

Chinese guideline for the diagnosis and treatment of childhood obstructive sleep apnea (2020)

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Introduction

Childhood obstructive sleep apnea (OSA) is a disorder of breathing during sleep characterized by prolonged partial upper airway obstruction and/or intermittent complete obstruction (obstructive apnea) that disrupts normal ventilation during sleep and normal sleep patterns in children.¹ OSA is one of the most serious sleep-disordered breathing (SDB) diseases in children. Because of its high prevalence and serious long-term complications, increasing numbers of families are affected by OSA. In 2012, the American Academy of Pediatrics (AAP) clinical practice guidelines reported that the prevalence of pediatric OSA was 1.2%–5.7%²; in 2010, the prevalence of pediatric OSA in Hong Kong, China was 4.8%.³ In contrast to OSA in adults, the main cause of upper airway obstruction in children is adenoid and/or tonsil hypertrophy. Obesity, craniofacial malformation, neuromuscular diseases, and

other factors may also contribute to the onset of pediatric OSA.⁴ Without timely diagnosis and effective intervention, pediatric OSA can lead to a series of serious complications, such as maxillofacial dysplasia, behavioral abnormalities, learning disabilities, growth restriction, neurocognitive impairment, endocrine metabolic disorders, hypertension, and pulmonary hypertension; it can also increase the risk of cardiovascular events in adulthood.^{5–8} Therefore, early detection and early diagnosis of pediatric OSA, as well as early intervention to correct this problem, are important considerations for improving patient prognosis.

There have been some controversies in the clinical diagnosis and treatment of pediatric OSA in China, which have restricted clinical diagnosis and treatment strategies, while hindering progress regarding diagnosis and treatment. The diagnosis and treatment of pediatric OSA is increasingly hampered by the absence of multi-

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disciplinary cooperation and guidelines. The numbers of pediatric OSA diagnosis and treatment guidelines and expert consensus are very limited, both in China and worldwide.^{1,2,5,9-13} The draft guideline for diagnosis and treatment of pediatric obstructive sleep apnea hypopnea syndrome issued in 2007 was mainly established on the basis of expert consensus.¹ In the past 10 years, there has been a lack of multi-disciplinary evidence-based diagnosis and treatment guidelines for pediatric OSA in China. Thus, evidence-based clinical practice guidelines are urgently needed. The purpose of the present guideline is to standardize the clinical diagnosis and treatment decision-making concerning pediatric OSA in China, provide scientific evidence for the diagnosis and treatment of pediatric OSA, promote multi-disciplinary integration, guide clinical practice for relevant medical staff, and ensure the use of a scientific approach for management of pediatric OSA.

Target population

This guideline is suitable for children aged 1–18 years with obstructive sleep apnea related to adenoid and/or tonsil hypertrophy, or related to obesity. The guideline is not applicable to children with central sleep apnea syndrome or hypoventilation syndrome. Moreover, they are not applicable to children with OSA who exhibit the following comorbidities: Down syndrome, severe craniofacial malformation, neuromuscular disease, chronic lung disease, sickle cell disease, metabolic disease, and/or laryngomalacia.

Users

This guideline is expected to be used by clinicians, nurses, technicians, and relevant teaching and scientific research staff engaged in sleep respiratory disease-related work in hospitals at all levels.

Definitions of relevant terms

The judgment of sleep events is consistent with the standard interpretation of children's sleep respiratory events formulated by the American Academy of Sleep Medicine (AASM).¹⁴ The interpretation and definition are as follows:

1. Obstructive apnea: $\geq 90\%$ reduction in airflow for at least two respiratory cycles, accompanied by respiratory efforts throughout the event.
2. Central apnea: $\geq 90\%$ reduction in airflow for at least 20 s; or with event-related arousal or oxygen desaturations of $\geq 3\%$ for at least two respiratory cycles; or heart rate reduction to ≤ 50 beats/min for at least 5 s; or heart rate < 60 beats/min for at least 15 s in at least two respiratory cycles (only for infants < 1 year of age). Each of these is accompanied by loss of chest and abdominal effort throughout the event.

TABLE 1 List of abbreviations

Abbreviations	Full terms
AAP	American Academy of Pediatrics
AASM	American Academy of Sleep Medicine
ASA	Australasian Sleep Association
AHI	Apnea hypopnea index
AI	Arousal index
ATS	American Thoracic Society
AUROC	Area under receiver operating characteristics curve
AMSTAR2	A measure tool to assess systematic reviews-second edition
AGREE-II	Appraisal of Guidelines for Research and Evaluation II
BMI	Body mass index
CI	Confidence interval
CPAP	Continuous positive airway pressure
ERS	European Respiratory Society
GPS	Good practice statement
GRADE	Grading of Recommendations Assessment, Development and Evaluation
ICSD	International Classification of Sleep Disorders
ICSD-3	International Classification of Sleep Disorders-Third Edition
LSaO ₂	Lowest oxygen saturation
MAA	Mandibular advancement appliance
MD	Mean differences
NLR	Negative likelihood ratio
NPPV	Non-invasive positive pressure ventilation
OAHI	Obstructive apnea hypopnea index
OAI	Obstructive apnea index
ODI	Oxygen desaturation index
OSA	Obstructive sleep apnea
OSA-18	Obstructive sleep apnea 18-item quality of life questionnaire
OR	Odds ratio
PLR	Positive likelihood ratio
PSG	Polysomnography
PSQ	Pediatric sleep questionnaire
RCT	Randomized controlled trial
RME	Rapid maxillary expansion
RR	Risk ratio
SDB	Sleep-disordered breathing
SMD	Standardized mean difference
WHO	World Health Organization
WMD	Weighted mean difference

3. Mixed apnea: $\geq 90\%$ reduction in airflow for at least two respiratory cycles, beginning without effort and concluding with inspiratory effort.
4. Hypopnea: $\geq 30\%$ reduction in airflow, accompanied by event-related arousal or oxygen desaturations of $\geq 3\%$, for at least two respiratory cycles.
5. Apnea hypopnea index (AHI): average number of apnea and hypopnea events per hour during sleep.
6. Obstructive apnea hypopnea index (OAHI): average number of obstructive apnea, mixed apnea, and hypopnea events per hour during sleep.
7. Obstructive apnea index (OAI): average number of obstructive apnea events per hour during sleep.

8. Oxygen desaturation index (ODI): average number of oxygen desaturation events of $\geq 3\%$ per hour during sleep.

Recommendation

The guideline includes 11 clinical questions and 24 recommendations for diagnosis and treatment, summarized in Table 2. Grading of evidence quality and recommendation strength is described in Table 3 by the Grading of Recommendations Assessment, Development and Evaluation (GRADE).

Clinical questions

Diagnosis questions

Clinical question 1: In the diagnosis of pediatric OSA, what clinical symptoms and signs should be considered?

Recommendations:

Regarding symptoms, the presence and frequency of snoring should be considered first. Snoring ≥ 3 nights/week merits clinical attention (1A).

Further considerations should include sleep apnea, mouth breathing, laborious breathing, restless sleep, enuresis, daytime drowsiness, attention deficit/hyperactivity, and poor academic performance (1B). For young children, mouth breathing, repeated arousal, and emotional and behavioral abnormalities should receive clinical attention (GPS).

Regarding physical signs, adenoid hypertrophy, tonsil hypertrophy, adenoid face, and obesity should be considered (1B).

Whether based on a single symptom/sign or a combination of multiple symptoms and signs, pediatric OSA cannot be reliably diagnosed without the use of polysomnography (PSG). Additional diagnostic methods are recommended to improve the accuracy of diagnosis (1B).

Evidence summary:

The guideline working group performed a qualitative analysis of 21 studies that described OSA-related symptoms and signs in children; these 21 studies included seven guidelines and three systematic reviews. The results were as follows: all 21 studies reported snoring symptoms (six reported snoring frequencies and four studies reported snoring frequencies of 3 nights/week). Additionally, attention deficit/hyperactivity, apnea, daytime sleepiness, and weight loss or gain were frequently reported, as were tonsil hypertrophy, adenoid hypertrophy.

Two systematic reviews assessed the accuracy of clinical history and/or signs for diagnosis of OSA, compared with the accuracy of PSG.^{15,16} Twelve original studies ($n = 1058$

patients) were included in a systematic review published in 2004¹⁵; these included six prospective cohort studies, four retrospective case series, one cross-sectional study, and one case-control study, with sample sizes ranged from 12 to 326 cases. There was significant heterogeneity among PSG-based diagnostic criteria, such as AHI events (apnea or hypopnea) and their ranges (1–15 episodes per hour). A meta-analysis based on data from 10 studies suggested that the positive predictive value (PPV) was 55.8% (95% confidence interval [CI]: 42.1–69.6); the sensitivities and specificities of the clinical evaluation parameters were $\leq 65\%$ in all studies.¹⁵ Methodological heterogeneity and clinical heterogeneity were evident among studies, but the results of the included studies were relatively consistent. The systematic review findings suggested that, compared with PSG, clinical symptoms and signs are not effective for diagnosis of OSA. Furthermore, 10 diagnostic tests ($n = 1525$ patients) were included in a systematic review published in 2012.¹⁶ Heterogeneity was observed among the included studies. Only six studies defined AHI $> 1/h$ as the threshold for diagnosis of pediatric OSA; no study described identification of symptoms and signs, nor did any study assess the consistency between observers. The systematic review results suggested that tonsil hypertrophy and snoring were highly sensitive parameters, but were not specific for OSA; daytime sleepiness, apnea, and nocturnal dyspnea were highly specific parameters, but were not sensitive for OSA. The sensitivity and specificity ranges of the seven assessed models (using combinations of symptoms and signs) were 4%–94% and 28%–99%,¹⁶ respectively. Area under the receiver operating characteristic curve (AUROC) results indicated that symptoms and signs have poor diagnostic ability for pediatric OSA. Therefore, compared with PSG, neither a single symptom/sign nor a combination of multiple symptoms and signs can effectively diagnose pediatric OSA^{15,16}; other diagnostic models are needed to improve the accuracy of diagnosis. Another systematic review assessed the diagnostic value of clinical history and physical examination, compared with PSG, in pediatric SDB¹⁷; its conclusions were consistent with the findings of previous analyses.

Justification:

This recommendation is based primarily on the evidence of symptoms and signs that occur with greater frequency. To formulate the working group's expert opinions based on the results of expert interviews and guidelines, some symptoms not included in the recommendations but observed in clinical practice (e.g., foaming at the mouth, prone position/head back/sitting/over-extension of the neck, and the three depression signs) are also worthy of clinical attention; these should be evaluated in clinical examinations, in combination with the above recommendations and individual child's performance. In addition, comprehensive assessment of upper airway

TABLE 2 Summary of questions and recommendations

Questions	Recommendations
Diagnosis questions	
1. In the diagnosis of pediatric obstructive sleep apnea (OSA), which clinical symptoms and signs should be considered?	Regarding symptoms, the presence and frequency of snoring should be considered first. Snoring ≥ 3 nights/week merits clinical attention (1A). Further considerations should include sleep suffocation, apnea, mouth breathing, laborious breathing, restless sleep, enuresis, daytime drowsiness, attention deficit/hyperactivity, and poor academic performance (1B). For young children, mouth breathing, repeated arousal, and emotional and behavioral abnormalities should receive clinical attention (GPS). Regarding physical signs, adenoid hypertrophy, tonsil hypertrophy, adenoid face, and obesity should be considered (1B). Whether based on a single symptom/sign or a combination of multiple symptoms and signs, pediatric OSA cannot be diagnosed without the use of polysomnography (PSG). Additional diagnostic methods are recommended to improve the accuracy of diagnosis (1B).
2. In PSG, what are the key indicators with direct diagnostic significance for pediatric OSA, and what is the recommended threshold for diagnosis?	PSG is the standard diagnostic method for pediatric OSA. Obstructive apnea hypopnea index (OAHI) $> 1/h$ is recommended as the threshold value for the early identification of children with sleep-disordered breathing who require intervention; additionally, apnea hypopnea index, obstructive apnea index, and lowest oxygen saturation (LSaO ₂) are important assessments for the evaluation of pediatric OSA (1A).
3. How should the severity of OSA be graded?	The severity of OSA is recommended to be graded based on PSG findings. The suggested grades are as follows (2B): mild, $1/h < OAHI \leq 5/h$; moderate, $5/h < OAHI \leq 10/h$; severe, $OAHI > 10/h$. The severity of OSA is not recommended to be graded on the basis of tonsil size (1B).
4. What is the diagnostic value of portable or alternative diagnostic tools (e.g., pulse oximeter)?	PSG is recommended for the diagnosis of pediatric OSA (1A). For hospitals with limited access to PSG, the use of clinically proven portable sleep monitoring equipment (e.g., pulse oximeter) is recommended. Other clinical information such as medical history, physical examination, and questionnaire results should be integrated for comprehensive diagnosis. If necessary, patients should be referred to medical institutions where PSG monitoring is available (2C).
5. What is the diagnostic value of pediatric OSA-related questionnaires or scales, such as the pediatric sleep questionnaire (PSQ) and the obstructive sleep apnea 18-item quality of life questionnaire (OSA-18)?	The PSQ and OSA-18 alone are not recommended to be used as diagnostic tools for pediatric OSA. A combination of medical history, physical examination, and sleep monitoring findings are recommended to increase the specificity of questionnaire-based diagnosis (2D).
Treatment questions	
6. What are the surgical indications for adenoidectomy and/or tonsillectomy in children with OSA?	When children are diagnosed with moderate or severe OSA and clinical findings are consistent with adenoid and/or tonsil hypertrophy, adenoidectomy and/or tonsillectomy is recommended for children without surgical contraindications (1B). For children diagnosed with OSA whose clinical findings are not consistent with adenoid and/or tonsil hypertrophy, a comprehensive assessment of the upper airway (including the oral and nasal cavities) is required; further treatments are recommended (GPS).
7. What are the risk factors for postoperative persistent OSA in children?	Critical evaluation of postoperative persistent OSA is recommended for obese children; supplementary treatments should be administered when necessary (1B). Children with OSA and the following characteristics are recommended to undergo postoperative monitoring: age < 3 years at the time of surgery; asthma and/or nasal diseases (e.g., allergic rhinitis or sinusitis); $OAHI > 10/h$ and/or lowest oxygen saturation $< 80\%$; family history of OSA (2B).
8. What are the efficacy and safety of nasal corticosteroids and leukotriene receptor antagonists in children with OSA?	For children with mild to moderate OSA, adenoid and tonsil evaluation should be performed. Until this evaluation has been completed, nasal corticosteroids or oral montelukast sodium are recommended to reduce sleep apnea events and improve symptom scores. Moreover, regular follow-up is recommended to evaluate efficacy and possible adverse reactions (1B). Regarding combination therapy, following adenoid and tonsil evaluation, nasal corticosteroids combined with oral montelukast sodium are recommended for children with mild or moderate OSA. Regular follow-up is recommended to evaluate efficacy and possible adverse reactions (2D). For children with OSA who do not respond favorably to medication or who experience recurrence after withdrawal, other treatments are recommended on the basis of comprehensive assessments of the upper airway (GPS).
9. What are the indications, efficacy, and long-term adverse reactions of non-invasive positive pressure ventilation (NPPV) for children with OSA?	For children with OSA who have surgical contraindications without adenoid and/or tonsil hypertrophy, as well as children with persistent OSA after adenoidectomy and/or tonsillectomy, combined with non-surgical treatments, NPPV is recommended as an effective treatment after comprehensive assessments of the upper airway (1B). NPPV is recommended as an alternative or a perioperative complementary treatment option for children with severe OSA (GPS). For children who are receiving NPPV, adjustment of ventilator parameters under PSG monitoring is recommended. Periodic evaluation of ventilator parameters is also recommended (GPS). The application of NPPV to children with OSA may result in mild adverse reactions, such as nasal symptoms, optic irritation, and skin damage. The long-term use of NPPV may cause craniofacial abnormalities; thus, regular evaluation is recommended (GPS).
10. What is the efficacy and safety of oral appliance therapy in the treatment of pediatric OSA?	Oral evaluation and oral appliance treatment are recommended for children with OSA who may exhibit oral and maxillofacial development problems, especially those with OSA who may not exhibit adenoid or tonsil hypertrophy, as well as those with persistent postoperative OSA, those who are inoperable, and those who are unable to tolerate NPPV treatment (GPS). After oral evaluation, children with OSA who require oral appliance treatment should receive maxillary expansion or mandibular anterior guidance according to the type of tooth and jaw deformity, as well as the site of airway obstruction. Maxillary arch expansion is effective for treatment of mild to moderate OSA, especially in children with middle palatal suture before bony healing (2D). Mandibular leading orthodontics is effective for children with mild to severe OSA. Treatment is recommended before puberty. Long-term treatment (> 6 months) is better than short-term treatment (1B).
11. What is the efficacy of weight loss in obese children with OSA?	For overweight or obese children with OSA, clinicians should recommend behavioral and dietary interventions to control weight (1D).

TABLE 3 Grading of quality of evidence and strength of recommendation

Category	Description
Quality of evidence	
High (A)	We are very confident that the true effect lies close to that of the estimate of the effect.
Moderate (B)	We are moderately confident in the effect estimate: the true effect is presumably close to the estimate of the effect, but it might be substantially different.
Low (C)	Our confidence in the effect estimate is limited: the true effect maybe substantially different from the estimate of the effect.
Very low (D)	We have very little confidence in the effect estimate: the true effect is presumably substantially different from the estimate of effect.
Strength of recommendation	
Strong (1)	Advantages of intervention considerably outweigh disadvantages, or disadvantages of intervention considerably outweigh advantages
Weak (2)	Advantages of intervention may outweigh disadvantages, or disadvantages of intervention may outweigh advantages
Good practice statement (GPS)	Recommendations based on indirect evidence or expert opinion/experience

obstruction in pediatric OSA should be emphasized, including the presence of allergic rhinitis, nasal septum deviation, nasopharyngeal mass, laryngeal space occupation, or tumor. Children’s symptoms and signs are an important basis for the initial diagnosis of pediatric OSA, but their diagnostic accuracy is low. Diagnosis of pediatric OSA solely based on a single symptom/sign or a combination of symptoms and signs is not recommended; additional diagnostic tools should be used. In addition, this recommendation is based on the 2019 recommendations of the European Respiratory Society (ERS), which distinguish among symptoms and signs according to age. For example, the main symptoms in younger children include snoring, mouth breathing, restless sleep, and abnormal emotional behavior, while the main symptoms in older children include snoring, apnea, daytime sleepiness, attention deficit/hyperactivity, learning difficulties, and memory decline.

Clinical question 2: In PSG, what are the key indicators with direct diagnostic significance for pediatric OSA, and what is the recommended threshold for diagnosis?

Recommendation:

PSG is the standard diagnostic method for pediatric OSA. OAHl > 1/h is recommended as the threshold value for the early detection of children with SDB who require intervention; additionally, AHI, OAI, and lowest oxygen saturation (LSaO₂) are important assessments for the evaluation of pediatric OSA (1A).

Evidence summary:

The 2012 AAP Guideline included a systematic review of 10 diagnostic studies (from 12 publications) since 2002, all of which used standard PSG for diagnosis of pediatric OSA.² However, the diagnostic criteria were inconsistent among studies. The key indicators for OSA diagnosis included AHI and OAI; the AHI thresholds were 1/h, 3/h,

and 5/h. A systematic review of 10 studies was published in 2012¹⁶; the results showed that the diagnostic thresholds used for diagnosis of pediatric OSA by PSG were inconsistent, such that six studies used AHI > 1/h and two studies used AHI > 5/h.

In a 2016 Chinese diagnostic trial (*n* = 1115 patients),¹⁸ PSG was applied to children who met the diagnosed criteria of American Thoracic Society (ATS) (AHI > 5/h or OAI > 1/h) and who were between the International Classification of Sleep Disorders (ICSD) and ATS thresholds (OAHl ≥ 1/h, while AHI ≤ 5/h and OAI ≤ 1/h), as well as children who met the ICSD criteria for primary snoring (OAHl < 1/h). The mean and longest durations of obstructive apnea were significantly longer in children between ICSD and ATS thresholds than in the ICSD primary snoring group (*P* < 0.01); moreover, LSaO₂ was lower in children between ICSD and ATS thresholds than in the primary snoring group (*P* < 0.05). Children between ICSD and ATS thresholds had obvious nocturnal symptoms, their daytime behavior was affected, and their PSG parameters were similar to those of children with OSA. Therefore, OAHl ≥ 1/h should be regarded as the diagnostic threshold of pediatric OSA; this approach is more conducive to the early identification of children with SDB who require intervention. A 2005 cross-sectional study (*n* = 48 patients) explored the value of PSG in the differential diagnosis of snoring in children.¹⁹ The results showed that the mean SaO₂, lowest SaO₂, and the SaO₂ < 95% times were significantly different between children with AHI < 1/h and those with AHI ≥ 5/h (*P* < 0.01), while there was no significant difference in snoring index or total number of snoring sounds; thus, AHI ≥ 1/h was more suitable for the diagnosis of OSA in children. A 2016 cross-sectional survey in China (*n* = 99 participants) analyzed the sleep-breathing parameters of healthy children.²⁰ OAI and OAHl were similar between children aged 3–5 years and those aged 6–14 years (OAI, 0.08 ± 0.12/h and 0.07 ± 0.14/h, respectively; OAHl, 0.18 ± 0.21/h

and $0.19 \pm 0.26/h$, respectively); the 95% CI for OAHl in healthy children was $< 1/h$.

Justification:

This recommendation is based on available evidence, as well as the 2017 ERS Guideline.²¹ It is consistent with the International Classification of Sleep Disorders-Third Edition (ICSD-3) (Table 4).²² OAHl $> 1/h$ was used as the diagnostic threshold for pediatric OSA. This recommendation emphasizes the importance of obstructive factors in the diagnosis of pediatric OSA. Central respiratory events in pediatric OSA are presumably associated with long-term obstructive apnea and hypoventilation. This recommendation is made with the presumption that obstructive factors constitute the root cause of pediatric OSA; these factors lead to a series of pathophysiological changes in children with OSA. Therefore, OAHl should be used as the main objective indicator for the diagnosis of OSA, rather than AHI.

Clinical question 3: How should the severity of OSA be graded?

Recommendations:

The severity of OSA is recommended to be graded based on PSG findings. The suggested grades are as follows (2B): mild, $1/h < \text{OAHl} \leq 5/h$; moderate, $5/h < \text{OAHl} \leq 10/h$; severe, $\text{OAHl} > 10/h$.

The severity of OSA is not recommended to be graded on the basis of tonsil size (1B).

Evidence summary:

A 2011 systematic review (20 studies) assessed tonsil size and PSG value for pediatric OSA severity rating.²⁵ The results showed an association between subjective tonsil size and objective OSA severity in 11 of the 20 studies, but revealed no association in the remaining nine studies. No difference was observed between high quality (score

3.22) and low quality (score 2.36) studies. Thus, a weak correlation was recorded between the severity of objective OSA and the size of children's tonsils. High-quality studies showed no association between subjective tonsil size and objective OSA severity.

Some studies used clinical parameters to assess the severity of pediatric OSA. The results suggested no correlation between tonsil size and AHI or ODI.²⁶ In preschoolers, a weak correlation has been observed between adenoid size and OSA severity; adenoid hypertrophy is considered the main cause of OSA in preschoolers with normal weight.²⁷ For OSA severity classification, standards have been inconsistent among studies, but most are based on obstructive AHI values of 5/h, 10/h, or 15/h.²⁸⁻³⁰ Some studies have referred to SpO₂ and total sleep time.²⁹ In 2014, the Australasian Sleep Association Guideline recommended OAHl as the standard for classification of pediatric OSA severity.²³ OAHl $< 1.2/h$ was regarded as normal, $1.2/h \leq \text{OAHl} < 5/h$ as mild abnormality, $5/h \leq \text{OAHl} < 10/h$ as moderate abnormality, and $10/h \leq \text{OAHl} < 30/h$ as severe abnormality. The 2007 Draft Guideline of the Chinese Medical Association used AHI or OAI as the criteria for OSA severity classification in children.¹ Specifically, $5/h \leq \text{AHI} \leq 10/h$ or $1/h \leq \text{OAI} \leq 5/h$ and LSAO₂ saturation between 0.85 and 0.91 were considered indicative of mild abnormality, while $10/h < \text{AHI} \leq 20/h$ or $5/h < \text{OAI} \leq 10/h$ and LSAO₂ saturation between 0.75 and 0.84 were considered indicative of moderate abnormality; $\text{AHI} > 20/h$ or $\text{OAI} > 10/h$ and LSAO₂ saturation < 0.75 were considered indicative of severe abnormality.

Justification:

The purpose of the severity rating in this recommendation is to guide the assessment of prognostic risk for pediatric OSA; "mild OSA", "moderate OSA", and "severe OSA" are established as indicated in Table 4. Notably, existing systematic reviews of tonsil size did not show an association with AHI or ODI. Uniform grading standards of OSA severity are not available; previous studies have

TABLE 4 Summary of diagnostic thresholds for pediatric OSA

Country/Region	Formulating institutions	Year	Mild	Moderate	Severe	Extreme severe	Reference type
America	American Academy of Sleep Medicine (AASM) ²²	2014	OAHl: ≥ 1	-	-	-	ICSD-3
Europe	European Respiratory Society (ERS) ²¹	2017	OAHl: $\geq 1-5$	OAHl: $>5-10$	OAHl: >10	-	Systematic review
Australasia	Australasian Sleep Association ²³	2014	OAHl: $\geq 1.2-5$	OAHl: $\geq 5-10$	OAHl: $\geq 10-30$	OAHl: >30	Guideline
America	American Society of Anesthesiologists ²⁴	2014	AHI: 1-5	AHI: 6-10	AHI: >10	-	Guideline
China	Editorial Board of <i>Chinese Journal of Otolaryngology Head and Neck Surgery</i> , Otolaryngology Branch of Chinese Medical Association ¹	2007	AHI: $\geq 5-10$ or OAI: $\geq 1-5$, LSaO ₂ : 0.85-0.91	AHI: $>10-20$ or OAI: $>5-10$, LSaO ₂ : 0.75-0.84	AHI: >20 or OAI: >10 , LSaO ₂ : < 0.75	-	Guideline

The units of OAHl, AHI and OAI are episodes/h. OAHl, obstructive apnea hypopnea index; AHI, apnea hypopnea index; OAI, obstructive apnea index; LSAO₂, lowest oxygen saturation; ICSD-3, International Classification of Sleep Disorders-Third Edition; -, not applicable.

used values established in systematic reviews, other original studies, and published guidelines (Table 4).²¹⁻²³ This recommendation uses $1/h < OAHl \leq 5/h$, $5/h < OAHl \leq 10/h$, and $OAHl > 10/h$ as criteria for pediatric OSA severity rating. Long-term follow-up of children with OSA is difficult; there remains a lack of cohort studies, both in China and globally, regarding the correlation between graded diagnosis of pediatric OSA and long-term effects on diseases and complications (e.g., changes in cognition, metabolism, cardiopulmonary function, and cardiovascular health). Therefore, long-term follow-up and cohort analysis of children with OSA is an important future research goal.

Clinical question 4: What is the diagnostic value of portable or alternative diagnostic tools (e.g., pulse oximeter)?

Recommendations:

PSG is recommended for the diagnosis of pediatric OSA (1A).

For hospitals with limited access to PSG, the use of clinically proven portable sleep monitoring equipment (e.g., pulse oximeter) is recommended. Other clinical information such as medical history, physical examination, and questionnaire results should be integrated for comprehensive diagnosis. If necessary, patients should be referred to medical institutions where PSG monitoring is available (2C).

Evidence summary:

The systematic review produced by the Steering Group included 13 studies ($n = 1633$ patients). Of these 13 studies, seven used pulse oximeters ($n = 1450$ patients) and six used portable sleep monitoring devices ($n = 183$ patients). Seven studies did not provide original data for descriptive analysis; of the remaining six studies, three used pulse oximeters ($n = 1019$ patients) and three used watch-PAT devices ($n = 114$ patients). The combined sensitivity and specificity of OSA diagnosis using PSG were 75.0% (95% CI: 53.0%–89.0%) and 88.0% (95% CI: 70.0%–96.0%), respectively. The positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were 6.2 (95% CI: 2.5–15.4) and 0.3 (95% CI: 0.1–0.7), respectively. The cumulative area under the receiver operating characteristic

curve was 0.89 (95% CI: 0.86–0.91, $P = 0.000$).

In 2013, a systematic review of 33 studies ($n = 1064$ patients; AMSTAR2 = 7.5) reported a comparison of PSG with 40 other diagnostic methods.³¹ One pulse oximeter and two portable sleep monitoring devices were compared with PSG (sample size ranged from 21 to 57) in studies published from 1995 to 2003. Two studies (both using OSA diagnostic criteria $AHI > 1/h$) reported sensitivities of 66.7% and 100%, whereas they reported specificities of 66.7% and 62.5%.

Justification:

This recommendation continues to support PSG as a standard diagnostic method for pediatric OSA. However, standard PSG monitoring involves equipment limitations, as well as a complex technical process, requirement for specialized personnel, and high cost. Therefore, clinicians are recommended to use pulse oximeters and other portable monitoring equipment to support the findings of clinical examinations when PSG monitoring is unavailable. Objective assessment and preliminary diagnosis of sleep breathing characteristics are recommended to obtain more objective diagnostic evidence before initiation of clinical treatment in children with OSA; this approach supports comprehensive assessment and individual treatment. It is also consistent with the 2012 AAP Guideline and 2014 Australasian Sleep Association Guideline.^{2,23} If use of the above portable equipment reveals severe OSA, affected patients should be referred to a medical institution with the ability to perform PSG, prior to treatment. In addition, the retrieval evidences of the above recommendations of the is not limited to the equipment type of evidence, but sleep monitoring III–IV level equipment have various kinds and the clinical question mainly focused on simple alternative diagnostic tools such as the diagnostic accuracy of pulse oximeter. For the method of pulse oxygen monitoring, the McGill oxygen score (Table 5) could be used.^{32,33} For children who do not meet the s the McGill oxygen score (e.g., children with $SaO_2 < 0.90$ fewer than three times and more than three clusters of SaO_2 decrease events, or children with $SaO_2 < 0.90$ more than three times and stable baseline $SaO_2 > 0.95$), PSG is recommended to facilitate a clear diagnosis.

TABLE 5 McGill Oximetry Score (MOS)^{32,33}

Score	Implication	Standard			
		No. of drops in $SaO_2 < 0.90$	No. of drops in $SaO_2 < 0.85$	No. of drops in $SaO_2 < 0.80$	Other
MOS 1	Normal study/inconclusive	<3	0	0	Baseline: stable (<3 clusters of desaturation) and >0.95
MOS 2	Mild	≥3	≤3	0	Three or more clusters of desaturation events
MOS 3	Moderate	≥3	>3	≤3	Three or more clusters of desaturation events
MOS 4	Severe	≥3	>3	>3	Three or more clusters of desaturation events

A cluster of desaturations was defined as ≥ 5 desaturations in a 10–30 minute period.³³ Each score was required to meet the criteria for “No. of drops in SaO_2 ” and “Others”.

Clinical question 5: What is the diagnostic value of pediatric OSA-related questionnaires or scales, such as the pediatric sleep questionnaire (PSQ) and the obstructive sleep apnea 18-item quality of life questionnaire (OSA-18)?

Recommendation:

The PSQ and OSA-18 alone are not recommended to be used as diagnostic tools for pediatric OSA. A combination of medical history, physical examination, and sleep monitoring findings are recommended to increase the specificity of questionnaire-based diagnosis (2D).

Evidence summary:

In total, eight studies were included in a comparison of diagnostic accuracy between OSA-related questionnaires or scales and PSG (OSA-18: four studies, $n = 1047$ patients; PSQ: four studies, $n = 472$ patients). The PSQ questionnaire here specifically refers to the sub-questionnaire of sleep-related breathing disorders, which cover the three major symptoms of pediatric OSA: sleep snoring, drowsiness, and hyperactivity. Four studies did not provide original data for descriptive analysis. The remaining four studies revealed the following respective combined sensitivity, specificity, PLR, NLR, and AUROC values for PSQ ($n = 307$ patients) and OSA-18 ($n = 743$ patients) in the diagnosis of pediatric OSA: 77% (95% CI: 55%–90%), 61% (95% CI: 38%–80%), 2.0 (95% CI: 1.2–3.3), 0.38 (95% CI: 0.19–0.76), and 0.75 (95% CI: 0.71–0.78, $P = 0.000$).

A systematic review (AMSTAR2 = 10) published in 2014 investigated the accuracy of PSG in diagnosis of SDB in children by comparing multiple physical examinations and questionnaires among four subgroups: questionnaire, questionnaire + physical examination, questionnaire + physical examination + other diagnostic methods, and physical examination + other diagnostic methods.¹⁷ Of the 11 included diagnostic tests, three assessed PSQ vs. PSG ($n = 102$ patients), PSQ + physical examination vs. PSG ($n = 61$ patients), and OSA-18 + physical examination + other diagnostic methods vs. PSG ($n = 527$ patients). The results suggested that the diagnostic accuracy of questionnaire-based assessment was insufficient to replace PSG or other objective examinations as an independent approach.

Justification:

The 2012 AAP Guideline² and 2014 Australasian Sleep Association Guideline²³ clearly emphasize the importance of clinical symptoms and questionnaires/scales in the preliminary diagnosis of OSA. For quantitative assessments of clinical symptoms, questionnaires are simple, convenient, and non-invasive. In 2011, a total of 6404 sleep assessment tools were available worldwide, including 183 children's sleep disorders questionnaire and scales. Unfortunately, few screening tools have been

evaluated for reliability and validity.³⁴ In terms of the questionnaires that have been scientifically validated and widely used in China, this recommendation mainly advocates the use of two questionnaires, PSQ and OSA-18. The PSQ has been translated into Portuguese,³⁵ Spanish,³⁶ Chinese^{37,38} and other versions; its reliability and validity have been confirmed. As a current approach to investigate the quality of life in children with OSA, the OSA-18 has been widely used; this questionnaire covers five dimensions (18 items): sleep disorder, physical symptoms, emotional distress, daytime conditions, and the degree of influence on guardians. However, current evidence suggests that the diagnostic accuracy of the questionnaire is low; thus, it cannot replace PSG or other objective examinations as an independent diagnostic tool. This questionnaire should be used in combination with other clinical diagnosis tools, including PSG (if necessary).

Treatment questions

Clinical question 6: What are the surgical indications for adenoidectomy and/or tonsillectomy in children with OSA?

Recommendations:

When children are diagnosed with moderate or severe OSA and clinical findings are consistent with adenoid and/or tonsil hypertrophy, adenoidectomy and/or tonsillectomy is recommended for children without surgical contraindications (1B).

For children diagnosed with OSA whose clinical findings are not consistent with adenoid and/or tonsil hypertrophy, a comprehensive assessment of the upper airway (including the oral and nasal cavities) is required; further treatments are recommended (GPS).

Evidence summary:

The results of qualitative studies are made as follows: 1) Seventy-seven studies were retrieved regarding surgical indications in children with OSA; these included 10 guidelines (recommendations are shown above), 3 systematic reviews, and 64 original studies. 2) The systematic reviews and original studies mainly discussed surgical efficacy, surgical methods, and complications related to adenoidectomy and/or tonsillectomy in children with OSA (inclusion criteria were pediatric OSA with adenoid and/or tonsil hypertrophy). 3) Two studies had a minimum age of 1 year in patients who underwent surgery, while 13 studies had a minimum age of 2 years; the remaining studies had a minimum age of 3 years. 4) The shortest course of OSA in children ranged from 3 to 6 months in patients who underwent surgery.

Justification:

Tonsillectomy and/or adenoidectomy are currently first-line treatments for pediatric OSA, especially in children with moderate to severe OSA, following comprehensive assessments of the upper airway (including nasal, nasopharyngeal, oropharyngeal, laryngopharyngeal, and laryngeal cavities) via endoscopy or imaging, in combination with fulfillment of clinical examination criteria for adenoidectomy and/or tonsillectomy without surgical contraindications (based on 2012 AAP Guideline).² Furthermore, the symptoms of children with OSA and their parents' requests to address these manifestations should be carefully considered. For children with mild OSA ($1/h < \text{OAHI} \leq 5/h$), proper clinical interventions are required after full evaluation, in accordance with the 2015 ERS recommendation for diagnosis and treatment of children aged 2–18 years with SDB.⁸ There is currently limited evidence concerning the benefits of medication or surgery for patients with mild OSA. On the basis of their experience, clinicians can perform medical treatments for children with mild OSA, especially those who exhibit nasal and pharyngeal symptoms. Furthermore, guidance can be provided to all children regarding proper sleep posture, while weight loss guidance can be provided to obese children. According to the 2017 ERS recommendation concerning obstructive sleep apnea in children aged 1–23 months, children aged < 3 years require postoperative hospitalization monitoring. Moreover, the reported minimum age for children to undergo adenoidectomy is 3 months, while the reported minimum age for children to undergo combined adenoidectomy and tonsillectomy is 6 months.²¹ Concerning the appropriate age ranges for children to undergo adenoidectomy and/or tonsillectomy, there is currently a lack of original research and systematic reviews. This problem has only been mentioned in a few guidelines and case reports; thus, surgeons must make treatment decisions on the basis of the degree of airway obstruction and their clinical experience. There are various methods available for morphological assessment of adenoid and tonsil hypertrophy. The present guideline used the Brodsky grading scale to determine tonsil size³⁹ and the Parikh classification to determine adenoid size.⁴⁰ Specifically, tonsils occupying >50% of the oropharynx is considered tonsil hypertrophy, while adenoid obstruction >50% is considered adenoid hypertrophy. For severely obese children with adenoid and/or tonsil hypertrophy, clinicians should consider the risks of tonsillectomy and/or adenoidectomy, as well as the advantages and disadvantages of other treatments. Major risks include anesthesia complications, postoperative respiratory failure, hemorrhage, palatopharyngeal insufficiency, and nasopharyngeal stenosis; minor risks include pain and postoperative dehydration.² For children with OSA who do not exhibit tonsil and/or adenoid hypertrophy, detailed assessments and examination of the upper airway (e.g., oral, nasal, and laryngeal cavities) and systemic

problems (e.g., neuromuscular diseases) are needed, as are assessments of obstructions and associated factors. If necessary, consultations from relevant departments should be arranged to assist in diagnosis and treatment.

Clinical question 7: What are the risk factors for postoperative persistent OSA in children?

Recommendations:

Critical evaluation of postoperative persistent OSA is recommended for obese children; supplementary treatments should be administered when necessary (1B).

Children with OSA and with the following characteristics are recommended to undergo postoperative monitoring: age < 3 years at the time of surgery; asthma and/or nasal diseases (e.g., allergic rhinitis or sinusitis); $\text{OAHI} > 10/h$ and/or lowest oxygen saturation < 80%; family history of OSA (2B).

Evidence summary:

A systematic review of 10 prospective cohort studies and two retrospective cohort studies was conducted ($n = 1655$ patients); four risk factors for postoperative persistent OSA were identified in pediatric patients. These factors were as follows: 1) Obesity (seven studies, $n = 682$ patients). Postoperative persistent OSA was more frequent in obese children with OSA than in normal-weight children (odds ratio [OR]: 4.11, 95% CI: 1.68–10.08, $P < 0.01$). On the basis of distinct diagnostic criteria, this review established three subgroups: $\text{AHI} \geq 1/h$ (OR: 3.77, 95% CI: 1.57–9.05, $P < 0.01$), $\text{AHI} \geq 2/h$ (OR: 7.96, 95% CI: 2.76–22.92, $P < 0.01$), and $\text{AHI} \geq 5/h$ (OR: 8.73, 95% CI: 4.50–16.94, $P < 0.01$). The results suggested that preoperative obesity is a risk factor for postoperative persistent OSA. 2) Overweight (three studies, $n = 224$ patients). Overweight children had no risk for postoperative persistent OSA, compared with normal-weight children (OR: 0.76, 95% CI: 0.20–2.96, $P = 0.70$). 3) Accompanying diseases (one study, $n = 85$ patients). The asthma (OR: 1.31, 95% CI: 0.50–3.41, $P = 0.58$) and allergic rhinitis (OR: 0.96, 95% CI: 0.39–2.39, $P = 0.93$) were not associated with elevated risk of postoperative persistent OSA. 4) Family history of diseases. SDB (two studies, $n = 194$ patients) (OR: 1.35, 95% CI: 0.62–2.91, $P = 0.45$), allergy (two studies, $n = 194$ patients) (OR: 2.24, 95% CI: 0.95–5.28, $P = 0.07$), and obesity (one study, $n = 84$ patients) (OR: 1.03, 95% CI: 0.20–5.32, $P = 0.98$) were not associated with elevated risk of postoperative persistent OSA. These findings suggested that obesity constitutes a risk factor for postoperative persistent OSA in pediatric patients.

A systematic review in 2015 (51 studies, $n = 3413$ patients, one randomized controlled trial [RCT] and other case studies or non-RCTs; AMSTAR2 = 7.5) showed that the postoperative AHI significantly decreased by 12.4–

fold in children with OSA, compared with preoperative AHI; however, LSaO₂ was enhanced in these children.⁴¹ The overall rate of postoperative AHI < 1/h was 51% (obese vs. non-obese vs. undifferentiated obesity groups: 34% vs. 49% vs. 56%), while the overall rate of AHI < 5/h was 81% (obese vs. non-obese vs. undifferentiated obese groups: 61% vs. 87% vs. 84%). Meta-regression analysis showed that the rate of postoperative AHI persistence was positively correlated with preoperative AHI and body mass index (BMI) Z-score. These results suggested that surgery can significantly improve sleep parameters in children with OSA, especially for non-obese patients. Postoperative persistent OSA is likely to occur in children with severe OSA and obesity.

Justification:

Notably, obesity is an independent risk factor for pediatric OSA. The current clinical evidence also suggests that obesity is a risk factor for postoperative persistent OSA. PSG or portable or simple alternative diagnostic tools can be used to evaluate postoperative persistent OSA. Supplementary treatments should be considered as appropriate, including non-invasive positive pressure ventilation (NPPV), orthodontic therapy, and weight loss. Current evidence indicates that accompanying diseases (e.g., asthma and allergic rhinitis) and family history of OSA do not increase the risk of postoperative persistent OSA. However, on the basis of existing guidelines and expert recommendations,^{2,42-44} clinicians should perform careful postoperative evaluation and airway management in children with OSA aged < 3 years, as well as those with accompanying diseases, severe OSA, hypoxemia, and/or relevant family history. In addition, clinicians should perform comprehensive assessments of the upper airway in children with OSA, especially those whose disease severity (based on PSG assessment) is not consistent with adenoid and/or tonsil hypertrophy (i.e., children with adenoid and/or tonsil hypertrophy who do not exhibit frequent sleep apnea events, or those with frequent sleep apnea events who do not exhibit clinically significant adenoid and/or tonsil hypertrophy). About the treatment of complications related to postoperative persistent OSA in children, 2014 Australasian Sleep Association Guideline recommended that children with age < 3 years plus a comorbidity or with very severe OSA (OAH or ODI ≥ 30; or oxygen saturation nadir < 70%; or McGill oximetry score 4) should be monitored post-operatively in a hospital with an onsite intensive care unit and should be considered for closer monitoring. Children with very severe OSA and morbid obesity (BMI > 35 kg/m²) should have a planned post-operative intensive care unit admission.²³

Clinical question 8: What are the efficacy and safety of nasal corticosteroids and leukotriene receptor antagonists in children with OSA?

Recommendations:

For children with mild to moderate OSA, adenoid and tonsil evaluation should be performed. Until this evaluation has been completed, nasal corticosteroids or oral montelukast sodium are recommended to reduce sleep apnea events and improve symptom scores. Moreover, regular follow-up is recommended to evaluate efficacy and possible adverse reactions (1B).

Regarding combination therapy, following adenoid and tonsil evaluation, nasal corticosteroids combined with oral montelukast sodium are recommended for children with mild or moderate OSA. Regular follow-up is recommended to evaluate efficacy and possible adverse reactions (2D).

For children with OSA who do not respond favorably to medication or who experience recurrence after withdrawal, other treatments are recommended on the basis of comprehensive assessments of the upper airway (GPS).

Evidence summary:

A systematic review was conducted, which included four, three, and two RCTs to evaluate the respective efficacy and safety of nasal corticosteroids, leukotriene receptor antagonists (e.g., montelukast sodium), and combined usage of these two drugs in children with OSA. The review included four RCTs ($n = 204$ patients) regarding the use of nasal corticosteroids in children with OSA. 1) The results of three RCTs ($n = 142$ patients) suggested that nasal corticosteroids reduced OAH (standardized mean difference [SMD]: -3.34, 95% CI: -4.66 to -2.01, $P < 0.0001$) and ODI (SMD: -2.18, 95% CI: -3.86 to -0.50, $P = 0.01$), compared with placebo; there were no significant differences between the two groups in arousal index (SMD: -1.32, 95% CI: -4.61 to 1.97, $P = 0.43$) or LSaO₂ (SMD: 2.06, 95% CI: -2.44 to 6.57, $P = 0.37$). Of the included studies, two reported adenoid morphology; the findings in one of these two studies suggested that nasal corticosteroids reduced adenoid morphology in children with OSA, compared with placebo, while the findings in the other study suggested no differences. 2) One RCT ($n = 62$ patients) constituted a randomized crossover trial of nasal budesonide, compared with placebo (normal saline), for 6 weeks. Data concerning the comparison between groups after random allocation were not reported; thus, that study was analyzed separately. All 62 patients in the RCT completed the first phase of the randomized crossover trial; 19 patients (five in the drug group and 14 in the placebo group) then withdrew from the trial. The results of the RCT suggested that nasal budesonide reduced the AHI in 48 patients (30 in the first phase and 18 in the second phase) who completed treatment, compared with 32 patients in placebo group in the first phase. 3) In terms of adverse reactions, two studies reported nausea, vomiting, and diarrhea, while the remaining two studies reported no events. 4) A meta-analysis revealed obvious clinical heterogeneity in three studies with respect to types

of nasal corticosteroids (mometasone furoate nasal spray in two studies and fluticasone propionate nasal spray in one study), number of medicine, and duration (4 weeks, 6 weeks, and 4 months).

The systematic review also included three RCTs ($n = 187$ patients) regarding the use of montelukast sodium in children with OSA.⁴⁵ 1) Compared with placebo (non-intervention group), the results of two RCTs ($n = 103$ patients) suggested that montelukast sodium reduced OAH (SMD: -0.99 , 95% CI: -1.40 to -0.58 , $P < 0.00001$), ODI mean difference [MD]: -2.83 , 95% CI: -3.86 to -1.79 , $P < 0.00001$), and AI (SMD: -1.02 , 95% CI: -1.47 to -0.57 , $P < 0.0001$), while elevating LSaO₂ (MD: 4.07 , 95% CI: 2.27 – 5.88 , $P < 0.00001$). The results of one RCT ($n = 46$ patients) showed that montelukast sodium relieved symptoms of snoring (SMD: -1.84 , 95% CI: -2.53 to -1.14 , $P < 0.00001$) and mouth breathing (SMD: -1.22 , 95% CI: -1.85 to -0.59 , $P = 0.0002$). The results of another RCT ($n = 57$ patients) suggested that there was no significant difference in tonsil morphology (MD: -0.20 , 95% CI: -0.46 to 0.06 , $P = 0.14$) and adenoid morphology (SMD: -0.58 , 95% CI: -1.19 to 0.03 , $P = 0.06$) between the two groups. The methodological quality in both RCTs was high, but the sample size was limited. 2) The results of another RCT ($n = 84$ patients; montelukast sodium combined with routine treatment vs. routine treatment) suggested that montelukast sodium reduced AHI (MD: -1.62 , 95% CI: -2.63 to -0.61 , $P = 0.002$), while improving LSaO₂ (MD: 2.53 , 95% CI: 0.88 – 4.18 , $P = 0.003$) and reducing adenoid morphology (RR: 0.15 , 95% CI: 0.04 – 0.64 , $P = 0.01$).

The review included two RCTs ($n = 234$ patients) regarding combined use of nasal corticosteroids and leukotriene receptor antagonists (montelukast sodium) in children with OSA. 1) The results of two RCTs ($n = 169$ patients; nasal corticosteroids combined with oral montelukast sodium vs. nasal corticosteroids) suggested that there was no significant difference in improving AHI between the two groups (SMD: -0.48 , 95% CI: -2.24 to 1.28 , $P = 0.59$), although the combination group showed better LSaO₂ (SMD: 1.11 , 95% CI: 0.79 – 1.44 , $P < 0.0001$), compared with the nasal corticosteroids group. One study reported no adverse reactions and another did not include outcome indicators. The results of one RCT ($n = 122$ patients; nasal corticosteroids combined with oral montelukast vs. oral montelukast) suggested that the combination treatment improved LSaO₂ (MD: 1.20 , 95% CI: 0.34 – 2.06 , $P = 0.006$) and reduced adenoid morphology (MD: -0.02 , 95% CI: -0.03 to -0.01 , $P = 0.002$) compared with oral montelukast, while there was no significant difference in AHI improvement (MD: 0.31 , 95% CI: -0.07 to 0.69 , $P = 0.11$) between the two groups. Of these two RCTs, one ($n = 195$ patients; oral montelukast vs. nasal corticosteroids [four patients were lost to follow-up] vs. nasal corticosteroids combined with

oral montelukast [eight patients were lost to follow-up]) mainly compared efficacy before and after treatment in three subgroups; it showed significant efficacy among the three groups in indicators including AHI, LSaO₂, snoring, and mouth breathing (but not tonsil morphology) after treatments, compared with baseline, although no comparison was made between groups. 2) Notably, there were no detailed descriptions of allocation concealment in these two studies, and no mention of blinding method; moreover, they had different extents of loss to follow-up.

Five systematic reviews compared drug treatments in children with OSA.^{44,46-49} A Cochrane systematic review in 2011 verified the efficacy and safety of anti-inflammatory drugs for children with OSA (AMSTAR2 = 14).⁴⁶ Two RCTs ($n = 87$ patients) evaluated nasal corticosteroids, while one RCT evaluated montelukast sodium (only the abstract was published). 1) The first RCT ($n = 25$ patients) showed that a 6-week-regimen of fluticasone propionate nasal spray reduced AHI in children with mild to moderate OSA, compared with placebo (MD: -7.20 , 95% CI: -13.96 to -0.44), whereas no significant difference was observed in LSaO₂ (MD: -1.20 , 95% CI: -5.06 to 2.66); moreover, no significant differences were recorded in tonsil morphology or clinical symptom scores reported by the patients' parents (e.g., snoring, apnea, and daytime sleepiness). Data concerning long-term safety and efficacy remain unclear; that study had high methodological quality, but used a small sample size. 2) The other published RCT was a randomized crossover trial with a 6-week cycle ($n = 62$ patients); the findings suggested that budesonide nasal spray reduced AHI, compared with placebo. This study was not performed on the basis of random assignment, so the results should be interpreted cautiously. A systematic review in 2015 included two RCTs and one case-control trial ($n = 105/27$ patients; AMSTAR2 = 7.5).⁴⁷ This review, based on single-group data comparison of 6-week nasal corticosteroids (fluticasone and budesonide) before and after treatment, suggested that nasal corticosteroids could reduce AHI in children with OSA (weighted mean difference [WMD]: 4.07 , 95% CI: 0.00 – 8.14 , $P < 0.00001$). Budesonide was confirmed to occasionally cause mild symptoms including epistaxis, diarrhea, and vomiting, but these did not lead to drug discontinuation. There were obvious methodological and clinical heterogeneities among the three studies; moreover, the randomly assigned drug group and controls were not compared. A systematic review in 2013⁴⁸ (two RCTs, $n = 76$ patients; AMSTAR2 = 10.5) suggested that, in children with OSA, montelukast sodium reduced AHI (OAI > 1/h or AHI > 5/h) (MD: -2.06 , 95% CI: -2.28 to -1.84 , $P < 0.00001$), AI (MD: -4.18 , 95% CI: -5.14 to -3.21 , $P < 0.00001$), and apnea index (MD: -1.18 , 95% CI: -1.28 to -1.08 , $P < 0.00001$), compared with placebo; however, there was no difference in mean blood oxygen saturation (MD: 0.75 , 95% CI: -0.32 to 1.83 , $P = 0.17$) and no adverse events were reported.

A systematic review in 2018⁴⁹ included six studies ($n = 668$ patients; one cross-sectional study, two prospective cohort studies, one retrospective cohort study, and two placebo-controlled RCTs) that investigated the efficacy of montelukast sodium for children with OSA. Among these studies, the results of two RCTs were consistent with the findings in the systematic review published in 2013.⁴⁸ The remaining two studies (a prospective cohort study and a retrospective cohort study; $n = 502$ patients) compared the efficacy of oral montelukast sodium combined with nasal corticosteroids before and after treatment; they revealed reduced AHI ($MD: -4.18$, 95% $CI: -6.33$ to -2.04 , $P < 0.0001$) and LSAT ($MD: 4.76$, 95% $CI: 4.46$ – 5.06 , $P < 0.000001$) after treatment. Four studies ($n = 511$ patients) included in the above systematic review reported adverse reactions. Three patients had mild nausea, headache, and epistaxis; no serious adverse reactions were reported. A reticular meta-analysis in 2017⁵⁰ (seven RCTs, $n = 499$ patients; AMSTAR2 = 7.5) showed that mometasone furoate ($WMD: 1.40$, 95% $CI: 1.17$ – 1.63), budesonide ($WMD: 3.50$, 95% $CI: 3.34$ – 3.66), fluticasone ($WMD: 7.20$, 95% $CI: 5.26$ – 9.14), and montelukast sodium ($WMD: 2.80$, 95% $CI: 1.01$ – 4.59) fully reduced AHI, compared with placebo; fluticasone had the greatest efficacy.

Justification:

Nasal corticosteroids and montelukast sodium are recommended for children with mild or moderate OSA who have adenoid and/or tonsil hypertrophy (especially those with adenoid hypertrophy), excluding other problems such as oral-maxillofacial defects and upper airway obstruction. In particular, nasal corticosteroids are recommended for children with OSA accompanied by rhinitis symptoms such as nasal congestion, runny nose, sneezing, and rhinolalia clausa. For children with moderate OSA and adenoid and/or tonsil hypertrophy, adenoidectomy and/or tonsillectomy remain first-line treatments. For children with surgical contraindications, those waiting for surgery, and those whose parents refuse surgery, the above drugs are recommended as conservative treatments. In terms of efficacy, the present systematic review suggested that nasal corticosteroids effectively reduced OAH and ODI in children with OSA, while oral montelukast sodium reduced OAH and improved symptom scores. In addition, there have been few high-quality RCTs to determine efficacy and adverse reactions related to the use of nasal corticosteroids combined with montelukast sodium; long-term follow-up data are limited. The efficacy of combined use of these drugs is an important research avenue concerning drug treatments for children with OSA and adenoid hypertrophy, consistent with the guidelines of the French Society of ear nose and throat and Head & Neck Surgery.⁴² On the basis of the above findings and instructions of these drugs, these drugs are recommended for use in children aged > 2 years. The current clinical studies are limited to short-term follow-

up and lack normative long-term prospective analysis. Additionally, the clinical indications for drug withdrawal and conversion to surgery require further evidence-based analyses. Possible adverse reactions should be monitored during drug treatments (e.g., epistaxis, headache, diarrhea, nausea, and/or vomiting). Notably, some studies have shown that montelukast sodium might be associated with psychiatric symptoms including nightmares, aggressive behaviors, depression, and suicide. In 2019, the United States Food and Drug Administration stated that montelukast sodium might cause a risk of neurological/psychiatric events, including depression, self-mutilation, and suicide.⁵¹ Clinicians should immediately discontinue medication and refer patients to an appropriate specialist if such symptoms develop. Comprehensive assessments are required after courses of treatment have been completed. For children with OSA who exhibit no clinically significant improvements in symptoms, signs, and OAH, as well as children who exhibit recurrence after drug withdrawal, clinicians should fully consider the etiology and re-evaluate obstructions of the upper airway (See recommendation 6).

Clinical question 9: What are the indications, efficacy, and long-term adverse reactions of non-invasive positive pressure ventilation (NPPV) for children with OSA?

Recommendations:

For children with OSA who have surgical contraindications without adenoid and/or tonsil hypertrophy, as well as children with persistent OSA after adenoidectomy and/or tonsillectomy, combined with non-surgical treatments, NPPV is recommended as an effective treatment after comprehensive assessments of the upper airway (1B).

NPPV is recommended as an alternative or a perioperative complementary treatment option for children with severe OSA (GPS).

For children who are receiving NPPV, adjustment of ventilator parameters under PSG monitoring is recommended. Periodic evaluation of ventilator parameters is also recommended (GPS).

The application of NPPV to children with OSA may result in mild adverse reactions, such as nasal symptoms, optic irritation, and skin damage. The long-term use of NPPV may cause craniofacial abnormalities; thus, regular evaluation is recommended (GPS).

Evidence summary:

For this recommendation, two RCTs were retrieved regarding the efficacy and adverse reactions of positive pressure ventilation in the treatment of children with OSA; the RCTs could not be combined due to clinical heterogeneity. One study ($n = 70$ patients) was a randomized, double-blind controlled trial (continuous

positive airway pressure [CPAP] combined with surgery vs. surgery alone); its findings suggested that combined treatment reduced AHI ($MD: -6.80$, $95\% CI: -10.62$ to -2.98 , $P = 0.0005$), but did not provide information regarding adverse reactions or complications. The study also indicated that other indicators were significantly altered in the CPAP group; these included improvements in the blood oxygenation and Epworth Sleepiness Score (ESS), as well as reductions in the partial pressure of carbon dioxide and apnea duration. The findings of study ($n = 67$ patients) with a lower methodological quality (CPAP combined with routine treatment vs. routine treatment alone) suggested that CPAP significantly reduced AHI while enhancing $LSaO_2$.

Justification:

The application of NPPV to children with OSA should be based on comprehensive airway assessments to identify upper airway obstructions. However, drug-induced sleep endoscopy and magnetic resonance imaging are not recommended for routine examinations. The use of NPPV should be combined with individual conditions and clinical requirements, and there is no restriction or recommendation regarding the age of application. CPAP is considered an effective alternative treatment for children with OSA²³; thus, it is used as an important supplementary treatment for children with severe OSA during the perioperative period,⁵² as well as a temporary intervention for special children with OSA who are waiting for craniofacial surgery.²¹ Children with OSA who are using CPAP or other noninvasive ventilation treatments must complete pressure titration during sleep monitoring; the parameters should be re-evaluated regularly. In 2016, the expert consensus of Sleep Cooperative Group, Respiratory Group, Chinese Pediatrics Society, Editorial Board of the *Chinese Journal of Practical Pediatrics*⁵³ reported that NPPV for children with OSA must be monitored and followed up for an extended period in a specialized medical center with pediatric NPPV to avoid or ensure timely identification of mask-related craniofacial abnormalities.

Clinical question 10: What is the efficacy and safety of oral appliance therapy in the treatment of pediatric OSA?

Recommendations:

Oral evaluation and oral appliance treatment are recommended for children with OSA who may exhibit oral and maxillofacial development problems, especially those with OSA who may not exhibit adenoid or tonsil hypertrophy, as well as those with persistent postoperative OSA, those who are inoperable, and those who are unable to tolerate NPPV treatment (GPS).

After oral evaluation, children with OSA who require oral appliance treatment should receive maxillary expansion or mandibular anterior guidance according to the type

of tooth and jaw deformity, as well as the site of airway obstruction. Maxillary arch expansion is effective for treatment of mild to moderate OSA, especially in children with middle palatal suture before bony healing (2D). Mandibular leading orthodontics is effective for children with mild to severe OSA. Treatment is recommended before puberty. Long-term treatment (> 6 months) is better than short-term treatment (1B).

Evidence summary:

A meta-analysis in 2017 (including one RCT, nine case series, two case reports, and five case-control studies, $n = 314$ patients) investigated the use of rapid maxillary expansion (RME) for the treatment of pediatric OSA in children with high palatal arch or upper palate stenosis (i.e., transverse maxillary hypoplasia).⁵⁴ The results showed that AHI decreased ($MD: -4.84$, $95\% CI: -8.47$ to -1.21) and $LSaO_2$ increased ($MD: 5.78$, $95\% CI: 1.99-9.58$). A systematic review in 2016 investigated rapid arch expansion for the treatment of pediatric OSA ($n = 215$ patients).⁵⁵ The results suggested that RME could reduce AHI by a mean of 6.86/h ($P < 0.0001$). In 2017, the results of a systematic review (five non-randomized controlled trials, $n = 137$ patients) suggested that rapid arch expansion could reduce AHI in children with OSA ($SMD: 3.24$, $95\% CI: 0.34-6.15$).⁵⁶ A systematic review published in 2019 included a descriptive analysis of six studies; the results suggested that rapid arch expansion achieved maxillary and nasal lateral wall widening by 3.4 mm and 3.3 mm, respectively; these distances decreased to 2.8 mm and 2.2 mm after puberty.⁵⁷ For arch expansion performed before puberty, the width of the upper alveolar seat and maxilla increased continuously and steadily during long-term follow-up; for the arch expansion performed after puberty, only the nasal lateral wall increased by 1.3 mm, compared with the control group, while the maxillary bony width did not increase. A 2016 Cochrane systematic review (quasi-RCT, $n = 23$ patients; AMSTAR2 = 15) compared personalized oral appliances with non-intervention treatment in children with OSA ($AHI > 1$).⁵⁸ The results suggested that orthodontic intervention could reduce AHI in children with mild OSA (risk ratio [RR]: 0.39, $95\% CI: 0.20-0.76$, $P = 0.0061$), while improving buccal respiration (RR: 0.16, $95\% CI: 0.04-0.59$, $P = 0.0060$), nasal stuffiness (RR: 0.18, $95\% CI: 0.05-0.69$, $P = 0.013$), and habitual snoring (RR: 0.18, $95\% CI: 0.06-0.55$, $P = 0.0028$). However, there remains insufficient evidence to support the use of orthodontic treatment for OSA.

A systematic review in 2019 (including three RCTs, one crossover RCT, and three non-randomized controlled trials, $n = 188$ patients; AMSTAR2 = 12) evaluated the efficacy of mandibular advancement appliance (MAA) in the treatment of pediatric OSA.⁵⁹ Two of the high-quality RCTs ($n = 34$ patients) showed that, compared

with placebo intervention, children with OSA in the MAAs group had lower AHI (*MD*: -1.75 , 95% *CI*: -2.07 to -1.44) and higher LSaO_2 (*RR*: 3.4, 95% *CI*: 0.9–5.9, $P = 0.007$). Scores on the Children's Sleep Questionnaire and Quality of Life and Behavior improved, whereas there was no difference in ODI between the two groups. Sensitivity analysis included other low-quality studies; the pooled results were consistent with those of the above two high-quality studies. With MAA treatment, subgroup analysis showed that the AHI values in patients with mild OSA ($\text{AHI} < 5$), moderate OSA ($5 < \text{AHI} < 10$), and severe OSA ($\text{AHI} > 10$) were reduced by 50% (1.72/3.5), 57% (4.27/7.5) and 76% (10.69/14.08), respectively. Furthermore, MAA treatment could reduce AHI in the younger group (age, 6–9.5 years) and the older group (age, 9.5–13 years). The results suggested that MAAs could be used to treat OSA in children < 13 years of age. However, minimal post-puberty data are available.

Justification:

Orthodontics is an important supplementary treatment for children with OSA. For clinical otolaryngologists and respiratory physicians, it is important to clarify the indications for orthodontic evaluation and establish the approach of diagnosis and treatment combined with comprehensive stomatology treatment. During orthodontic treatment, it is particularly necessary for children with OSA to complete regular orthodontic follow-up; sleep monitoring should be carried out systematically for 3–6 months after discontinuation of treatment.⁴² For children with OSA who exhibit mouth breathing, oral muscle function training can be used as adjuvant therapy.

Clinical question II: What is the efficacy of weight loss in obese children with OSA?

Recommendation:

For overweight or obese children with OSA, clinicians should recommend behavioral and dietary interventions to control weight (1D).

Evidence summary:

A systematic review in 2016 ($n = 359$ participants, including 163 patients with OSA; AMSTAR2 = 5.5) included 16 studies, among which four investigated two types of weight loss (using descriptive analysis): surgical (two retrospective studies, $n = 260$ participants, including 117 patients with OSA) and behavioral (two prospective studies, $n = 99$ participants, including 46 patients with OSA).⁶⁰ In the surgical weight loss analysis, among 34 obese children (obesity defined as $\text{BMI} \geq 95$ th percentile) included in one study, 19 obese children with OSA (obesity defined as $\text{BMI} > 40 \text{ kg/m}^2$) underwent gastric bypass surgery. Among 10 patients who underwent

postoperative follow-up, the mean BMI values before and after surgery were $60.8 \pm 11.07 \text{ kg/m}^2$ and $41.6 \pm 9.5 \text{ kg/m}^2$, respectively. The mean AHI decreased from 9.1 to 0.65 ($P < 0.01$) and the rate of OSA persistence was 10% (1/10). In another study, 98 obese children with OSA (obesity defined as $\text{BMI} > 40 \text{ kg/m}^2$) underwent laparoscopic condom gastrectomy and the rate of OSA persistence was 18% (18/98); no BMI or AHI information were recorded before and after surgery. Two other studies investigated behavioral weight loss (i.e., dietary restriction, physical activity, and psychological support) as an intervention for obese children with OSA (in one study, obesity was defined as $\text{BMI} > 40 \text{ kg/m}^2$). The AHI was reduced by weight loss intervention; OSA persistence rates were 38% (8/21) and 33% (3/9), respectively.

A case series study in 2018 ($n = 24$ patients) investigated the efficacy of physical exercise combined with dietary changes as weight loss intervention for children with OSA ($n = 14$ patients; $\text{AHI} \geq 2$).⁶¹ Subgroup analysis showed no significant change in AHI after 9 months of weight loss intervention.

Justification:

For obese children with OSA, clinicians should recommend weight control,^{1,2} in addition to other treatments. Normal weight standards for school-age children are provided in the "People's Republic of China Health Industry Standard (WS/T 586-2018) Overweight and Obesity Screening for School-age Children and Adolescents",⁶² and in the "Clinical Intervention Guideline for Obese Children" published by the European Endocrine Society and Pediatric Endocrinology Society.⁶³ However, there is currently a lack of high-quality research concerning the efficacy of weight loss therapy on OSA in children, because the available studies mainly constitute case series of patients with very high BMI ($> 40 \text{ kg/m}^2$), older age (> 15 years), and limited data.

Guideline development process and methods

Guideline development methodology

The guideline was developed in accordance with the most recent standards of the Institute of Medicine,⁶⁴ and the development methodology was based on the development process described in the 2015 World Health Organization (WHO) Handbook for Guideline Development and related methodological standards,⁶⁵ as well as the second version of the Appraisal of Guidelines for Research and Evaluation II (AGREE-II).⁶⁶ The guideline was reported based on the Reporting Items for Practice Guidelines in Healthcare.⁶⁷

Proposal and registration of the guideline

The guideline was registered on the International Practice Guidelines Registry Platform (<http://guidelines-registry>).

cn/; registration number IPGRP-2018CN058). The proposal of guideline has been published in the 1st issue of *Chinese Journal of Evidence-based Medicine* in 2020.⁶⁸

Guideline working group

The guideline working group was established in July 2018, consisting of four groups: steering group, guideline development group, evidence synthesis and evaluation group, and external review group. The working group was composed of clinical experts, guidance methodology experts, evidence-based medicine experts, clinical epidemiology experts, health statistics experts, editors of professional journals, and experts from other fields. Clinical experts included otorhinolaryngologists, head and neck surgeons, respiratory medicine experts, stomatologists, chronic disease management experts, and developmental behavior experts; notably, pediatricians comprised 78% of the clinical experts. Patients and guardian preferences were considered during the selection of outcome indicators and the formation of recommendations.

The methodological support and guidance for this guideline were jointly provided by the Evidence-based Medicine Center of Lanzhou University/Chinese GRADE Centre, the Peking University Evidence-based Medicine Center/Peking University School of Public Health, and the Center for Clinical Epidemiology and Evidence-based Medicine, Beijing Children's Hospital, Capital Medical University.

Statement of conflict of interest

All participants involved in the formulation of the guideline, including the steering group, the guideline development working group, evidence synthesis and evaluation group, and the external review group have completed the required declaration of interest forms. All participants declare no financial and non-financial conflicts of interest directly related to this guideline.

Collection and selection of clinical questions and outcomes

The list of clinical questions and outcomes were formulated following the published OSA-related guidelines and systematic reviews. Then the duplicated questions and outcomes were removed and several questions and outcomes were combined if necessary. During the selection of clinical questions, two rounds of Delphi surveys were conducted and a face-to-face consensus meeting was held. The core members of guideline development group, repeatedly discussed and identified 11 clinical questions relevant to this guideline, including five diagnostic clinical questions and six treatment clinical questions. The clinical questions were constructed by clinical experts and methodologists on the basis of the Population, Intervention, Comparison, and Outcome (PICO) principle. The formulation of the

list of outcomes was based on the retrieved literature and in-depth interviews, and considering the patients/guardians' preferences and values. After various degrees of discussion, the guideline development group agreed upon outcomes for use in this guideline.

Search, synthesis, and evaluation of evidence

This guideline was formulated following retrieval and evaluation of OSA, adenoidectomy, and/or tonsillectomy-related guidelines, as well as OSA-related systematic reviews/meta-analyses at different stages of topic and scope determination; evidence synthesis and evaluation was also performed. During the development of systematic reviews, the corresponding original studies and data analyses were retrieved and evaluated.

Inclusion and exclusion criteria

Inclusion criteria: 1) Participants: children diagnosed with OSA/obstructive sleep apnea syndrome /obstructive sleep apnea-hypopnea syndrome, aged 1 to 18 years; 2) Intervention and comparative measures: no limitation; 3) Outcomes: no limitation; 4) Study types: Searching guidelines and consensuses related to OSA and adenoidectomy and/or tonsillectomy; Searching OSA-related systematic reviews/meta-analyses; Searching relevant primary research.

Exclusion criteria: patients with primary snoring, central apnea or hypopnea syndrome, and children with OSA complicated by other congenital or severe diseases, such as Down syndrome, craniofacial deformities, neuromuscular diseases (e.g., cerebral palsy), chronic lung disease, sickle cell disease, metabolic disease, and/or laryngomalacia. Intervention measures involving traditional Chinese medicine (e.g., Chinese herbal medicine, proprietary Chinese medicine, and/or acupuncture). Documents and data published in multiple articles or formats.

Data sources and search strategies

Data sources include 1) Database search: English databases include PubMed, Excerpt Medica Database (EMBASE), the Cochrane Library; Chinese databases including China Biomedical Literature Database, Chinese National Knowledge Infrastructure (CNKI), VIP and Wanfang databases. The retrieval time is from the inception of the database to September 2019. 2) Related resources of the guide: NGC (<http://www.ngc.gov>), NICE (<https://www.nice.org.uk/guidance>), GIN (<https://www.g-i-n.net>), WHO (<http://www.who.int/publications/guidelines/en/>), Uptodate (<https://www.uptodate.com/contents/search>) and Medical Maitong. 3) PROSPERO (International prospective register of systematic reviews) registration platform for systematic review/meta-analysis of related retrieval resources. 4) Resources related to clinical trials: WHO International Clinical Trial Registry Platform. 5) Supplementary search: investigation of

OSA-related research references and Baidu academic supplementary investigation.

Main search terms included three aspects: OSA, children's population, and study type. The PubMed search strategy is shown in Table 6.

Evidence screening and data extraction

Evidence screening and data extraction were performed independently by at least two reviewers, in accordance with the above inclusion and exclusion criteria. First, the reviewers assessed titles and abstracts to exclude irrelevant literature; they then consulted the full texts of presumably relevant articles and determined whether the studies were appropriate for inclusion criteria and exclusion criteria. The relevant data were extracted by at least two reviewers,

TABLE 6 PubMed search strategy

Number	Searching strategy
#1	"Snoring"[Mesh]
#2	"Sleep Apnea Syndromes"[Mesh:NoExp]
#3	"Sleep Apnea, Obstructive"[Mesh]
#4	((sleep* AND (apnea* OR apnoea* OR hypopn* OR obstruct*OR disorder* OR disturb*)) OR snore* OR snoring*)
#5	#1 OR #2 OR #3 OR #4
#6	"Infant"[Mesh]
#7	"Child, Preschool"[Mesh]
#8	"Child"[Mesh]
#9	"Adolescent"[Mesh]
#10	(child*[Title/Abstract] OR pediat*[Title/Abstract] OR paediat*[Title/Abstract] OR infan*[Title/Abstract] OR youth*[Title/Abstract] OR toddler*[Title/Abstract] OR adolesc*[Title/Abstract] OR teen*[Title/Abstract] OR boy*[Title/Abstract] OR girl*[Title/Abstract] OR bab*[Title/Abstract] OR preschool*[Title/Abstract] OR pre-school*[Title/Abstract])
#11	#6 OR #7 OR #8 OR #9 OR #10
#12	#5 AND #11
#13	"Meta-Analysis" [Publication Type]
#14	"Meta-Analysis as Topic"[Mesh]
#15	Meta analysis
#16	Meta analyses
#17	Systematic review
#18	Systematic reviews
#19	OR/13–18
#20	#12 AND #19

using a pre-designed data extraction form. Disagreements were resolved by discussion; when necessary, a third researcher was consulted to achieve consensus.

Evidence evaluation

The AGREE-II tool was used to evaluate the methodological quality of the relevant guidelines. The AMSTAR2 scale was used to evaluate the methodological quality of included systematic reviews.⁶⁹ High quality systematic review and/or meta-analysis was used directly and it would be updated if the study had published for more than 2 years, among which Chinese children's evidence was also collected and evaluated. The Cochrane Risk of Bias tool was used to evaluate the risk of bias of included RCTs. The Quality Assessment of Diagnostic Accuracy Studies tool was used to evaluate the methodological quality of included diagnostic tests. The Newcastle-Ottawa scale was used to evaluate the methodological quality of included cohort and case-control studies. The evaluation process was completed by two independent reviewers; disagreements were resolved by discussion or consultation with a third reviewer to achieve consensus.

Quality evaluation of the evidence body was conducted based on the GRADE System in evidence summary of each clinical question (Table 3). The quality of evidence was graded as high, moderate, low, or very low; the strength of commendation was considered strong or weak (<http://www.gradeworkinggroup.org/>). The evidence was downgraded according to five criteria (i.e., risk of bias, inconsistency, indirectness, imprecision, and publication bias) or upgraded according to three criteria (i.e., large magnitude of effect, dose-response gradient, or plausible confounding can increase confidence in estimated effects). Evidence was presented through a summary of finding tables and evidence profiles.

Formulation of recommendation

The guideline development working group established 27 recommendations based on the systematic review evidence related to each clinical question and the systematic review evidence developed by the guideline development working group. Recommendations on individual issues are combined relevant guideline evidence; the preferences and values of Chinese children and their guardians; the cost of intervention; and other advantages and disadvantages. Through three rounds of Delphi surveys and a face-to-face expert consensus meeting held in Beijing, China, on August 25, 2019, a total of 82 suggestions were collected and 24 final recommendations were formed. During this period, the guideline working group discussed and finalized all recommendations and quality of evidence grades.

Draft external review of the guideline

The guideline was reviewed by seven external peer

experts and improved on the basis of their feedback and suggestions. Finally, the guideline development working group submitted the guideline to the steering group for approval.

Dissemination and implementation of this guideline

The guideline was disseminated and promoted in the following ways: 1) Introduction and interpretation in relevant academic conferences; 2) Presentation at gatherings of otorhinolaryngologists, respiratory physicians, sleep monitoring technicians, nurses, and other relevant medical workers throughout China to learn the relevant contents of the guideline and use it correctly; 3) Dissemination through the Internet.

Estimation of advantageous and disadvantageous factors that may affect implementation of the guideline. Advantageous factors: snoring and sleep apnea are gradually recognized by the public, parents closely monitor their children's sleep problems, and clinicians at all levels strongly demand pediatric OSA-related guideline. Disadvantageous factors: 1) OSA is a type of sleep disorder for which the main clinical manifestations are snoring and sleep apnea. Sleep disorders cover a wide range, and now tend to require combined diagnosis and treatment by clinicians in otorhinolaryngology, head and neck surgery, respiratory, stomatology, and developmental behavior specialties. This guideline mainly focus on OSA in children with enlarged tonsils, adenoids, and/or obesity; however, they do not consider primary snoring, central apnea or hypopnea syndrome, and other congenital or severe diseases. 2) The study population for which evidence was obtained in this guideline rarely included 14–18-year-old children/adolescents. The growth and development of older children/adolescents is similar to that of adults, but is quite different from that of young children. Therefore, older children/adolescents exhibit adult morbidity characteristics; they can be treated in accordance with the principles of diagnosis and treatment for adult OSA. 3) This guideline aimed to address the efficacy and safety of leukotriene receptor antagonists in the treatment of pediatric OSA. Montelukast sodium was the main focus of the available clinical evidence, as there was no evidence regarding other leukotriene receptor antagonists.

Updates of the guideline

The preparation team plans to update this guideline 3–5 years after their publication. The update method will be implemented in accordance with the international guidelines update process.

Version statement

There are two versions of this guide, Chinese and English. The Chinese version of this guideline will be jointly published by the *Chinese Journal of Otorhinolaryngology*

and *head and neck surgery* and the *Chinese Journal of Evidence-based Medicine*, while the English version will be jointly published by *Pediatric Investigation* and *World Journal of Otorhinolaryngology-Head and Neck Surgery*. The supporting data of the guideline are stored in the National Center for Children's Health/Beijing Children's Hospital, Capital Medical University.

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CONFLICT OF INTEREST

None.

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