hoey L, Bromwich M, Momoli F, Chan T, Goldberg R, Patel A, Yin LI, et al. Predictors of postoperative respiratory complications in children undergoing adenotonsillectomy. *J Clin Sleep Med*. 2020;16:41–48. doi: 10.5664/jcsm.8118
158. Hawkins S, Huston S, Campbell K, Halbower A. High-flow, heated, humidified air via nasal cannula treats CPAP-intolerant children with obstructive sleep apnea. *J Clin Sleep Med*. 2017;13:981–989. doi: 10.5664/jcsm.6700
159. Ehsan Z, Ishman SL, Kimball TR, Zhang N, Zou Y, Amin RS. Longitudinal cardiovascular outcomes of sleep disordered breathing in children: a meta-analysis and systematic review. *Sleep*. 2017;40:zsx015. doi: 10.1093/sleep/zsx015
160. Lee C-H, Kang K-T, Chiu S-N, Chang I-S, Weng W-C, Lee P-L, Hsu W-C. Association of adenotonsillectomy with blood pressure among hypertensive and nonhypertensive children with obstructive sleep apnea. *JAMA Otolaryngol Head Neck Surg*. 2018;144:300–307. doi: 10.1001/jamaoto.2017.3127
161. Teo DT, Mitchell RB. Systematic review of effects of adenotonsillectomy on cardiovascular parameters in children with obstructive sleep apnea. *Otolaryngol Head Neck Surg*. 2013;148:21–28. doi: 10.1177/0194599812463193
162. Ng DK, Wong JC, Chan CH, Leung LC, Leung SY. Ambulatory blood pressure before and after adenotonsillectomy in children with obstructive sleep apnea. *Sleep Med*. 2010;11:721–725. doi: 10.1016/j.sleep.2009.10.007
163. Kang KT, Chiu SN, Lin CY, Weng WC, Lee PL, Hsu WC. Effect of adenotonsillectomy on ambulatory blood pressure in pediatric obstructive sleep apnea: 6-month follow-up study. *Otolaryngol Head Neck Surg*. 2019;160:911–921. doi: 10.1177/0194599818825462
164. Hsu WC, Kang KT, Chiu SN, Weng WC, Lee PL, Lin CY. 24-hour ambulatory blood pressure after adenotonsillectomy in childhood sleep apnea. *J Pediatr*. 2018;199:112–117.e116. doi: 10.1016/j.jpeds.2018.03.072
165. Vlahandonis A, Walter LM, Horne RS. Does treatment of SDB in children improve cardiovascular outcome? *Sleep Med Rev*. 2013;17:75–85. doi: 10.1016/j.smrv.2012.04.004
166. Venekamp RP, Chandrasekharan D, Abel F, Blackshaw H, Kreis IA, Evans HER, Schilder AGM. Research into childhood obstructive sleep-disordered breathing: a systematic review. *Chest*. 2017;152:51–57. doi: 10.1016/j.chest.2016.12.001
167. Kuo YL, Kang KT, Chiu SN, Weng WC, Lee PL, Hsu WC. Blood pressure after surgery among obese and nonobese children with obstructive sleep apnea. *Otolaryngol Head Neck Surg*. 2015;152:931–940. doi: 10.1177/0194599815573927
168. Chervin RD, Ruzicka DL, Giordani BJ, Weatherly RA, Dillon JE, Hodges EK, Marcus CL, Guire KE. Sleep-disordered breathing, behavior, and cognition in children before and after adenotonsillectomy. *Pediatrics*. 2006;117:e769–e778. doi: 10.1542/peds.2005-1837
169. Kheirandish L, Goldbart AD, Gozal D. Intranasal steroids and oral leukotriene modifier therapy in residual sleep-disordered breathing after tonsillectomy and adenoidectomy in children. *Pediatrics*. 2006;117:e61–e66. doi: 10.1542/peds.2005-0795
170. Mitchell RB, Archer SM, Ishman SL, Rosenfeld RM, Coles S, Finestone SA, Friedman NR, Giordano T, Hildrew DM, Kim TW, et al. Clinical practice guideline: tonsillectomy in children (update). *Otolaryngol Head Neck Surg*. 2019;160:S1–S42. doi: 10.1177/0194599818801757