AMERICAN THORACIC SOCIETY DOCUMENTS

Management of Persistent, Post-adenotonsillectomy Obstructive Sleep Apnea in Children

An Official American Thoracic Society Clinical Practice Guideline

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Abstract

Background: Obstructive sleep apnea (OSA) is the most common sleep-related breathing disorder. Although adenotonsillectomy is first-line management for pediatric OSA, up to 40% of children may have persistent OSA. This document provides an evidence-based clinical practice guideline on the management of children with persistent OSA. The target audience is clinicians, including physicians, dentists, and allied health professionals, caring for children with OSA.

Methods: A multidisciplinary international panel of experts was convened to determine key unanswered questions regarding the management of persistent pediatric OSA. We conducted a systematic review of the relevant literature. The Grading of Recommendations, Assessment, Development, and Evaluation approach was used to rate the quality of evidence and the strength of the clinical recommendations. The panel members considered the strength of each recommendation and evaluated the benefits and risks of applying the intervention. In formulating the recommendations, the panel considered patient and caregiver values, the cost of care, and feasibility.

Results: Recommendations were developed for six management options for persistent OSA.

Conclusions: The panel developed recommendations for the management of persistent pediatric OSA based on limited evidence and expert opinion. Important areas for future research were identified for each recommendation.

Keywords: pediatrics; OSA

Overview

The purpose of this guideline is to assess currently available evidence, combined with expert opinion, to provide best practice and evidence-based management guidelines for children with persistent (after adenotonsillectomy) obstructive sleep apnea (OSA). A summary of recommendations follows, with full descriptions of the evidence profile and assessment of that evidence later in the document.

Recommendations

1. We suggest that children with persistent OSA who do not qualify for site-specific upper airway treatment may be considered candidates for treatment with continuous positive airway pressure (CPAP) (conditional recommendation, very low certainty in the estimates of the effect).
2. We suggest that children with persistent OSA with specific craniofacial features may be considered candidates for orthodontic and dentofacial orthopedic treatment (conditional recommendation, very low certainty in the estimates of the effect).
3. We suggest that children with persistent OSA who are overweight or obese undergo weight loss intervention (conditional recommendation, very low certainty in the estimates of the effect).
4. We suggest that children with persistent OSA with lingual tonsillar hypertrophy may be considered candidates for

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Contents

lingual tonsillectomy (conditional recommendation, very low certainty in the estimates of the effect).

5. We suggest that children with persistent OSA and sleep dependent laryngomalacia be considered candidates for supraglottoplasty (conditional recommendation, very low certainty in the estimates of the effect).
6. We suggest that children with persistent OSA who are on intranasal steroids be, may be treated with montelukast (conditional recommendation, very low certainty in the estimates of the effect).

Introduction

OSA is characterized by repeated episodes of upper airway obstruction during sleep. It is the most common sleep-related breathing disorder, prevalent in up to 5% of children. It is an independent risk factor for neurocognitive, cardiovascular, and metabolic sequelae (1) and, when untreated, is associated with neurocognitive deficits, behavioral changes, low academic performance, and lower quality of life (QOL) (1, 2). Although adenotonsillectomy (AT) is first-line management for pediatric OSA (3, 4), up to 40% of children may have persistent OSA (herein defined as OSA that persists despite AT), leaving 2% of all children at risk for this condition (5). The prevalence is particularly high in those with baseline severe OSA—defined as an obstructive apnea–hypopnea index (oAHI) $\geq$ 10/h (10–15% prevalence), obesity (50% prevalence), underlying medical complexities (chronic cardiopulmonary and neuromuscular disorders), and genetic disorders (50% prevalence in Down syndrome) (3, 5–7). With the global epidemic of childhood obesity and the improving survival of children with medical complexities, there are a significant and increasing number of children with persistent, severe, and untreated OSA (as AT has a low cure rate in these children) entering adulthood and posing a significant public health concern.

Currently, two guidelines addressing persistent OSA management are the 2012 American Academy of Pediatrics (AAP) and the 2015 Pediatric Society of New Zealand clinical practice guidelines on management of pediatric OSA, which recommend CPAP for children with persistent OSA (3, 8). The AAP guideline was limited to otherwise healthy children treated in the primary care setting, thus excluding the growing cohort of children with medical complexity and comorbid OSA. Moreover, this guideline did not address other non-CPAP treatment options for persistent OSA. Since the publication of these guidelines, there is new and emerging evidence regarding non-CPAP therapies for persistent OSA management.

There are multiple reasons to focus on non-CPAP therapies for these children, including the following.

- The AAP CPAP recommendation was based on low-quality evidence (three small retrospective studies) (9–11).
- Adherence to CPAP therapy is low, particularly in children with medical complexity (30–75% overall adherence) (12, 13).
- There are concerns about CPAP use leading to aerosolization to family members, first highlighted during the coronavirus disease (COVID-19) pandemic.
- Studies suggest that long-term use of CPAP in children (particularly those who are compliant) can lead to a negative impact on midface growth and dental anatomy (14, 15).
- Evidence suggests that OSA remission is seen in only 30% of children as they reach adulthood, thus contributing to the huge medical burden of OSA in adults (16).
- Despite a lack of evidence-based guidelines, clinicians frequently prescribe non-CPAP treatment options for persistent OSA, including upper airway surgeries, orthodontic treatment, and medical therapy (17–19).
- Additional guidance is needed to inform shared decision making.

Herein, we appraised currently available evidence in a robust and systematic fashion. Our goal was to improve the quality of care by providing evidence-based recommendations, coupled with expert opinion, for management of children with persistent OSA. In addition, as the sleep community progresses to phenotyping and personalized management of OSA, formal guidance is needed to address two key

clinical questions: *1*) should CPAP be the primary option for children with surgically modifiable or correctable causes of persistent OSA? And *2*) what are the treatment options for persistent OSA in children who are not adherent to CPAP?

Use of This Guideline

This guideline was developed to inform clinicians, patients, and other stakeholders regarding the management of persistent OSA focusing on questions that address significant management issues. As the first guideline for children with persistent OSA, we also highlighted known gaps in the literature to encourage further research in this area. These guidelines are not intended to impose a standard of care. They provide the basis for rational decisions in the management of persistent OSA in children. Clinicians, patients, third-party payers, institutional review committees, other stakeholders, and/or the courts should never view these recommendations as dictates. No guidelines and recommendations can take into account all of the often-compelling unique individual clinical circumstances. Therefore, no one charged with evaluating clinicians' actions should attempt to apply the recommendations from these guidelines by rote or in a blanket fashion. Statements about the underlying values and preferences as well as qualifying remarks accompanying each recommendation are its integral parts and serve to facilitate more accurate interpretation. They should never be omitted when quoting or translating recommendations from these guidelines.

Definition of Persistent OSA

It is debatable whether a single parameter can determine the severity of OSA. Nevertheless, oAHI cutoffs from in-laboratory polysomnography (PSG) are often used to dictate care. The oAHI corresponds to the sum of obstructive apneas, mixed apneas, and hypopneas per hour of total sleep time (central apneas not included). The panel voted to determine the appropriate oAHI cutoff for diagnosis. Persistent OSA was defined as an oAHI ≥ 1 event/h. For oAHI ≥ 1 and <5 events/h (mild OSA), the literature reported on the use of antiinflammatory medications (intranasal steroids with or without montelukast), whereas treatment with CPAP or surgery was typically reserved for those with persistent symptoms or oAHI ≥ 5 events/h (20, 21). Because there is limited guidance for management options and a higher risk of neurocognitive sequela in children with oAHI > 5 events/h (1), the panel focused their attention on this population, except for the assessment of antiinflammatory medication use. Of note, for the search strategy, if the authors only reported the AHI, then oAHI was not used.

Target Population

The target population for this guideline was children under 18 years of age with persistent OSA, regardless of race, comorbidity, or other demographic attributes. Because current studies typically include a mix of children with and without comorbid medication conditions, there were no patient-level exclusions.

Methods

This guideline was developed using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach in accordance with American Thoracic Society (ATS) policies and procedures (22). The systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement (23).

Committee Composition

The guideline proposal submitted by the two co-chairs (Z.E. and S.L.I.) was selected by the ATS Documents Development and Implementation Committee during the guideline proposal application cycle of 2020. The project was approved by the ATS Board of Directors. The guideline panel included 13 international experts from key multidisciplinary specialties, including otolaryngology, dentistry, pediatric sleep medicine, plastic surgery, and nursing, with expertise in pediatric OSA. A senior ATS methodologist (I.S.) and an ATS methodology scholar (A.T.N.H.) were appointed to assist the panel, with the help of a medical librarian (K.S.).

Confidentiality Agreement and Conflict of Interest Management

All committee members disclosed potential conflicts of interest before all meetings, which were reviewed by the ATS Conflict of Interest Department. F.R.A. is on the clinical advisory board of Somnomed, a company that produces OA for adults. There were no conflicts of interest identified for the rest of the panel. Funding and guidance were provided by ATS. However, ATS did not influence the topic of discussion or the recommendations in the guideline.

Meetings

All meetings were held via video conference from March 2021 to October 2022 and were recorded. Additional meetings were held by the methodologists and the co-chairs as needed.

Formulating Clinical Questions

Sixteen questions, in the patient, intervention, comparison, outcome (PICO) format were initially proposed (*see* Table E13 in the online supplement). After priority ranking using a 9-point scale, six were selected as key questions to be addressed. For each question, the panel selected and prioritized a list of clinically important and patient-centric outcomes *a priori*. These were ranked from 1 to 9 (score of 7–9 considered critical, score of 4–6 important, and score <4 having limited importance). Only critical and important outcomes were evaluated (GRADE approach). These included resolution of OSA (reduction in oAHI < 1 event/h), improvement of OSA (improvement in oAHI to <5 events/h), QOL, cognitive function, behavioral changes, adverse events, and weight loss (for the weight loss question). Important outcomes included mood, weight changes, snoring, daytime sleepiness, and oxygen desaturation.

Literature Search

The panel proposed a list of search terms based on the key questions. With the assistance of the medical librarian, a literature search for each key question was performed on Medline, EMBASE, Scopus, CINAHL, and the Cochrane Database of Systematic Reviews using search strategies agreed on by the expert panel. The methodologist team screened the titles and abstracts based on the inclusion criteria in duplicate. Case reports, narrative reviews, and expert opinions were excluded. Because of a limited number of studies on interventions in children with persistent OSA, studies with at least 10 patients, at least 75% of whom were post-AT, were included. Any conflict was resolved via discussion. Relevant full-text articles were reviewed. The list of the final studies was confirmed with the expert panel to ensure there were no missing studies and to obtain any studies not found on literature review. Details on the number of studies screened are provided in the online supplement (Figures E1–E6).

Evidence Review and Development of Clinical Recommendations

Data were extracted from relevant studies. If there were adequate data that could be pooled, the Cochrane Collaboration Review Manager Software, version 5.3 was used to perform a meta-analysis. When meta-analysis was not possible, a narrative review was performed. Risk of bias was determined using the Cochrane risk of bias in nonrandomized studies of interventions tool (ROBINS-I) (4).

There were no eligible studies found for PICO question 3 (Should obese children with persistent OSA undergo weight loss intervention?). The methodology team performed a pragmatic review of weight loss interventions in children with OSA without a history of AT. Two systematic reviews (24, 25) were found and appraised using the Documentation Appraisal Review Tool (5). All full-text studies included in the two systematic reviews were retrieved, and data were extracted directly from the studies.

Based on the GRADE approach, a summary of evidence was presented to the expert panel using the GRADEpro Guideline Development Tool online application (https://www.gradepro.org/) (26). The certainty of evidence for each outcome was classified as high, moderate, low, or very low. The panelists reviewed the evidence and formulated the recommendations for each question using the evidence to decision framework (7). This was based on discussions of the balance of desirable and undesirable effects, the certainty of the evidence, patient's values, resources needed, cost-effectiveness, effect on health equity, acceptability, and feasibility of the intervention. The recommendations were finalized and approved after the panel voted on their direction and strength. The term "we recommend" is used for strong recommendations, and "we suggest" is used for weak or conditional recommendations. Evidence quality and implications of the different degrees of recommendation are described in Tables E14 and E15.

Manuscript Preparation

The initial manuscript was prepared by the two co-chairs and the panel members, reviewed by the entire panel, and, after achieving consensus, it was submitted for external peer review. The guideline was reviewed anonymously by content experts and one methodologist. After revision, it was reviewed and approved by a multidisciplinary board of directors.

Recommendations

Question 1: Should children with persistent OSA be treated with CPAP?

Background. CPAP has traditionally been the default treatment option for pediatric OSA (both surgically naive and after AT). When used appropriately and consistently, it is effective in improving OSA-related symptoms, disease severity (as measured by the oAHI), sleep architecture, and sleep quality, and mitigating neurocognitive and behavioral sequelae. The impact of treatment on blood pressure, cardiovascular stress, and metabolic dysfunction is less certain (27).

Barriers to CPAP include poor adherence due to mask fit/side effects from wear, and intolerance to pressure. Over the past decade, there has been a paradigm shift in the management of persistent OSA as alternate treatment options have emerged and gained favor in children who do not tolerate or are not ideal candidates for CPAP (28). For children with persistent OSA who have surgically modifiable sites of upper airway obstruction, surgery may improve or resolve OSA—an appealing tradeoff to CPAP, which is often a long-term or lifelong commitment to therapy. However, long-term data regarding surgical outcomes, as well as ongoing CPAP compliance, are needed to best inform these decisions. Considering this, we focused on the use of CPAP, to determine whether therapy impacts critical and important outcomes.

Summary of the evidence (includes description of evidence and quality). We identified four observational studies reporting CPAP use in persistent OSA. Primary outcomes of therapy were not uniform across studies. One study reported on the resolution of OSA, stating that 26 of 73 children "no longer required CPAP"; it was not stated if PSG was performed to confirm this (11). One study assessed improvement in OSA severity (defined as an oAHI < 5 events/h after treatment) and reported that 101 of 109 children had an improvement in oAHI. Median follow-up was 110 days (interquartile range [IQR], 55–182 d) (29). Three studies reported an improvement in OSA severity (using the oAHI) as an outcome measure. One reported a decrease in oAHI from a median (IQR) of 12.1 (7.6–21.5) events/h to 0.8 (0.2–2) events/h. Different modes of PAP were used in 109 patients: 10% used bilevel, 11% used autotitrating PAP, and 79% used CPAP (29). Another reported a decrease in AHI from a mean $\pm$ SD of 28.4 $\pm$ 31.8 to 8 $\pm$ 4.1 events/h, where 32% ($n = 46$) of children used bilevel and 68% were on CPAP (30). The third study assessed different modes of PAP therapy and reported that 12/13 children using CPAP had a decrease in mean AHI from 22 $\pm$ 11 to 2 $\pm$ 3 events/h. Data from 39/43 children on Bi-Flex showed a decrease in mean AHI from 18 $\pm$ 15 to 2 $\pm$ 2 events/h (31).

Only one study reported on the impact of PAP (CPAP and bilevel) on cognitive function and behavioral problems. In this study cohort of 41 children, 13 (32%) had deteriorating school performance. After starting PAP therapy, improvement was seen for all 37 patients for whom data were available. The authors also reported that 8/45 children (18%) had hyperactivity or behavioral problems, which decreased to 3/44 children (7%) after starting PAP therapy (30).

Adverse events were reported in three studies. One reported that 11/46 (24%) children had adverse events, mainly due to mask fit (30). Waters and colleagues reported 8/32 (25%) children had CO_2 retention or increased central apneas, and 16 reported CPAP nonacceptance (8 parental and 8 child nontolerance). Other adverse effects, each reported in one child, were induced breathing disorder, inadvertent high pressure, and provider nonacceptance (11). Marcus and colleagues reported that none of the patients recruited had serious complications (31).

Cielo and colleagues reported oxygen saturation increased from a median (IQR) of 87% (79–89%) to 93% (92–95%) in 109 patients (29). Although Uong and colleagues reported a mean saturation increase from of 75.7% $\pm$ 15.2% to 87.8% $\pm$ 8.1% in 44 children (30). Marcus and colleagues reported an increase in oxygen saturation from 81% $\pm$ 12% to 92% $\pm$ 3% in 12/13 patients on CPAP and from 78% $\pm$ 13% to 90% $\pm$ 4% in 43/49 patients on Bi-Flex (31).

Only one study reported on the resolution of snoring. Uong and colleagues reported 41/46 children had snoring complaint, and all resolved (data available for 45 children) after starting PAP therapy (30).

Uong and colleagues reported 40/45 children suffered from excessive daytime sleepiness, which decreased to 3/44 children after starting PAP (30). Marcus and colleagues reported Epworth sleepiness scale results for PAP, which decreased from 8 $\pm$ 5 to 6 $\pm$ 3 for 12/13 children on CPAP

and from 10 ± 6 to 5 ± 5 for 43/39 children on Bi-Flex (31).

We did not find any literature describing the outcomes of mood and QOL in children with persistent OSA treated with CPAP.

Certainty assessment (risk of bias) has been provided in the evidence profile (Table E1). With no Randomized Controlled Trial evaluating the use of CPAP versus no CPAP for children with persistent OSA, the panel's confidence in the accuracy of these estimated effects of CPAP on the critical outcomes was very low. Given the limited availability of pediatric data, this recommendation is based on the presented data as well as extrapolation from adult data.

Adherence to CPAP was not uniformly defined in included studies. Cielo and colleagues reported the percentage of nights with CPAP use (including use >4 h/night) and duration (minutes) of CPAP used per night (29). Uong and colleagues defined adherence using adult criteria—CPAP use of >4 h/night of use and ⩾5 nights/wk (30). Marcus and colleagues used the mean number of minutes used per night as a primary measure of adherence (31). Waters and colleagues did not define adherence in their cohort (11).

ATS Recommendation 1: We suggest that children with persistent OSA who do not qualify for site-specific upper airway treatment may be considered candidates for treatment with CPAP (conditional recommendation, very low certainty in the estimates of the effect).

Justification and implementation. The panel suggests a collaborative approach when evaluating children with persistent OSA to determine the most suitable treatment options. This is best accomplished with a multidisciplinary team. A drug-induced sleep endoscopy (DISE) with other imaging modalities as available (cine magnetic resonance imaging [MRI] or orthodontic evaluation, for example) may be considered if CPAP is not desired, adherence is poor, or surgically modifiable sites of airway obstruction are suspected. This recommendation places a high priority on the need to identify upper airway abnormalities that are amenable to surgery and/or orthodontic care.

Once the decision to use CPAP is made, physicians must determine the need for an in-laboratory titration study (based on availability or if partial response occurs after autoadjusting CPAP) versus empiric autoadjusting CPAP therapy (e.g., healthy adolescents). The panel suggests regular download of CPAP data to assess adherence and clinical visits to assess facial appearance/growth and side effects.

After starting CPAP, an initial visit within 30–90 days (preferably within a few weeks) is recommended. There is variation in practice for follow-up visits, which is based on tolerability/adherence (and within the United States, at times, determined by third-party payor types). For children who have a partial response or have adherence issues, a behavioral psychologist may also be useful. CPAP coordinators/liaisons may be helpful in monitoring patients. Based on the panel's experience, providing CPAP may be challenging in resource-limited countries or regions.

In general, adherence reported in the literature has not accounted for the duration of nighttime sleep in children (32–40); this is surprising because of the importance of sleep for a developing child. To this effect, the recent European Respiratory Society statement on chronic CPAP and non invasive ventilation use in children decided that the use of CPAP/noninvasive ventilation during the entire sleep time should be the goal (27). Numerous predictors of adherence have been identified (27) and can be identified using the Adherence Barriers to CPAP questionnaire (35). Several strategies/tools can be used to improve adherence and include behavioral therapy (41), therapeutic education sessions by a respiratory therapist (38), token economy (42), medical hypnosis (43), and shared decision-making tools (44). It is critical to heavily focus on patient and caregiver education from the start of CPAP therapy, as early successful use is associated with long-term success. Patients should therefore be enrolled in an intensive follow-up program in the first weeks after initiation.

Desirable consequences and their magnitude. Although the data are limited, the panel determined the anticipated desirable effects are large, particularly if data from adults are extrapolated. Significant improvements in school performance and decrease in daytime somnolence has been reported in children with persistent OSA adherent to CPAP (30).

Undesirable consequences and their magnitude. The panel determined that, in general, the undesirable effects of CPAP are small. However, some (rare) side effects may not be as trivial. Children may experience facial ulcers that require delay in treatment and mask refitting. The impact on facial growth is a concern, particularly in those with good adherence to therapy; however, there are limited data published in this regard, and it is focused on patients with prolonged PAP use, such as children with craniofacial malformation and spinal muscular atrophy (15). Facial deformities have been described in children using chronic CPAP, especially after initiation in infancy and in certain underlying conditions that already favor these abnormalities. Fauroux and colleagues described a prevalence of 68% of global facial flattening in their cohort (45). This deformity was more common in patients with OSA or neuromuscular disease. Maxillary retrusion was observed in 37% of the patients, whereas most of these patients had an underlying disease that could favor maxillary retrusion. Daily use (>10 h/d) was associated with this complication (45). Roberts and colleagues compared a cohort of compliant and noncompliant pediatric patients on CPAP therapy and demonstrated that CPAP-adherent children experienced a negative mean annual change (retrusion) of the midface compared with forward growth in noncompliant subjects (15).

Values and preferences. There are no data on family/patient preferences related to CPAP for this population. Most patients/caregivers may have decisional conflicts about the efficacy of the treatment options, whether CPAP or surgery, and it may affect the acceptability of the interventions. The panel agreed that every patient's family will value the benefit but may disagree as to their child's ability to use CPAP. Acceptance may be low if parents/patients rely on previous experience from family members or friends. Alternatively, for families of children with craniofacial abnormalities, CPAP may be a more acceptable option when compared with the alternative of facial surgery.

Cost/implementation. There are no data regarding costs or cost-effectiveness of CPAP therapy for children with persistent OSA. The cost of therapy varies worldwide and is largely dependent on device/mask and payor type. The panel believed the cost may be significant, as treatment is long term. Moreover, if there are other options for treatment (e.g., surgery), the cost-effectiveness of CPAP may be lower. As such, CPAP is cost-effective if it is the only viable treatment option.

If coverage is provided by insurance, proof of "good" adherence to the therapy is typically required. Currently, insurance

companies use adult criteria for determining adherence, which further complicates things (46). Even if covered, the supplies are expensive and often require repeated out-of-pocket costs. For children with craniofacial abnormalities, some patients may not be able to find a good-fitting mask, and custom masks are not easy to obtain.

Within the United States and worldwide, inequities exist regarding access to specialists, sleep laboratories, centers for pediatric mask fitting, or home care services. The importance of access to centers with pediatric-specific expertise is higher for children with persistent OSA, who often have medical complexities. In regions with limited access to PSG, treatment with autoadjusting CPAP is encouraged/preferred. Last, at the time of writing, there are large supply chain issues with obtaining CPAP machines, and there has been a global recall on some devices, which has significantly impacted availability (47).

What others are saying. The AAP and the Pediatric Society of New Zealand both recommend the use of CPAP in children with persistent OSA (3, 8).

Remarks/future research opportunities. There is a need for:

- Well-designed studies examining short- and long-term adherence to treatment, with a particular focus on what constitutes acceptable adherence in children.
- Large, multicenter studies focusing on outcomes that have not been adequately targeted (QOL, mood, weight changes, cognitive function, behavioral changes, adverse events, snoring, sleepiness [subjective and Epworth sleepiness scale], oxygen saturation).
- A focus on the long-term impact of CPAP masks on facial growth and the use of custom masks.
- Comparative effectiveness data and cost-effectiveness of CPAP compared with other therapies
- Standardization of variables used to define OSA, such as AHI, oAHI, and respiratory disturbance index, as well as pediatric definitions for effectiveness and adherence.

Question 2: Should children with persistent OSA undergo orthodontic/dentofacial orthopedic treatment?

Background. Rapid maxillary expansion (RME) therapy has been used since 1860 to correct maxillary constriction (also known as transverse maxillary deficiency), which is often clinically manifested as a crossbite. The prevalence of posterior crossbite varies depending on the assessment criteria but can range between 8% and 22% (48). RME is often performed using a cemented intraoral orthopedic appliance, ideally before puberty and after permanent first molars have erupted (typically 6–7 years of age). Activation of the expander screw lasts from 1 to 2 weeks, and the device remains in place for a few more weeks, without activation, to consolidate the expansion achieved. Early treatments are preferred. Of note, maxillary/mandibular advancement surgery is often used to treat pediatric OSA with or without concurrent maxillary expansion; however, the role of bony skeletal surgery is not addressed in this question.

Summary of the evidence (includes description of evidence and quality). We identified two observational studies on maxillary expansion in persistent OSA (Table E2). Guilleminault and colleagues conducted a randomized crossover trial of AT and maxillary expansion (49) in 31 children (average age, 6.5 yr) with enlarged tonsils and narrow maxilla associated with a high and narrow palate. For the purpose of this review, we describe the 16 children who started the trial with AT. Four weeks after AT, the AHI dropped from 12.5 to 4.9 events/h and further decreased to 0.9 after 3 months of maxillary expansion (appliance still in place).

In a retrospective assessment of children who had AT and RME by Guilleminault and colleagues, AT was performed in 601 children, and 377 were considered cured. Of the 224 children with persistent OSA, 121 underwent RME, although only 29 reported follow-ups at pubertal stages. Of these 29 children, the mean age at follow-up was 14.4 years (9 girls and 20 boys), the baseline AHI was 9 events/h, AHI after AT was 3 events/h, and AHI after RME was 0.5 events/h. At the pubertal assessment, nine (seven girls and two boys) children were asymptomatic (mean AHI, 0.5 events/h), and five had loud snoring (mean AHI, 3.1 events/h), with flow limitation and mouth breathing during sleep also seen (49).

School performance was reported in 15/29 children in one study; however, no baseline was reported. Snoring improved in 24/29. Adverse events of RME were also reported. Inability to make clicking sounds with the tongue was reported in 18/29, 15 were unable to protrude their tongue up toward their nose, 6 had difficulties holding a button between their lips, and 2 had difficulty swallowing liquids (50).

When combined, the mean improvement in AHI was 3.3 events/h (95% Confidence interval [CI], 1.8–4.8 events/h), whereas oxygen saturation improved by 2.8% (95% CI, 2.3–3.5%) after RME (49, 50).

We did not find any literature describing the outcomes of OSA resolution, QOL, behavioral changes, mood, weight, or daytime sleepiness in children with persistent OSA treated with RME.

ATS Recommendation 2: We suggest that children with persistent OSA with specific craniofacial features may be considered candidates for orthodontic/dentofacial orthopedic treatment (conditional recommendation, very low certainty in the estimates of the effect). The panel believed these children must also have an indication for orthodontic treatment based on a constricted maxilla (high and narrow palate, and often, but not always, posterior crossbite) and that RME be the preferred therapy.

Justification and implementation. The panel suggests children with persistent OSA be evaluated for maxillary constriction and referred to the appropriate orthodontist/dentofacial specialist for ongoing care if a deficiency is suspected. This is typically best addressed between 6 and 13 years of age. A crossbite may be a diagnostic clue to look for in the nonspecialist's office. Once appropriate evaluation is performed (detailed oral exam, imaging), a decision can be made whether the child is a good candidate for RME. In children with a narrow maxilla and OSA who have access to an orthodontist and dental coverage, as well as behavioral and homecare allowing them to receive the treatment, RME provides a favorable risk-to-benefit profile.

Desirable consequences and their magnitude. RME in children with maxillary constriction leads to a small improvement in OSA in patients with persistent OSA after AT (mean reduction of 3.3 events/h). Additional retrospective research in children with mild to moderate OSA and maxillary transverse hypoplasia demonstrates a more significant improvement of OSA, but the study population and previous treatment are poorly described (51). The panel concluded that if data are extrapolated from children with mild to moderate OSA with narrow maxilla/maxillary transverse hypoplasia/maxillary

constriction, there is a moderate improvement expected.

Undesirable consequences and their magnitude. The undesirable effects of RME include alterations in tongue and lip function, difficulty drinking quickly, inflammation of the gums/palate, speech difficulty, and difficulties with cleaning the appliance. Because these effects are transient in nature and this therapy is very commonly prescribed and tolerated for patients without OSA, these effects are considered trivial.

Values and preferences. Children with behavioral issues may have difficulty tolerating RME. Cooperation from the child and the need for parental supervision and assistance can make the proper implementation of home care and expansion difficult.

Cost/implementation. There are no published studies regarding the cost of RME for pediatric OSA. In the United States, this is typically considered a dental intervention; thus, medical insurance will usually not cover the cost, but dental insurance may. One should expect high initial costs for establishing care with an orthodontist and for treatment (expenses may range from $2,000 to $4,000, depending on location and other factors). In addition, orthodontic treatments (e.g., RME) may have a maximum lifetime limit, and future orthodontic costs may not be fully covered by insurance in some countries.

What others are saying. There are no existing guidelines specifically focusing on RME in the context of persistent OSA in children.

Remarks/future research opportunities. There is a need for:

- Larger studies determining the role of RME in persistent OSA specifically assessing its role for children with obesity and those with genetic and craniofacial syndromes.
- Comparative effectiveness studies assessing the impact in children with and without maxillary constriction.
- Future studies with outcome measurements (QOL, behavioral changes, mood, daytime sleepiness, weight changes) as well as cost-effectiveness analysis.
- Studies comparing RME to slow maxillary expansion and in combination with functional jaw orthopedic appliance and/or myofunctional therapy.
- Prospective studies including outcomes (benefits/risks) in younger children (<6 yr) focused on the efficacy of maxillary expansion compared with normal growth.
- Prospective studies comparing preadolescent RME efficacy with or without AT.
- Studies on orthopedic mandibular advancement for children with retropositioned mandibles and OSA with or without AT.

Question 3: Should children with obesity and persistent OSA undergo weight loss intervention?

Background. AT is associated with high failure rates in children with obesity (52). Although up to 76% of children with obesity have persistent OSA, only 15–37% of nonobese children have persistent OSA (25). The definition of obesity and overweight were based on current CDC guidance (53).

Summary of the evidence (includes description of evidence and quality). There are no randomized controlled trials that evaluate the efficacy of medical or surgical weight loss interventions for persistent OSA in children with obesity. We identified 12 observational studies that evaluated the effect of medical (8 studies) or surgical weight loss (4 studies) in children with OSA who had not undergone AT. Data were present for five outcomes of interest and could not be pooled for all outcomes because of differences in defining the outcomes (Table E3).

Three studies reported resolution of OSA by medical weight-loss interventions. Roche and colleagues reported in 2019 that 6/13 (46%) children with OSA who enrolled in a 9-month-long residential weight-loss program had resolution of OSA (defined as oAHI $<$ 2 events/h) (54). A second study reported resolution of OSA (defined as AHI $<$ 2 events/h) in 11/20 (55%) children with obesity who underwent a 9- to 12-month multidisciplinary weight-loss program (55); however, the degree of overlap between studies is unclear. Van Eyck and colleagues (56) reported resolution of OSA (defined as oxygen desaturation index $<$ 2 events/h) in 63/79 (80%) children with obesity who underwent a multidisciplinary weight-loss program over 6 months (ITT, 58%; 108 patients recruited).

Six studies reported an improvement in AHI after medical weight loss, with two specifically reporting AHI $<$ 5 events/h. Verhulst and colleagues reported that 19/21 (90%) children who enrolled in a residential multidisciplinary weight-loss program for 6 months had a decrease in AHI to $<$5 events/h (57). Corgosinho and colleagues reported that 8/12 (66.6%) children who underwent an outpatient multidisciplinary weight-loss program for 1 year had a decrease in AHI to $<$5 events/h as well as a reduction in median AHI (range) from 11.6 (6.2–22.6) to 2.3 (0.4–13.8) events/h ($P < 0.05$) (58). Siegfried and colleagues reported a nonsignificant reduction in mean respiratory disturbance index from 4.1 $\pm$ 4.9 to 3.3 $\pm$ 3.0 events/h in 38 children who participated in a residential weight-loss program over 5.9 $\pm$ 1.6 months (59). Roche and colleagues reported in 2018 a nonsignificant reduction in mean AHI from 2.7 $\pm$ 3.4 to 2.3 $\pm$ 2.5 events/h ($P = 0.32$) in 24 patients who participated in a 9-month residential weight-loss program and a reduction in mean AHI from 6.2 $\pm$ 4.9 to 3.0 $\pm$ 3.9 events/h ($P < 0.01$) in 20 patients who underwent a 9- to 12-month weight-loss program (60). Van Hoorenbeeck and colleagues reported in 2013 a reduction in median AHI (range) from 2.2 (0.0–58.3) to 0.87 (0.0–27.7) events/h ($P < 0.001$) in 50/68 patients who underwent a multidisciplinary weight-loss program over 4.1 to 6 months (61).

Three studies reported resolution of OSA by surgical interventions. Alqahtani and colleagues reported OSA remission (based on pediatric sleep questionnaire [PSQ] scores) for 98 patients (aged 5–21 yr) who underwent sleeve gastrectomy as 81% (80/98) at 6 months, as defined by improvement in PSQ scores (62). OSA was defined as AHI $>$ 2 events/h and PSQ = 0.33. These authors also reported that 15/98 (15.3%) patients had "improvement" of OSA at 6 months, defined as improvement in PSQ score. Kalra and colleagues performed laparoscopic Roux-en-Y gastric bypass on 25 children. Ninety percent (9/10) had improvement of AHI to $<$5 events/h and reduction in median AHI from 9.1 to 0.65 events/h ($P < 0.01$) (63). In a 2020 study of 59 adolescents (age 17.7 $\pm$ 1.5 yr), 54% had OSA and 69% had resolution of OSA at 1-year follow-up after laparoscopic adjustable gastric banding, with a concomitant significant decrease in body mass index (BMI) (40.9 $\pm$ 6.4 vs. 34.4 $\pm$ 6.3 kg/m^2) (64). A retrospective review of 81 patients (age 16.9 $\pm$ 2.0 yr) who underwent bariatric surgery showed a baseline OSA prevalence of 54% (oAHI

> 5 events/h) (65). Of the 23 patients with a postsurgery PSG results, 66% had remission of OSA and were noted to have a lower mean presurgery BMI and weight than nonresponders.

No studies reported adverse events for medical weight loss. One study reported adverse events for sleeve gastrectomy ($n = 226$, aged 5–21 yr); nine (3.98%) had adverse events (one bleeding, one readmission, two wound infections, one nausea and vomiting, and four GERD). There were no reports of reoperation, mortality, leak, pulmonary embolism, or pneumonia.

Meta-analysis of studies focusing on medical weight loss reported a reduction in BMI, with a mean decrease of 6.63 kg/m^2 (95% CI, 9.82–3.45 kg/m^2), mean reduction in BMI *z*-score of 0.68 (95% CI, 1.03 to 0.33), and mean reduction in absolute weight of 11.53 kg (19.9–3.15 kg). Corgosinho and colleagues reported a decrease in median weight (range) from 107.3 kg (92.8–145.2 kg) to 93.8 kg (72–146.1 kg) ($P < 0.05$) in 12 adolescents who underwent a 1-year outpatient multidisciplinary weight-loss program (58).

Two studies reported weight loss after surgery. Alqahtani and colleagues reported a decrease in median (IQR) BMI after sleeve gastrectomy ($n = 226$, aged 5–21 yr) from 48.2 ± 10.1 to 34.8 ± 8.1 at 6 months. Mean BMI *z*-score decreased from 2.99 ± 0.4 to 2.4 ± 0.6 in the same time frame. Data for patients with OSA were not reported separately (62). Kalra and colleagues also reported a decrease in BMI from 60.8 ± 11.1 to 41.6 ± 9.5 ($P < 0.01$) 4 to 6 months after performing laparoscopic Roux-en-Y gastric bypass in 10 patients with OSA. Weight decreased from 173.1 ± 27.8 kg to 118.3 ± 21.7 kg ($P < 0.01$) (63).

Roche and colleagues reported in 2018 an increase in the snoring index for 24 patients with obesity undergoing multidisciplinary weight-loss intervention for 9 months (199 ± 183 to 238 ± 295 events/h) ($P = 0.33$) (60). No studies evaluated the impact of weight loss on cognitive function, behavioral changes, mood, or QOL metrics.

ATS Recommendation 3: We suggest that children with obesity and persistent OSA undergo weight-loss intervention (conditional recommendation, very low certainty in the estimates of the effect).

Justification and implementation. The panel suggests weight-loss interventions through diet, exercise, and behavioral modification ideally as part of a multidisciplinary weight-loss program in all obese children with persistent OSA. If weight loss is not achieved successfully, then consideration should be given to surgical weight loss for eligible children. This recommendation accounts for the fact that such expertise may not be available at all centers.

Desirable consequences and their magnitude. We are uncertain about the effect of weight loss on the treatment of persistent OSA in children, as there are no studies in this patient group, although the panel believed that extrapolating data from children with OSA before AT was reasonable. The potential for benefit to children with OSA and other comorbidities resulting from obesity versus the trivial side effects favor medical weight-loss interventions. However, in the available studies, intense residential and nonresidential programs were used; neither is readily available, and both are limited by cost/coverage and patient acceptance. For surgical interventions, data are very limited. The sustainability of weight loss after completion of either medical or surgical management is unknown.

Undesirable consequences and their magnitude. Adverse events from medical therapy are unreported in children who undergo weight-loss interventions, but these are likely trivial. The undesirable effects are small for surgical interventions. The number of adverse events in the surgical studies is small; this is supported by data from adult trials, which report few side effects using current surgical techniques (including sleeve gastrectomy). Roux-en-Y gastric bypass had more complications in terms of frequency and severity and is no longer the standard of care.

Values and preferences. Regardless of whether medical or surgical intervention is chosen, there is probably no important uncertainty about or variability in how much patients/caregivers value the main outcomes that were chosen. There may be cultural norms regarding weight (e.g., some Pacific Islander cultures) that may decrease acceptability for weight loss.

Insurance coverage for medical residential or nonresidential or surgical weight-loss programs may not be readily available. The potential of long-term benefit will have to be weighed against the costs associated with the interventions. Patient/family acceptance is also variable for residential or outpatient intense programs.

Cost/implementation. There were no cost-effectiveness studies identified. For medical interventions, there is limited availability of weight-loss programs, variable coverage of costs, and questionable sustainability once the program is completed. For surgical interventions, the main limitations are cost and surgical candidacy (comorbidities and ability to participate in lifestyle changes to maintain long-term results).

What others are saying. A European Respiratory Society Statement and an AAP guideline for the treatment of OSA in children recommend weight loss in addition to other therapy in children with OSA who are overweight or obese (66, 67).

Remarks/future research opportunities. There is a need for:

- Randomized controlled trials to evaluate the efficacy of medical and surgical weight-loss interventions in children for OSA resolution, QOL, OSA-related morbidity including metabolic data, long-term sustainability of weight loss, as well as cost-effectiveness.
- Studies of patients with Down syndrome undergoing either medical or surgical weight-loss programs.

Question 4: Should children with lingual tonsillar hypertrophy and persistent OSA undergo lingual tonsillectomy?

Background. Tongue-base obstruction caused by lingual tonsillar hypertrophy (LTH) is a common cause of persistent OSA. LTH is defined as ⩾50% airway obstruction (typically measured with DISE or imaging) and may cause the posterior tongue to prolapse and lead to persistent OSA in up to 85% of affected children (68). The lingual tonsil is a component of the Waldeyer ring of lymphoid tissue located at the base of the tongue, and its hypertrophy can result from lymphoid hyperplasia from prior AT, obesity, and/or laryngopharyngeal reflux (69–71). LTH is more common in children with comorbidities and is seen most frequently in children with Down syndrome (72).

LTH can be diagnosed by awake flexible laryngoscopy, plain neck X-rays, computed tomography, or MRI studies such as cine MRI (73). Awake flexible endoscopy and DISE are the preferred and most widely used

techniques to diagnose LTH (74, 75). Lingual tonsillectomy is performed transorally via direct or endoscopic access using radiofrequency ablation, suction cautery, or microdebridement (73). Lingual tonsillectomy can be performed as a stand-alone tongue procedure, with or without a midline glossectomy, or in addition to multilevel upper airway surgery.

Summary of the evidence. We identified eight studies that included 316 patients and reported data on five outcomes of interest (Table E4). Five studies ($n = 93$) reported resolution of oAHI to <1 event/h after lingual tonsillectomy, with a risk difference of 0.26 (95% CI, −0.03 to 0.54); most studies involved children with Down syndrome (76–80). Six studies ($n = 161$) reported an improvement in the severity of OSA (assessed with a reduction to AHI < 5 events/h), with a risk difference of 0.61 (0.37–0.85) (76–81). Five studies (143 children) reported on a change in mean AHI as a marker for severity of OSA, which was 6.6 events/h lower after surgery (4.7–8.5 events/h) (77–79, 81, 82).

Four studies reported adverse events. Abdel-Aziz and colleagues reported 3/16 children (19%) developed airway edema. None developed an infection, hemorrhage, or need for reintubation (76). DeMarcantonio and colleagues reported adverse events in 92 children with lingual tonsillectomy performed for OSA and recurrent tonsillitis as follows: nine ED visits, four hospitalizations, three decreased oral intake/dysphagia, four voice changes, four bleeding. There was no breakdown for complications for patients with OSA alone (78). Lin and Koltai reported 2/26 children (8%) developed adhesions between the epiglottis and tongue base (although some experts do not consider this an adverse event) (83). Skirko and colleagues reported 11/39 children (28%) developed minor obstruction requiring oxygen, and 1 (3%) had postoperative vomiting, 1 (3%) developed bleeding that spontaneously resolved, and 3 (8%) had dehydration (80).

Outcomes of daytime sleepiness, QOL, cognitive function, behavioral changes, and mood were not reported.

Overall, lingual tonsillectomy is associated with improvement in AHI in most children. However, studies to date have used PSG as the main outcomes measure and have not included QOL and behavior measures that would allow better evaluation of the clinical significance of reduction in AHI/improvements in hypoxemia. Furthermore, it is unknown if lingual tonsillectomy is only indicated for children with moderate to severe OSA or is also an option for children with mild OSA.

Recommendation 4: We suggest that children with lingual tonsillar hypertrophy and persistent OSA may be considered candidates for lingual tonsillectomy (conditional recommendation, very low certainty in the estimates of the effect).

Justification and implementation. This recommendation places a high priority on the need to identify LTH in children with persistent OSA, particularly if risk factors are present (e.g., Down syndrome). This can be done with awake nasopharyngoscopy, DISE, or imaging (cine MRI or computed tomography).

Desirable consequences and their magnitude. Lingual tonsillectomy leads to improvement of OSA, but complete resolution of OSA (AHI < 1) is infrequently reported and estimated to be only 20%. A mean AHI change of 6.6 is likely to improve all children from moderate to mild OSA and some children from severe to mild OSA, leading to approximately 50% of the population having mild persistent OSA. As such, most children will have less severe but persistent OSA after lingual tonsillectomy, with mild persistent OSA in approximately 50%.

Undesirable consequences and their magnitude. The undesirable consequences of lingual tonsillectomy include bleeding, voice changes, and decreased oral intake. These occur at a frequency like that seen with AT. None of the studies reported on long-term adverse outcomes, such as dysphagia.

Values and preferences. Children with and without comorbidities may have similar outcomes. Children who are overweight/obese or those with Down syndrome are expected to have the least improvement after lingual tonsillectomy. In the studies, the majority of obese children also had Down syndrome, and no data are available comparing obese to normal-weight children with or without Down syndrome. Of note, studies on lingual tonsillectomy in children without Down syndrome are limited. However, children with Down syndrome are more likely to have additional factors, making resolution of OSA in this population more difficult than in nonsyndromic children (i.e., midface hypoplasia and hypotonia with relative macroglossia). To this effect, the favorable outcomes from lingual tonsillectomy are encouraging, in that nonsyndromic children with LTH and no other airway obstruction may have equivalent if not improved outcomes. Weight loss/nutritional advice is advised before lingual tonsillectomy.

Cost/implementation. Costs are unknown and have not been reported. It is likely that the cost of lingual tonsillectomy is comparable to palatine tonsillectomy, including postoperative monitoring. The procedure does not require additional anesthesia or surgical expertise.

What others are saying. Weighing the risks and benefits, lingual tonsillectomy is an acceptable procedure/option in selected patients for key stakeholders.

Remarks/future research opportunities. There is a need for:

- Prospective multiinstitutional studies on outcomes of lingual tonsillectomy for children with persistent OSA.
- Future studies that include an ethnically diverse population of children to improve the external validity of the results.
- Long-term data on outcomes of lingual tonsillectomy beyond the first 6 months after surgery.

Question 5: Should children with obstruction at the supraglottis and persistent OSA undergo supraglottoplasty?

Background. Sleep-dependent laryngomalacia is preferentially diagnosed by DISE and is commonly caused by inspiratory collapse of redundant supra-arytenoidal mucosa (type 1 laryngomalacia) (81, 84). Sleep-dependent laryngomalacia is increasingly recognized as a cause of persistent OSA (17, 85). Sleep-dependent laryngomalacia is treated with supraglottoplasty, making it one of the most performed surgical interventions for children with persistent OSA (17).

Supraglottoplasty is performed under general anesthesia and includes division of shortened aryepiglottic folds and trimming of redundant supra-arytenoidal mucosa by either cold steel instruments, microdebrider, or laser (86). Immediate postoperative complications include respiratory distress, postoperative bleeding, feeding difficulties, and aspiration. Aspiration is uncommon and limited to children with neuromuscular disorders (87, 88). Long-term complications are rare and include supraglottic stenosis

and the possible need for revision surgery (89).

Studies on the outcomes of supraglottoplasty for congenital laryngomalacia and OSA show clinically meaningful improvements in PSG parameters (reduction in AHI and improvement in minimal oxygen saturation during sleep) (90). There are few studies on the outcome of supraglottoplasty alone in children with persistent OSA (90). These children usually undergo several procedures addressing multilevel upper airway obstruction, making the contribution of supraglottoplasty difficult to measure.

Summary of the evidence. We identified two published studies that met the inclusion criteria: Chan and colleagues (81) and Digoy and colleagues (91), including a total of 60 children (aged 6–55 mo) and four outcomes of interest (Table E5). Both studies reported a reduction in AHI after surgery. Chan and colleagues reported a decrease in mean AHI from 14.9 ± 2.8 to 4.9 ± 1.1, with 21/24 children (88%) showing an improvement in AHI (81). Digoy and colleagues reported a decrease in mean AHI from 13.3 ± 12.9 to 4.1 ± 5.0 ($P = 0.001$), with 33/36 children (92%) showing a decrease in AHI (91). Neither study specifically reported resolution of OSA as an outcome.

Chan and colleagues reported a mean oxygen saturation from 88% ± 1.2% at baseline to 88.8% ± 0.6% postoperatively (81). Digoy and colleagues reported a mean increase in oxygen saturation from 83.0% ± 8.6% to 86.5% ± 4.9% postoperatively ($P = 0.015$); 58% of patients experienced an increase in saturation (91). These improvements may be especially clinically relevant if the child has medical complexity, including cardiopulmonary comorbidity.

Snoring improvement was reported by Digoy and colleagues in 25/29 children (86%), with resolution in 15 and improvement in 10 (91).

Outcomes of daytime sleepiness, QOL, cognitive function, behavioral changes, and mood were not reported.

Adverse effects were only reported by Digoy and colleagues, with postoperative dysphagia in seven children, transient dysphagia in five, and dysphagia for >6 months in two others. Postoperative coughing and throat clearing were reported in three children (91).

Recommendation 5: We suggest that children with sleep-dependent laryngomalacia and persistent OSA may be considered candidates for supraglottoplasty (conditional recommendation, very low certainty in the estimates of the effect).

Justification and implementation. This recommendation places a high priority on the need to identify obstruction at the level of the supraglottis (sleep-dependent or congenital laryngomalacia) using DISE in children with persistent OSA.

Desirable consequences and their magnitude. The magnitude of the desirable consequences is difficult to judge, because we only identified two small, retrospective studies. Both studies reported an improvement in OSA severity (AHI and oxygen saturation) after supraglottoplasty.

Undesirable consequences and their magnitude. The undesirable consequences of supraglottoplasty (dysphagia) are usually transient and considered small. None of the studies reported on long-term adverse outcomes, such as supraglottic stenosis.

Values and preferences. For dysphagia, different populations (e.g., those at high risk of aspiration) may not benefit from supraglottoplasty. This complication was reported to be transient because of the surgery and should be part of shared decision making before obtaining consent. Cough is transient and should not be considered a reason to not proceed with a supraglottoplasty.

Cost/implementation. Costs are unknown. The authors believe that the cost of supraglottoplasty is comparable to tonsillectomy. Decisions regarding the need and environment for postoperative monitoring are determined by each institution. Access to a pediatric ICU or step-down unit/intermediate care may be required for high-risk patients (i.e., those with severe OSA or significant comorbidities or known preoperative hypercarbia).

The procedure does not require significant additional ear, nose, and throat expertise beyond initial training.

Safe swallowing ability should be assessed before discharge (may need speech swallow evaluation if persistent).

What others are saying. After considering the balance of benefit, surgical risk, and cost, supraglottoplasty is acceptable to key stake holders.

Remarks/future research opportunities. There is a need for:

- Data on the use of supraglottoplasty in children with persistent OSA.
- Studies of children with persistent OSA in whom supraglottoplasty is performed as the sole procedure rather than as part of a multilevel approach.
- Information on treatment outcomes in specific subgroups, such as children with comorbidities.
- Investigation of the effect of the procedure on cognitive function and behavior, daytime sleepiness, and QOL.
- Cost and cost-effectiveness studies of supraglottoplasty.

Question 6: Should children on intranasal steroids with persistent OSA after AT be treated with montelukast?

Background. Intranasal steroids and/or montelukast administered for 6 to 12 weeks have been used to decrease the severity of mild-to-moderate OSA in children before AT (66). Based on clinical experience with antiinflammatory medications in children who have not undergone AT, it has been speculated that intranasal steroids and/or montelukast administered after AT for persistent OSA may have beneficial effects on residual adenoidal tissue and upper airway mucosa inflammation (92, 93). It remains unclear whether children should be treated with intranasal steroids and montelukast or intranasal steroids alone. In 2020, the U.S. Food and Drug Administration (FDA) issued a black box warning stating serious behavior and mood-related changes with montelukast (Singulair and generics). Therefore, the panel believed this question was imperative to guide physicians on the use of montelukast in persistent OSA.

Summary of the evidence (includes description of evidence and quality). There are no randomized controlled trials comparing the efficacy of intranasal steroids in combination with montelukast to intranasal steroids only for persistent OSA. We identified one small observational study of children with mild OSA (AHI > 1 and <5) that recruited 22 study children (aged 2–10 yr) and 14 control subjects (94). They reported data on three outcomes of interest: severity of OSA, oxygen desaturation, and adverse events (Table E6). Participants were treated with montelukast and intranasal budesonide (open label) for 12 weeks, and PSG was repeated at the end of the course. Mean oAHI decreased from 3.9 ± 1.2 to 0.3 ± 0.3 events/h in the treatment group

and increased from 3.6 ± 1.4 to 4.7 ± 1.5 events/h in the control groups ($P < 0.001$). Treatment with intranasal budesonide and oral montelukast was also associated with significant improvement in oxygen nadir (87.3 ± 3.2 to 92.5 ± 3.0, $P < 0.01$), and respiratory arousal index (4.6 ± 0.6 to 0.8 ± 0.3, $P < 0.001$) but nonsignificant changes in the control group. Although these results are encouraging, the risk of bias in this study is very high because there is possible confounding and selection of participants into the study, the study is small in size, and results may lack generalizability. Moreover, it is suspected that negative small trials have been performed but not published.

This article reported few side effects; one child developed epistaxis in the montelukast/budesonide group that resolved within 3 days of stopping the intervention and did not recur on reinitiation of the intervention. No adverse events were reported in the control group.

Outcomes of daytime sleepiness, snoring, QOL, cognitive function, behavioral changes, and mood were not reported.

Recommendation 6: We suggest that children on intranasal steroids with persistent OSA may be treated with montelukast (conditional recommendation, very low certainty in the estimates of the effect).

Justification and implementation. The panel suggests a treatment course of up to 12 weeks if other treatment interventions are not available and provided that: *1*) the child is closely monitored for potential behavior and mood-related changes; and *2*) PSG is considered if symptoms of OSA persist at the end of the treatment course.

Desirable consequences and their magnitude. We are uncertain about the magnitude of montelukast additive effects on oAHI when it is coadministered with intranasal steroids compared with the efficacy of intranasal steroids only, because there are no available studies. Based on the single small observational study, the favorable effects of the drug combination on AHI relative to no treatment are substantial (mean difference, −4.4/h; 95% confidence interval, −5.2/h to −3.6/h) taking under consideration that recruited children had only mild persistent OSA (94). Studied outcomes have not included frequency of OSA resolution, QOL, OSA-related morbidity, or snoring.

Undesirable consequences and their magnitude. In the single observational study, one child in the montelukast/budesonide group developed epistaxis that resolved within 3 days of discontinuing the intervention and did not recur on reinitiation of the medications (94). In 2020, the FDA strengthened existing warnings about serious behavior and mood-related changes related to montelukast, including suicidal thoughts or actions. The FDA has recommended that the benefits of montelukast may not outweigh the risks, especially when the disease symptoms are mild and can be adequately treated with other medications.

Values and preferences. Parents may prefer intranasal steroids with or without montelukast as an intervention to reduce severity of persistent OSA over CPAP or additional surgical interventions.

Cost/implementation. The cost of the combination of intranasal steroids and montelukast for a 12-week course can be high for some families, especially if medications are not covered by insurance. Parental preferences should be taken under consideration after explaining uncertainty about medication efficacy, morbidity accompanying even OSA of mild severity, alternative treatment interventions for mild-to-moderate persistent OSA (i.e., CPAP, further surgical interventions), cost of medications, and potential serious adverse effects of montelukast.

What others are saying. Despite the FDA warning, in Europe montelukast is used as second-line controller medication for asthma in children 11 years of age or younger (95).

Remarks/future research opportunities. There is a need for:

- Randomized controlled trials to evaluate the efficacy of intranasal corticosteroids alone compared with placebo.
- Randomized controlled trials to evaluate the efficacy of intranasal steroids with and without the additive effects of montelukast.
- Trials of children with moderate persistent OSA.
- Inclusion of outcomes in these trials, including oAHI, OSA resolution, QOL, OSA-related morbidity, and snoring.

Conclusions

Over the last decade, significant advances have been made in the clinical management of persistent pediatric OSA, and yet no guidelines have been published by any professional society solely focusing on this population. Clinicians confronted with children with persistent OSA should personalize treatment decisions based on symptoms, relative benefits versus risks, and medical comorbidity, as suggested by these recommendations. Future head-to-head randomized controlled trials of treatment interventions are necessary to better address research gaps, including the impact of race, socioeconomic status, and other social determinants of health. Some treatment options with potential clinical benefit (e.g., maxillomandibular surgery) in pediatric persistent OSA were not addressed in this guideline. This and other treatment interventions, such as hypoglossal nerve stimulation, high-flow nasal cannula, and myofunctional therapy, as well other pertinent new evidence that may become available, will be addressed in a future update by the committee. This guideline was reviewed by the ATS Quality Improvement and Implementation Committee. None of the recommendations are considered suitable for performance measure development. ■

This official clinical practice guideline was prepared by an *ad hoc* subcommittee of the ATS Assembly on Sleep and Respiratory Neurobiology.

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