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# Upper Airway Treatable Traits in Obstructive Sleep Apnea: Bridging Otolaryngology and Respiratory Medicine

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**Abstract:** Obstructive sleep apnea (OSA) is a heterogeneous disorder in which recurrent upper-airway obstruction reflects variable combinations of anatomical vulnerability and non-anatomical physiology. A treatable-traits framework may help move management beyond the apnea-hypopnea index by linking clinically relevant, modifiable characteristics to specific interventions. This narrative review focuses on adult upper-airway traits at the interface of otolaryngology, respiratory medicine, and sleep medicine. Nasal obstruction, tonsillar hypertrophy, palatal and lateral pharyngeal collapse, tongue-base obstruction, craniofacial restriction, epiglottic collapse, and position-dependent obstruction may be actionable, but the strength of evidence supporting treatment selection varies by trait. Drug-induced sleep endoscopy (DISE) can characterize dynamic collapse and may change management in selected patients, although visualization of a collapse pattern is not equivalent to validated prediction of treatment response. Positive airway pressure remains foundational, while oral appliance therapy, positional therapy, site-directed surgery, maxillomandibular advancement, hypoglossal nerve stimulation, nasal treatment, and weight-directed treatment may be appropriate for selected phenotypes. We propose an evidence-informed, iterative approach that distinguishes direct therapeutic targets from enabling traits and emerging treatment-selection markers, emphasizes selective rather than routine use of DISE, and incorporates clinical and objective reassessment tailored to treatment and context. The goal of precision OSA care is not maximal phenotyping, but clinically useful phenotyping that changes management while acknowledging uncertainty.

**Keywords:** Obstructive Sleep Apnea; Treatable Traits; Upper Airway; Drug-Induced Sleep Endoscopy; Phenotype; Endotype; Otolaryngology; Sleep Medicine

## 1. Introduction

Obstructive sleep apnea (OSA) is commonly summarized by the apnea-hypopnea index (AHI), yet patients with similar AHIs may differ substantially in symptoms, hypoxic burden, patterns of upper-airway obstruction, physiological mechanisms, comorbidity, treatment tolerance, and response. Contemporary physiological models emphasize interacting traits including anatomical collapsibility, pharyngeal dilator muscle responsiveness, ventilatory control instability (loop gain), and arousal threshold [1,2]. These mechanisms do not operate independently: the same anatomical airway can remain stable in one patient but repeatedly collapse in another because neuromuscular compensation, ventilatory control, sleep stage, body position, or arousal responses differ. This heterogeneity helps explain why treatment response varies even among patients with comparable conventional OSA severity.

The treatable-traits concept was developed as a precision-medicine framework for heterogeneous airway disease: a trait should be recognizable, clinically relevant, and linked to an intervention with measurable benefit [3]. Applied to OSA, the concept is useful only if it improves clinical decision-making rather than simply creating a longer list of phenotypes. For clinical organization, this review distinguishes direct therapeutic targets, enabling traits, and

emerging treatment-selection markers. These categories describe clinical roles and translational status, not a hierarchy of evidence certainty. A direct target can still have limited treatment-selection evidence, while an enabling trait can be supported by clinically meaningful evidence for treatment delivery or acceptance.

Upper-airway anatomy is especially relevant to otolaryngology because nasal, oropharyngeal, retroglossal, craniofacial, and epiglottic abnormalities can be directly examined and, in selected patients, modified. However, identification of an abnormal structure does not by itself establish that correcting that structure will improve clinically important OSA outcomes. This distinction is central to the present review. A visible finding may be descriptive, may alter a treatment plan, or may have validated predictive value for treatment response; these are separate evidentiary steps.

Drug-induced sleep endoscopy (DISE) illustrates this problem clearly. DISE can characterize sleep-like patterns of dynamic collapse [4,5], but a collapse pattern is not automatically a treatment-response biomarker. Similarly, the effectiveness of a therapy in a selected OSA population does not prove that a particular endoscopic or anatomical feature can reliably identify responders. The purpose of this review is therefore not only to catalogue upper-airway abnormalities, but to ask how strongly each finding can support a treatment decision, what outcome should be used to judge success, and where uncertainty remains. This perspective is intended to bridge otolaryngologic examination with respiratory and sleep-medicine assessment rather than to privilege one specialty or intervention over another.

## 2. Review Approach and Literature Selection

This narrative review focuses on adult OSA; pediatric treatment pathways are outside its scope. PubMed/MEDLINE was the principal bibliographic database used during manuscript development and revision, supplemented by targeted searches of official society, regulatory, journal, and publisher websites. No formal lower date limit was applied. Searches were updated through 21 October 2026. Search concepts were combined around the following domains: "obstructive sleep apnea" or "OSA" with "treatable traits", "phenotype", "endotype", "upper airway", "nasal obstruction", "tonsillectomy", "palatal surgery", "lateral pharyngeal wall", "tongue base", "craniofacial", "epiglottic collapse", "drug-induced sleep endoscopy", "mandibular advancement", "maxillomandibular advancement", "hypoglossal nerve stimulation", "positional therapy", "obesity treatment", "loop gain", "arousal threshold", "older adults", "COPD", and "asthma". Searches were repeated with therapy-specific terms when a clinical question required direct evidence about treatment efficacy, patient selection, or follow-up.

Priority was given to clinical practice guidelines and official statements, randomized controlled trials, pivotal prospective studies, systematic reviews and meta-analyses, and recent studies that directly informed treatment selection or its limitations. When several sources addressed the same question, the most recent high-quality synthesis was preferentially used together with a pivotal original trial when that trial clarified patient selection, effect size, safety, or an important limitation. Older landmark studies were retained when they defined a classification system, physiological construct, or treatment platform that remains clinically relevant. Case reports and very small uncontrolled series were not used as the principal basis for general treatment recommendations. English-language adult studies were prioritized for the clinical synthesis; non-English guidance was considered when an English abstract provided relevant methodological or consensus information.

The search was deliberately targeted rather than exhaustive. This was not a systematic review: no protocol was registered, no Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram was generated, and no formal risk-of-bias or certainty-of-evidence grading was performed. Reference lists of key sources were checked for additional clinically relevant studies, and a final targeted update was performed for anatomical traits supported by older literature. That update identified newer evidence including a 2025 randomized trial of adult tonsillectomy, a 2025 meta-analysis comparing palatopharyngeal surgical modifications, a recent review of epiglottic collapse, and a 2026 meta-analysis of hypoglossal nerve stimulation [6–9]. The final synthesis therefore emphasizes transparency about the type, recency, and limitations of supporting evidence rather than implying comprehensive evidence grading.

Evidence was interpreted at two distinct levels. First, we considered whether a therapy has demonstrated benefit in an appropriate OSA population. Second, we considered whether the specific trait under discussion has been validated as a treatment-selection marker for that therapy. These questions are not interchangeable. For example, oral appliance therapy and upper-airway surgery can be effective in selected adults, but an isolated tongue-base or

palatal finding does not necessarily have validated predictive accuracy for treatment response. This distinction is carried through the text and tables. AI-assisted manuscript preparation is described in the AI Use Statement; no figures are included in the revised manuscript.

## 3. From Phenotypes and Endotypes to Clinically Usable Treatable Traits

### 3.1. A Practical Evidence-Aware Definition

For this review, a clinically useful treatable trait is a characteristic that can be identified with reasonable reliability, is relevant to disease expression or treatment delivery, and is linked to an intervention that may provide benefit in an appropriate patient population. Detectability is not equivalent to validated treatment selection. A trait may be easy to observe and biologically plausible while still lacking evidence that its presence predicts benefit from a specific intervention. Conversely, an enabling trait may not reduce AHI substantially but can still produce clinically meaningful benefit by improving tolerance, adherence, or feasibility of an established treatment.

The category of direct therapeutic target is used when the trait itself is a principal object of intervention. Marked tonsillar hypertrophy, position-dependent obstruction, craniofacial restriction, obesity-related loading, and selected dynamic collapse patterns can fall into this category, but the strength of treatment-selection evidence varies. Enabling traits are factors whose modification helps another therapy succeed; nasal obstruction and positive airway pressure (PAP)-related barriers are common examples. Emerging treatment-selection markers include physiological endotypes and selected dynamic findings for which measurement is increasingly feasible but prospective evidence linking the marker to superior treatment selection remains incomplete [2].

This distinction also changes how success should be measured. A direct target may be judged by objective respiratory outcomes, symptoms, treatment burden, and safety. An enabling trait may be judged by nasal symptoms, mask tolerance, PAP use, pressure requirements, or whether the patient can sustain an otherwise effective treatment. An emerging marker should be judged not only by measurement validity but by whether using the marker changes treatment choice and improves outcomes compared with usual care. This classification therefore separates clinical role from the strength and limitations of treatment linkage rather than presenting the categories as evidence grades.

### 3.2. Physiological Endotypes and Their Current Clinical Status

Upper-airway collapsibility, pharyngeal muscle responsiveness, loop gain, and arousal threshold provide a mechanistic framework for OSA [1,2]. Collapsibility reflects passive mechanical vulnerability; muscle responsiveness reflects the ability of dilator muscles to compensate; loop gain reflects ventilatory-control instability; and arousal threshold influences when respiratory events are terminated by cortical arousal. These traits help explain why apparently similar anatomy can produce very different disease expression and why an anatomically directed treatment may be highly effective in one patient but incomplete in another.

Estimation of endotypes from routine polysomnography is increasingly feasible, and newer work on loop gain illustrates the movement from specialized physiological laboratories toward scalable signal-derived measures [10]. However, clinically validated cutoffs, reproducibility across platforms, and prospective evidence that endotype-guided selection improves patient-important outcomes remain limited [2,10]. These measures should therefore be described as promising mechanistic or treatment-selection markers rather than established routine decision tools. Their present value is strongest when they clarify why a conventional intervention may have an incomplete effect or when they are used within research and specialized clinical pathways.

### 3.3. Multiple Traits and Combination Therapy

OSA often reflects several interacting mechanisms. A patient may simultaneously have nasal obstruction, obesity-related loading, retroglossal vulnerability, and supine-predominant obstruction. In such cases, combination therapy can be a rational planned strategy rather than evidence of treatment failure. Nasal treatment may enable PAP, weight reduction may reduce mechanical loading, a mandibular advancement device may improve retroglossal patency, and positional therapy may address residual supine events. The relevant question is not whether one intervention corrects every abnormality, but whether the combined strategy achieves acceptable control with tolerable burden.

Trait interactions can also create apparent contradictions. PAP intolerance can directly change a treatment pathway, but conceptually it remains an enabling or treatment-related trait because the clinical objective is to overcome a barrier to effective treatment or select an acceptable alternative. Likewise, obesity is a direct systemic/mechanical target but does not replace treatment of persistent airway obstruction when residual OSA remains. The clinical task is to identify which traits are dominant, modifiable, and sufficiently supported by evidence to alter management at a particular point in care.

## 4. Anatomical Upper-Airway Traits and the Strength of Treatment Linkage

### 4.1. Nasal Obstruction: Primarily an Enabling Trait

Septal deviation, turbinate hypertrophy, rhinitis, polyposis, and nasal valve dysfunction are readily identifiable through history, nasal examination, and endoscopy. These findings matter clinically because nasal resistance can increase breathing discomfort and can interfere with nasal PAP interfaces. Importantly, the outcome of interest should match the role assigned to the trait. If nasal obstruction is treated as an enabling trait, improvement in nasal symptoms, mask tolerance, PAP pressure requirements, adherence, or willingness to continue treatment may be more relevant than a large change in AHI.

A recent systematic review found that isolated nasal surgery improves subjective sleep quality, sleepiness, nasal resistance, and snoring, but generally produces little change in objective polysomnographic severity; it may also reduce required continuous positive airway pressure (CPAP) titration pressures and increase CPAP use [11]. These findings support nasal treatment as a facilitator of established OSA therapy rather than a routine stand-alone cure. Medical therapy for inflammatory disease should be optimized first when appropriate, while septoplasty, turbinate procedures, or functional nasal surgery may be considered when a structural abnormality remains clinically important. The decision should be driven by symptoms and treatment feasibility rather than by the assumption that correction of nasal anatomy alone will normalize OSA.

### 4.2. Tonsillar, Palatal, and Lateral Pharyngeal Obstruction

Marked palatine tonsillar hypertrophy is one of the more intuitive direct anatomical targets because the obstructing tissue is visible and removable. The older systematic review and meta-analysis of adult tonsillectomy demonstrated substantial improvement in selected patients with enlarged tonsils, particularly in less severe disease [12]. A 2025 randomized controlled trial has now added contemporary evidence: among 29 adults with primarily mild-to-moderate OSA and body mass index (BMI) no greater than 35 $kg/m^2$, tonsillectomy produced a clinically meaningful reduction in AHI over one year compared with lifestyle counseling [6]. The trial was small, but it supports the concept that tonsillectomy can be an effective treatment option in carefully selected adults rather than an intervention extrapolated only from uncontrolled cohorts.

Palatal and lateral pharyngeal wall obstruction are more heterogeneous. Collapse may be anteroposterior, lateral, or concentric and may coexist with downstream obstruction. The SAMS randomized clinical trial showed that combined palatal and tongue surgery improved AHI and daytime sleepiness compared with ongoing medical management in selected adults with moderate-to-severe OSA after failure of conventional therapy [13]. A 2025 meta-analysis of 45 studies involving 1,501 adults undergoing palatopharyngeal surgery without concomitant tonsillectomy further demonstrated that these procedures are not interchangeable: pooled AHI reduction varied substantially by technique, and the responder rate was 51% in the 23 studies (728 patients) reporting that outcome, with stronger reductions reported for powered, muscle-relocation, and suture-based techniques than for several older approaches [7]. This heterogeneity argues against treating “palatal surgery” as a single exposure.

These treatment data should not be overextended into a claim that a particular DISE pattern has validated predictive value for one specific procedure. A lateral-wall or palatal collapse pattern can contribute to anatomical reasoning and surgical planning, but predictive accuracy depends on technique, multilevel disease, obesity, physiological traits, and patient selection. The practical implication is to use anatomical information to define a plausible target and to counsel patients about expected benefit and uncertainty, rather than to equate a visually prominent collapse with guaranteed surgical success.

### 4.3. Tongue-Base and Craniofacial Restriction

Retroglossal obstruction can reflect tongue volume, lingual tonsillar tissue, mandibular position, craniofacial restriction, or dynamic posterior displacement. Clinical and dental examination may reveal retrognathia, limited retrolingual space, dental constraints, or other features relevant to treatment feasibility. Selected imaging can clarify skeletal and soft-tissue relationships, although most imaging is obtained awake and should not be treated as a direct substitute for sleep-state airway behavior.

Oral appliance therapy has guideline support for adults who prefer an alternative to PAP or cannot tolerate PAP, particularly using custom titratable mandibular advancement devices [14]. The efficacy of the therapy is established at the population level, but an isolated retroglossal finding has not been validated as a universal response marker. Jaw-thrust maneuvers during DISE may add supportive information, yet negative maneuvers should not automatically exclude treatment, as discussed below [15]. Dental health, temporomandibular-joint status, degree of mandibular advancement that can be achieved, and patient preference remain important practical determinants.

Maxillomandibular advancement (MMA) addresses skeletal and multilevel airway restriction through advancement of both jaws. A 2025 meta-analysis of 31 studies and 1,597 patients found substantial mean reductions in AHI and improvement in oxygen saturation nadir after MMA [16]. Patient-reported quality-of-life outcomes also improve in published cohorts [17]. These benefits must be balanced against the burden of major craniofacial surgery and procedure-specific adverse effects, including persistent lower-facial sensory disturbance in a subset of patients. MMA is therefore best discussed as an effective option for appropriately selected patients rather than as a default response to retrognathia or tongue-base collapse.

### 4.4. Epiglottic Collapse

Epiglottic collapse may be occult during wakefulness and can be revealed by DISE. It can occur as an isolated pattern or as one component of multilevel obstruction, and different morphologic behaviors have been described. The older systematic review highlighted limited evidence and uncertainty regarding the clinical significance of this finding [18]. More recent literature confirms growing recognition of epiglottic collapse but also emphasizes wide variation in reported prevalence, inconsistent diagnostic criteria, and the need for standardized treatment pathways [8].

Management can include PAP, positional or mandibular strategies, or selected epiglottic procedures. In some patients, PAP is effective; in others, the interaction between applied pressure and a highly mobile epiglottis may be complex. Surgical options described in the literature include epiglottis-stabilizing or tissue-reducing procedures, usually in highly selected cases. Because the evidence base is dominated by observational studies and heterogeneous surgical series, epiglottic collapse should not be treated as a stand-alone surgical indication. The finding is most useful when integrated with symptoms, PAP response, multilevel collapse, and the effect of positional or mandibular maneuvers.

### 4.5. Position Dependence and Multilevel Obstruction

Position dependence is a clinically measurable trait with a direct therapeutic implication when supine events predominate. Body position can modify tongue-base, palatal, lateral-wall, and epiglottic behavior through gravitational and lung-volume effects. Positional therapy can reduce supine respiratory events and may be sufficient in selected patients with a strong positional phenotype, although PAP generally produces greater overall AHI reduction when OSA is not strongly position dependent [19]. Durability and adherence vary with the device or behavioral strategy used, and treatment response should be interpreted in relation to the diagnostic study that established positional dependence.

Multilevel obstruction is common and weakens one-site/one-treatment logic. A patient may have enlarged tonsils, retropalatal collapse, and retroglossal narrowing simultaneously, while obesity or high loop gain amplifies overall instability. In such patients, the objective is not to label one structure as the sole cause, but to identify dominant, actionable contributors and choose a treatment strategy with acceptable expected benefit and burden. **Table 1** summarizes upper-airway and related treatable traits according to clinical role, practical judgment, treatment implications, supporting evidence, treatment-selection validity, and key limitations.

**Table 1.** Clinically actionable traits: Role, judgment, treatment linkage, and limitations.

| Trait/Example | Clinical Role | Assessment and Decision Criteria | Potential Treatment Implication | Supporting Evidence and Treatment-Selection Validity | Main Limitation |
|---|---|---|---|---|---|
| Nasal obstruction | Enabling trait | Symptoms + nasal exam/endoscopy; identify structural/inflammatory cause | Medical therapy; selected nasal surgery; facilitate PAP | Systematic-review evidence supports improvement in nasal symptoms and PAP facilitation [11]; evidence for OSA resolution or treatment selection based on nasal findings alone remains limited. | AHI may change little despite improved nasal breathing |
| Marked tonsillar hypertrophy | Direct therapeutic target—anatomical | Large tonsils with compatible narrowing; assess whole airway | Tonsillectomy in selected adults | A 2025 randomized trial [6] and systematic-review evidence [12] support tonsillectomy in selected adults; broader phenotype remains important. | Residual multilevel/non-anatomical disease |
| Palatal/lateral-wall collapse | Direct therapeutic target—dynamic anatomical | Awake assessment; DISE only if result may change treatment | Selected reconstructive/multilevel pharyngeal surgery | SAMS RCT supports multilevel surgery in selected adults [13], and a 2025 meta-analysis shows technique-dependent palatopharyngeal outcomes [7]; DISE pattern alone is not a validated response predictor [4,5,20,21]. | Collapse pattern alone does not establish outcome benefit |
| Tongue-base/retroglossal vulnerability | Direct therapeutic target—anatomical/dynamic | Clinical/dental assessment; selected imaging or DISE | MAD; MMA; selected surgery; HNS by phenotype | MAD is guideline-supported [14], but an isolated retroglossal finding is not a validated response marker; MMA is supported in selected cohorts [16]. | No single finding reliably predicts response |
| Craniofacial restriction | Direct therapeutic target—structural | Dental/craniofacial examination; selected imaging | MAD or MMA in selected patients | MMA outcome and patient-reported evidence support selected patients [16,17]; treatment matching remains individualized. | Major procedure burden; imaging is usually static |
| Epiglottic collapse | Direct therapeutic target—dynamic anatomical | DISE when clinically relevant | PAP; positional/mandibular strategies; selected surgery | Recent review evidence confirms clinical relevance but heterogeneous prevalence and treatment evidence [8,18]; treatment-selection validity remains limited. | Often multilevel; heterogeneous data |
| Position-dependent obstruction | Direct therapeutic target—sleep-state dependent | Sleep-study evidence of supine predominance | Positional therapy; combination treatment | Meta-analysis supports positional therapy in selected patients [19]. | Definitions, adherence, durability vary |
| PAP-related barriers | Enabling trait—treatment-related | PAP-use data + clinical assessment | Interface, nasal, pressure, behavioral or sleep interventions | Evidence depends on the specific barrier/intervention; assess PAP use/adherence and treatment burden. | Not an anatomical OSA mechanism |
| Physiological endotypes | Emerging treatment-selection marker | Research/PSG-derived collapsibility, loop gain, arousal threshold, muscle compensation | Mechanism-informed therapy under evaluation | Mechanistic validity is strong [1,2,10]; routine treatment-selection utility is not established. | Methods/cutoffs and prospective utility need validation |
| Obesity-related loading | Direct therapeutic target—systemic/mechanical | BMI + clinical context | Weight-directed treatment plus established OSA therapy as needed | Randomized trials support tirzepatide in obesity-related OSA [22]; residual OSA requires reassessment. | Residual OSA may persist despite weight loss |

Note: Abbreviations: AHI, apnea-hypopnea index; BMI, body mass index; DISE, drug-induced sleep endoscopy; HNS, hypoglossal nerve stimulation; MAD, mandibular advancement device; MMA, maxillomandibular advancement; OSA, obstructive sleep apnea; PAP, positive airway pressure; PSG, polysomnography; RCT, randomized controlled trial; SAMS, Sleep Apnea Multilevel Surgery. Clinical-role categories describe primary decision-making roles, not evidence-certainty grades; some traits may span roles. Enabling-trait success may be reflected by nasal symptoms, PAP use/adherence, or treatment burden rather than AHI alone.

## 5. Dynamic Assessment of the Upper Airway

### 5.1. Awake Assessment, Imaging, and DISE

History, nasal and oropharyngeal examination, flexible endoscopy, craniofacial assessment, and selected imaging remain the foundation of anatomical assessment. These tools are inexpensive relative to procedural sleep-state evaluation and can identify many clinically relevant findings, including nasal obstruction, large tonsils, craniofacial restriction, dental limitations, lingual tonsillar enlargement, and laryngeal abnormalities. Their main limitation is state dependence: wakefulness preserves neuromuscular tone and may not reproduce the configuration or severity

of collapse during sleep.

DISE adds sleep-like dynamic information and can describe the site, degree, and configuration of collapse using systems such as the velum, oropharyngeal lateral walls, tongue base, and epiglottis (VOTE) classification [4,5]. Its most defensible role is selective treatment planning when the result is likely to change management, not routine staging of every patient with OSA. Examples include evaluation of candidates for selected surgical procedures or hypoglossal nerve stimulation, clarification of suspected epiglottic or multilevel collapse, and assessment of how mandibular advancement or positional maneuvers alter dynamic obstruction.

The distinction between information and utility is essential. DISE can provide information unavailable from an awake examination, but additional information is not automatically beneficial if it does not alter a treatment decision or improve outcomes. Sedative agent, dose, depth of sedation, body position, and scoring variability can influence findings [5]. For that reason, clinically useful DISE requires standardized technique, a clear pre-procedure decision question, and interpretation in the context of objective OSA severity, symptoms, comorbidity, and treatment history. **Table 2** summarizes the clinical roles and limitations of principal assessment methods.

**Table 2.** Assessment methods: Clinical role and limits.

| Assessment | What It Adds | When It Can Change Management | Important Limitation | Example Implication |
|---|---|---|---|---|
| History + routine examination | Symptoms, nasal disease, tonsils, dentition, craniofacial features, treatment barriers | In objectively confirmed OSA, guides initial treatment selection and identifies barriers or referral needs | Awake/static and partly subjective | Treat rhinitis; optimize PAP; refer for dental/ENT assessment |
| PSG/HSAT | Objective OSA confirmation, oxygenation, position; PSG adds sleep stage and arousals | Diagnosis and follow-up; PSG is preferred when significant cardiorespiratory disease or hypoventilation is present [23] | HSAT is appropriate for selected uncomplicated adults; PSG and HSAT are not interchangeable in all patients [23] | Severity/context; positional phenotype; residual disease assessment |
| Imaging (selected) | Craniofacial and soft-tissue anatomy | When skeletal/structural information affects dental/surgical planning | Usually awake/static; cost/radiation depending modality | MMA planning; selected complex anatomy |
| DISE | Dynamic site, degree, configuration of collapse | When result is likely to alter non-PAP treatment selection | Sedation effects, observer variability, incomplete outcome-prediction evidence | Surgical planning; HNS eligibility; selected MAD/positional assessment |
| VOTE classification (DISE reporting) | Structured description of velum, oropharyngeal lateral wall, tongue-base, and epiglottic collapse | Standardizes communication of DISE findings | A reporting framework, not an independent test or physiological endotype measure | Supports structured interpretation; does not itself validate a treatment choice [4] |
| Jaw thrust during DISE | Change in collapse with simulated mandibular advancement | May support MAD consideration | Negative result should not exclude MAD; incremental value uncertain | Positive response can strengthen rationale for MAD |
| PSG-derived endotyping | Estimated collapsibility, loop gain, arousal threshold, muscle compensation | Research and selected advanced phenotyping | Methods/cutoffs/clinical utility not fully standardized | Potential future mechanism-directed therapy |
| Post-treatment sleep testing | Residual AHI, hypoxemia, position/REM pattern | After oral appliance and most non-PAP therapies; positional therapy may not require repeat testing when efficacy was already demonstrated during the diagnostic study [24] | Routine retesting is not recommended for asymptomatic patients stable on PAP; follow-up testing should match the clinical question [24] | Continue, combine, or modify treatment based on clinical and objective reassessment |

Note: Abbreviations: AHI, apnea-hypopnea index; DISE, drug-induced sleep endoscopy; ENT, otolaryngology; HNS, hypoglossal nerve stimulation; HSAT, home sleep apnea testing; MAD, mandibular advancement device; MMA, maxillomandibular advancement; OSA, obstructive sleep apnea; PAP, positive airway pressure; PSG, polysomnography; REM, rapid eye movement; VOTE, velum, oropharyngeal lateral walls, tongue base, and epiglottis.

## 5.2. Dynamic Maneuvers: Useful Signals, Not Exclusion Tests

Mandibular advancement or jaw-thrust maneuvers during DISE can simulate one component of oral appliance therapy. In a prospective study, a positive jaw-thrust response was associated with favorable oral-appliance response; however, a negative response was not a significant predictor of treatment failure [15]. A positive jaw-thrust response may therefore strengthen the rationale for oral appliance therapy, but a negative response should not be used to exclude treatment. The incremental value of performing DISE solely to predict oral-appliance efficacy remains uncertain [15].

Positional maneuvers can be interpreted similarly. Improvement with lateral positioning during DISE may sup-

port the biological plausibility of positional therapy, but the diagnostic sleep study remains the primary method for establishing a reproducible positional phenotype. Likewise, mouth closure or chin-lift maneuvers may generate treatment hypotheses without constituting validated response tests. Dynamic maneuvers are best viewed as supportive signals that can refine an already plausible treatment pathway rather than binary inclusion or exclusion criteria.

### 5.3. What DISE Can and Cannot Establish

Three questions should be kept separate: whether DISE can reliably describe a collapse pattern; whether the finding changes the clinician's treatment plan; and whether DISE-guided selection improves patient-centered outcomes. Evidence is strongest for description and selected eligibility decisions. Comparative studies and systematic reviews have yielded mixed findings on whether preoperative DISE improves surgical outcomes. A 2023 meta-analysis of seven comparative studies including 791 patients found no significant improvement in surgical success, AHI, minimum oxygen saturation, or Epworth Sleepiness Scale with preoperative DISE, while emphasizing the low overall level of evidence [20]. A 2024 systematic review of eight studies likewise found inconsistent evidence that DISE improves surgical outcomes [21].

These findings do not imply that DISE is useless. They indicate that its incremental outcome benefit should be distinguished from its ability to describe collapse patterns, reveal otherwise occult sites, and modify treatment plans. Outcome studies are also complicated by heterogeneity in surgical techniques, patient selection, sedation protocols, scoring systems, and definitions of success. A test can be clinically valuable for selected decisions even when a universal improvement in surgical outcomes has not been demonstrated across heterogeneous populations.

A practical decision rule is therefore to ask before DISE: what treatment choice could change because of this result? If the answer is unclear, routine DISE is less compelling. If the result could determine eligibility for a device, clarify suspected epiglottic or multilevel obstruction, or alter the type or extent of a planned intervention, the procedure may provide more actionable information. Standardized reporting and explicit acknowledgment of uncertainty remain essential [4,5].

## 6. Matching Traits to Therapy: Indication, Effect, and Limitation

### 6.1. PAP Remains Foundational

Positive airway pressure (PAP) pneumatically splints the upper airway across multiple levels and remains a cornerstone of therapy. From a treatable-traits perspective, PAP is notable because it can overcome anatomical collapsibility without requiring precise localization of every obstruction site. The presence of a surgically modifiable abnormality therefore does not automatically make surgery the preferred initial treatment. American Academy of Sleep Medicine guidance on surgical referral emphasizes discussion of surgical consultation for appropriate PAP-intolerant patients while also supporting PAP as initial therapy in many adults with major upper-airway anatomical abnormalities [25].

Clinical failure of PAP should be separated into efficacy failure and implementation failure. Many patients can achieve excellent control when PAP is worn but struggle with nasal obstruction, mask leak, discomfort, pressure intolerance, claustrophobia, insomnia, or practical burden. These are enabling or treatment-related traits rather than evidence that pneumatic splinting is physiologically ineffective. Interface adjustment, humidification, pressure optimization, treatment of nasal disease, behavioral support, and insomnia management may convert apparent PAP intolerance into successful treatment. When such measures fail or conflict with patient preference, non-PAP pathways become more relevant.

### 6.2. Oral Appliance and Positional Therapy

Custom titratable mandibular advancement devices are guideline-supported for adults who prefer an alternative to continuous positive airway pressure (CPAP) or are CPAP-intolerant [14]. Their principal mechanical effect is to advance the mandible and associated soft tissues, increasing pharyngeal dimensions and reducing collapsibility, particularly in the retroglossal region. However, treatment selection should not be reduced to the presence or absence of a single tongue-base finding. Dental status, achievable protrusion, OSA severity, body position, craniofacial morphology, patient preference, and tolerance all influence feasibility and effectiveness.

Positional therapy is most rational when a reproducible supine-predominant phenotype is present and can also complement a partially effective primary therapy [19]. For example, a mandibular advancement device may control most events but leave residual supine obstruction; adding positional therapy can be more acceptable than abandoning an otherwise useful treatment. Follow-up sleep testing is recommended after oral appliance therapy [14, 24]. For positional therapy, repeat testing may be unnecessary when its efficacy has already been demonstrated during the diagnostic sleep study, although reassessment is appropriate when symptoms persist, weight changes substantially, or the clinical picture changes [24].

### 6.3. Upper-Airway Surgery and MMA

Surgery should be framed as a referral and selection process rather than an automatic consequence of finding an anatomical lesion. Procedure choice depends on the target, multilevel disease, operative burden, comorbidity, prior therapy, and patient goals [25]. The evidence base is heterogeneous because different operations act on different structures and have different risk profiles. Contemporary palatal procedures increasingly emphasize reconstruction, stabilization, or repositioning rather than indiscriminate tissue removal, while multilevel surgery may combine palatal and tongue-directed components.

In the SAMS randomized clinical trial of 102 adults with moderate-to-severe OSA in whom conventional therapy had failed, multilevel palatal and tongue surgery produced greater improvement than ongoing medical management at six months: the baseline-adjusted between-group difference was −17.6 events/h for AHI and −6.7 points for the Epworth Sleepiness Scale [13]. Among the 50 operated participants, two (4%) experienced serious adverse events judged potentially related to the procedure [13]. This trial demonstrates efficacy of multilevel soft-tissue surgery in selected patients, but did not validate a specific DISE collapse pattern as a treatment-response biomarker. The newer palatopharyngeal meta-analysis similarly shows that surgical technique matters and that pooled response is heterogeneous [7].

MMA is a broader structural intervention. In a 2025 meta-analysis of 31 studies including 1,597 patients, mean AHI decreased by 41.9 events/h and oxygen saturation nadir increased by 6.3 percentage points after MMA [16]. The pooled incidence of lower facial numbness at follow-up beyond one year was 32.7% [16]. Patient-reported outcomes also improved [17]. These results describe selected surgical populations and should not be interpreted as direct comparative superiority over non-surgical therapies tested in different populations. The decision to recommend MMA should therefore balance expected physiological benefit against invasiveness, dental and skeletal considerations, sensory complications, recovery burden, and patient preference.

### 6.4. Hypoglossal Nerve Stimulation

Hypoglossal nerve stimulation (HNS) augments upper-airway neuromuscular control rather than removing tissue. The STAR trial established proof of efficacy in carefully selected adults with PAP intolerance [26]. Since then, evidence has expanded substantially. A 2026 systematic review and meta-analysis of 38 studies comprising 3,220 patients reported a pooled Sher responder rate of approximately 74%, along with clinically important reductions in AHI, oxygen desaturation index, and sleepiness, but also substantial between-study heterogeneity [9]. This heterogeneity is important because it shows that even an effective therapy does not yet have perfectly defined response determinants.

Eligibility remains device- and jurisdiction-specific. For the U.S. Food and Drug Administration-approved Inspire system, current labeling includes moderate-to-severe OSA within specified AHI limits, inability to use or tolerate PAP, and absence of complete concentric collapse at the soft-palate level; current device labeling and local regulatory requirements should be checked rather than generalized across all stimulation systems [27]. DISE is therefore directly linked to eligibility in some HNS pathways, but this is different from claiming that every observed collapse pattern is a validated quantitative predictor of response.

### 6.5. Obesity and Weight-Directed Treatment

Obesity is an upstream mechanical and systemic trait. Increased peripharyngeal tissue, altered lung volume, and changes in airway mechanics can increase collapsibility, while metabolic and inflammatory effects may contribute more broadly to sleep-disordered breathing. Weight-directed treatment should therefore be considered part of OSA management when obesity is clinically relevant, but weight loss and airway-directed therapy are not

mutually exclusive.

In the two 52-week phase 3 SURMOUNT-OSA trials of adults with obesity and moderate-to-severe OSA, tirzepatide produced estimated treatment differences in AHI versus placebo of −20.0 events/h in participants not receiving PAP and −23.8 events/h in participants receiving PAP at baseline; gastrointestinal adverse events were the most frequent and were generally mild to moderate [22]. These results demonstrate that treatment of an upstream systemic trait can meaningfully reduce OSA burden in an appropriate population. They do not establish equivalence or superiority to airway-directed treatments tested in different populations, and residual OSA should be objectively reassessed before established therapy is withdrawn.

### 6.6. Combination Therapy and Reassessment

When multiple traits coexist, combination therapy may be planned from the outset or added after partial response. Examples include nasal treatment to facilitate PAP, an oral appliance plus positional therapy, weight management plus PAP, or surgery followed by lower-pressure PAP. Combination treatment is particularly logical when interventions address different mechanisms and when each component reduces treatment burden enough to improve adherence to the overall strategy.

Clinical and objective reassessment should be matched to treatment and clinical context. American Academy of Sleep Medicine guidance recommends follow-up polysomnography or home sleep apnea testing to assess response to non-PAP interventions, while routine retesting is not recommended for asymptomatic patients who are stable on PAP; repeat testing may also be appropriate after clinically significant weight change or when sleep-related hypoxemia or hypoventilation requires reassessment [24]. Reassessment should integrate symptoms, adherence, treatment burden, residual OSA, adverse effects, and whether remaining traits require additional therapy. A trait-based approach is therefore iterative rather than a one-time classification exercise.

## 7. Beyond Anatomy: Physiological Modifiers of an Anatomical Airway

Anatomy does not act in isolation. The same structural vulnerability can produce different clinical expression depending on pharyngeal muscle compensation, loop gain, arousal threshold, sleep stage, and body position [1,2]. A highly collapsible airway may require substantial PAP pressure or a strong structural intervention, whereas a moderately collapsible airway may become clinically unstable primarily because ventilatory-control or neuromuscular factors are unfavorable. This interaction explains why treatment effect cannot always be predicted from the apparent severity of one anatomical finding.

Upper-airway muscle responsiveness is particularly relevant to the interface between anatomy and physiology. During wakefulness, dilator muscle activity can compensate for a narrow airway. Sleep reduces this compensation, and some patients recruit pharyngeal muscles more effectively than others as respiratory drive rises. HNS targets one component of this physiology by augmenting neuromuscular activation, while PAP bypasses the need for adequate compensation by providing a pneumatic splint. These different mechanisms illustrate why the same anatomical phenotype can be approached in more than one way.

Loop gain describes the stability of ventilatory control. High loop gain can amplify cycles of obstruction and recovery because ventilatory responses overshoot and undershoot after a disturbance. Scalable estimation methods are improving, and recent work has focused on translating loop gain from laboratory endotyping toward clinically accessible measures [10]. Nevertheless, prospective evidence that routine loop-gain-guided therapy improves outcomes is not yet sufficient for universal use. The same caution applies to arousal-threshold and muscle-compensation estimates: mechanistic validity is not equivalent to treatment-selection utility.

Rapid eye movement (REM) sleep can worsen obstruction through state-dependent changes in neuromuscular tone and respiratory control [28], while supine positioning can increase mechanical disadvantage. REM-predominant or position-dependent phenotypes therefore provide examples in which disease expression changes without a change in fixed anatomy. These observations reinforce the central premise of the review: upper-airway findings should be interpreted within the physiological conditions under which collapse occurs, and treatment response should be judged by what happens across the patient's typical sleep architecture and body positions.

## 8. An Evidence-Informed Multidisciplinary Pathway

A practical pathway begins with objective confirmation and characterization of OSA rather than with upper-airway localization. Polysomnography or appropriately selected home sleep apnea testing establishes the presence of disease, event distribution, oxygenation, position dependence, and—when polysomnography is used—sleep stage and arousals [23]. The first treatment decision can often be made from this information together with symptoms, comorbidity, nasal and oropharyngeal examination, craniofacial and dental assessment, treatment preference, and practical barriers.

Targeted upper-airway assessment should be added when anatomical information has a realistic chance of changing management. Large tonsils, major nasal obstruction, obvious craniofacial restriction, or dental constraints may be actionable without DISE. Selected imaging can support dental or skeletal planning. DISE is reserved for questions that require sleep-like dynamic information, such as clarification of multilevel collapse, assessment of epiglottic behavior, device-specific HNS eligibility, or situations in which the planned surgical approach could change according to the observed pattern.

The next step is trait-informed treatment selection. PAP remains the default high-efficacy option for many patients, but non-PAP therapy becomes important when preference, intolerance, anatomy, position dependence, obesity, or prior treatment response justifies an alternative or adjunct. Direct therapeutic targets, enabling traits, and emerging markers should not be given equal weight. A direct target should have a plausible and evidence-supported intervention; an enabling trait should be judged by whether it improves treatment delivery; and an emerging marker should not drive irreversible treatment without adequate validation.

Finally, treatment should be followed by clinical and, when indicated, objective reassessment. Residual symptoms, poor adherence, persistent hypoxemia, or residual respiratory events should prompt re-evaluation of the trait profile rather than automatic escalation of the same therapy. This creates an iterative loop: confirm disease, identify clinically actionable traits, select therapy according to evidence and patient context, reassess, and refine. The pathway is evidence-informed but has not itself been prospectively validated as an integrated management strategy.

## 9. Patient Context: Older Adults and Chronic Respiratory Disease

### 9.1. Older Adults and Frailty

In older adults, the question is not only whether a trait is biologically modifiable, but whether the intervention is clinically appropriate. Frailty, cognition, manual dexterity for PAP setup, dentition for oral appliances, aspiration risk, perioperative burden, multimorbidity, caregiver support, life expectancy, and patient goals may change the preferred treatment even when the anatomical phenotype is similar. Very old and frail adults remain underrepresented in randomized trials, which limits direct extrapolation of evidence [29].

These factors have direct implications for upper-airway treatment selection. A visually correctable lesion does not automatically justify surgery if perioperative burden or recovery risk is disproportionate to expected symptomatic benefit. Conversely, older age alone should not exclude an effective non-PAP intervention in a functionally independent patient who understands the trade-offs. Oral appliance therapy may be limited by dentition, while PAP success may depend on dexterity, cognition, caregiver assistance, or interface tolerance. In a frail patient, an enabling intervention that improves comfort or adherence may be more valuable than pursuing maximal AHI normalization through an invasive procedure. The treatable-traits framework therefore requires a parallel assessment of treatment burden and functional reserve.

### 9.2. Chronic Obstructive Pulmonary Disease (COPD), Asthma, and Gas-Exchange Complexity

In chronic obstructive pulmonary disease (COPD)-OSA overlap, nocturnal hypoxemia, airflow limitation, and, in selected patients, hypercapnia can alter treatment priorities and may require broader respiratory assessment rather than an upper-airway intervention alone [30, 31]. The presence of an anatomical upper-airway target remains relevant, but the consequences of residual OSA may be magnified by impaired pulmonary reserve. A patient with significant nocturnal desaturation or suspected hypoventilation may require full polysomnography, gas-exchange assessment, PAP or ventilatory optimization, and careful consideration of whether an anatomical intervention will address the dominant physiological problem.

This changes the sequence of treatment selection. Correcting nasal obstruction may improve tolerance of PAP in a patient with COPD, but nasal surgery does not replace management of lower-airway disease or nocturnal hypoventilation. Similarly, upper-airway surgery may reduce obstructive events yet leave clinically important gas-exchange abnormalities that require separate treatment. Respiratory disease therefore functions as a contextual modifier of the expected benefit and safety of upper-airway intervention rather than as a reason to ignore upper-airway traits.

In asthma-OSA overlap, obesity, rhinitis, reflux, and sleep disruption can coexist as modifiable traits [32]. Nasal inflammatory disease may be an enabling trait for PAP tolerance, while obesity can amplify both asthma burden and OSA. However, treatment of one airway compartment should not be assumed to predictably improve the other. The practical implication is to coordinate upper- and lower-airway management and to define which outcome is being targeted—OSA control, PAP adherence, asthma symptoms, nocturnal oxygenation, or overall sleep quality—before attributing benefit to a single intervention.

## 10. Current Gaps and Future Directions

The main research gap is not the ability to generate additional phenotypes, but the ability to show that a measured trait changes treatment choice and improves outcomes. Future studies should distinguish descriptive associations from predictive biomarkers and should test treatment-by-trait interactions prospectively. A useful treatment-selection marker should demonstrate more than correlation with response: it should improve decision quality or outcomes compared with a strategy that does not use the marker.

DISE is a priority area for this distinction. Standardization of sedation, positioning, scoring, and reporting is necessary, but standardization alone does not prove outcome benefit [5,20,21]. Prospective studies should identify clearly defined decision points—for example, whether DISE changes the choice between two non-PAP therapies—and should measure whether that change improves objective control, symptoms, adverse events, treatment burden, or adherence. Similar principles apply to jaw-thrust maneuvers and other treatment simulations.

Physiological endotyping requires the same translational discipline. Scalable estimation of loop gain, arousal threshold, collapsibility, and muscle compensation is increasingly feasible, but clinical adoption should depend on prospective evidence that using these measures improves therapy selection [2,10]. Combination-therapy trials are particularly relevant because many patients have more than one actionable mechanism. Rather than comparing each therapy only as monotherapy, future work should test rational combinations that address distinct traits and quantify whether the added complexity is justified by greater effectiveness or lower treatment burden.

The evidence base for individual anatomical traits also remains uneven. The recent tonsillectomy randomized trial, contemporary palatopharyngeal meta-analysis, and updated epiglottic review strengthen areas previously dominated by older observational literature [6–8], but sample sizes, surgical techniques, and outcome definitions remain heterogeneous. HNS evidence has expanded substantially, yet the 2026 meta-analysis still identified considerable unexplained between-study heterogeneity despite an overall responder rate near three-quarters [9]. Better predictors of response, not simply more pooled efficacy estimates, are therefore needed.

Artificial intelligence may eventually assist DISE interpretation and multimodal phenotyping. A 2026 prospective proof-of-concept study evaluated a large language model in only 16 DISE cases; such work addresses feasibility and interpretive agreement, not improved patient outcomes [33]. AI systems require multicenter validation, reproducibility testing, bias assessment, and demonstration of incremental clinical value before routine use. More generally, precision OSA care should favor selective phenotyping: perform an additional test when the result has a realistic chance of changing management, rather than pursuing maximal phenotyping for its own sake [34].

## 11. Conclusions

Upper-airway treatable traits provide a clinically useful bridge between otolaryngology and respiratory sleep medicine, but their evidentiary status is not uniform. Some findings, such as position dependence, marked tonsillar enlargement, specific device-eligibility criteria, and clearly defined craniofacial abnormalities, can directly influence established treatment pathways. Others, including nasal obstruction and PAP-related barriers, often function as enabling traits whose value is measured by improved treatment delivery or tolerance rather than by AHI reduction alone. Physiological endotypes offer important mechanistic information but remain incompletely validated as

routine treatment-selection tools.

DISE is most useful when selectively applied to a decision that may change because of the observed collapse pattern. It can reveal dynamic anatomy and support selected eligibility or planning decisions, but it should not be interpreted as a universal predictor of treatment response. Recent randomized and meta-analytic evidence strengthens the case for selected tonsillar, palatal/multilevel, skeletal, neurostimulatory, and weight-directed interventions, while also highlighting heterogeneity of response and treatment burden [6,7,9,13,16,22].

The practical value of a treatable-traits approach is therefore not to replace standard OSA diagnosis or to mandate more testing. It is to improve the sequence of decisions: confirm OSA objectively, identify traits that are clinically relevant and actionable, distinguish direct targets from enabling factors and emerging markers, select treatment according to evidence and patient context, and reassess outcomes with measures appropriate to the intervention. Precision OSA care should be judged by whether it produces better and more acceptable treatment, not by the number of traits that can be measured. In parallel, established positive airway pressure guidelines emphasize patient education and practical troubleshooting to support sustained treatment use [35].

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## AI Use Statement

OpenAI ChatGPT was used during earlier manuscript development for initial drafting suggestions, structural organization, identification and organization of potentially relevant literature and topics, and English-language refinement. GPT-5.6 Sol was used during the final revision; exact model versions were not consistently recorded across earlier sessions. AI assistance influenced initial wording or organization in portions of Sections 1–11 and preliminary conceptual planning of figures that were subsequently removed during the first revision. The author independently evaluated original cited sources, determined study selection and evidence prioritization, reviewed and revised all substantive scientific statements, and verified reference details. AI was not used to autonomously determine study eligibility, perform independent data extraction or statistical analyses, conduct a formal risk-of-bias assessment, or make final clinical or scientific judgments. The revised manuscript contains no figures, whether AI-assisted or otherwise. The author takes full responsibility for the accuracy, originality, and integrity of the final text.

## References


1. Eckert, D.J.; White, D.P.; Jordan, A.S.; et al. Defining phenotypic causes of obstructive sleep apnea: Identification of novel therapeutic targets. *Am. J. Respir. Crit. Care Med.* **2013**, *188*, 996–1004. [CrossRef]
2. Tolbert, T.M.; Schmickl, C.N.; Gell, L.K.; et al. Research priorities for translating endophenotyping of adult obstructive sleep apnea to the clinic: An official American Thoracic Society Research Statement. *Am. J. Respir. Crit. Care Med.* **2025**, *211*, 1562–1583. [CrossRef]
3. Agusti, A.; Bel, E.; Thomas, M.; et al. Treatable traits: Toward precision medicine of chronic airway diseases. *Eur. Respir. J.* **2016**, *47*, 410–419. [CrossRef]
4. Kezirian, E.J.; Hohenhorst, W.; de Vries, N. Drug-induced sleep endoscopy: The VOTE classification. *Eur. Arch. Otorhinolaryngol.* **2011**, *268*, 1233–1236. [CrossRef]
5. Sleep Respiratory Diseases Working Committee, Respiratory Physician Branch, Chinese Medical Doctor Association. Expert consensus on the application of drug-induced sleep endoscopy in the diagnosis and treatment of obstructive sleep apnea (2025 edition). *Zhonghua Yi Xue Za Zhi* **2025**, *105*, 3384–3393. (in Chinese) [CrossRef]
6. Makkonen, J.; Blomster, H.; Raappana, A.; et al. Adult obstructive sleep apnea treated with tonsillectomy: A randomized controlled clinical trial. *Acta Otolaryngol.* **2025**, *145*, 989–996. [CrossRef]
7. Tschopp, S.; Meinert, F.; Mantokoudis, G.; et al. Effectiveness of palatopharyngeal surgery modifications in obstructive sleep apnea: A meta-analysis. *OTO Open* **2025**, *9*, e70144. [CrossRef]
8. Chen, D.; Zhou, L.; Zeng, Q.Y.; et al. Epiglottis collapse in individuals with obstructive sleep apnea. *World J. Otorhinolaryngol. Head Neck Surg.* **2026**, *12*, 486–493. [CrossRef]
9. Heiser, C.; Braun, M.; Huntley, C.; et al. Hypoglossal nerve stimulation for obstructive sleep apnea: A systematic review and meta-analysis on responder-based outcomes and between-study heterogeneity. *J. Clin. Med.* **2026**, *15*, 5180. [CrossRef]
10. Li, C.; Wang, C.; Zhang, Y.; et al. Loop gain in obstructive sleep apnea: From physiological endotype to clinical translation. *Nat. Sci. Sleep* **2026**, *18*, 616733. [CrossRef]
11. Correa, E.J.; Conti, D.M.; Moreno-Luna, R.; et al. Role of nasal surgery in adult obstructive sleep apnea: A systematic review. *Sleep Sci.* **2024**, *17*, e310–e321. [CrossRef]
12. Camacho, M.; Li, D.; Kawai, M.; et al. Tonsillectomy for adult obstructive sleep apnea: A systematic review and meta-analysis. *Laryngoscope* **2016**, *126*, 2176–2186. [CrossRef]
13. MacKay, S.; Carney, A.S.; Catcheside, P.G.; et al. Effect of multilevel upper airway surgery vs medical management on the apnea-hypopnea index and patient-reported daytime sleepiness among patients with moderate or severe obstructive sleep apnea: The SAMS randomized clinical trial. *JAMA* **2020**, *324*, 1168–1179. [CrossRef]
14. Ramar, K.; Dort, L.C.; Katz, S.G.; et al. Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: An update for 2015. *J. Clin. Sleep Med.* **2015**, *11*, 773–827. [CrossRef]
15. Veugen, C.C.A.F.M.; Kant, E.; Kelder, J.C.; et al. The predictive value of mandibular advancement maneuvers during drug-induced sleep endoscopy for treatment success of oral appliance treatment in obstructive sleep apnea: A prospective study. *J. Clin. Sleep Med.* **2024**, *20*, 353–361. [CrossRef]
16. Walker, A.; Kassir, M.F.; Sama, V.; et al. Maxillomandibular advancement safety and effectiveness in obstructive sleep apnea: Systematic review and meta-analysis. *Otolaryngol. Head Neck Surg.* **2025**, *172*, 1142–1154. [CrossRef]
17. Al-Bayyati, H.H.R.; Hassing, G.J.; van der Hoeve, E.P.; et al. Patient-reported outcomes with focus on health-related quality of life in patients with obstructive sleep apnea treated with maxillomandibular advancement surgery: A systematic review and meta-analysis. *J. Oral Maxillofac. Surg.* **2025**, *83*, 543–557. [CrossRef]
18. Torre, C.; Camacho, M.; Liu, S.Y.C.; et al. Epiglottis collapse in adult obstructive sleep apnea: A systematic review. *Laryngoscope* **2016**, *126*, 515–523. [CrossRef]
19. Gao, Y.; Zhu, S.; Li, W.; et al. Comparative efficacy of sleep positional therapy, oral appliance therapy, and CPAP in obstructive sleep apnea: A meta-analysis of mean changes in key outcomes. *Front. Med. (Lausanne)* **2025**, *12*, 1517274. [CrossRef]
20. Lisan, Q.; Baudouin, R.; Lechien, J.R.; et al. Is drug-induced sleep endoscopy associated with better outcomes after soft tissue surgery for sleep apnea? A systematic review and meta-analysis. *Clin. Otolaryngol.* **2023**, *48*, 122–129. [CrossRef]
21. Di Bari, M.; Colombo, G.; Giombi, F.; et al. The effect of drug-induced sleep endoscopy on surgical outcomes for obstructive sleep apnea: A systematic review. *Sleep Breath.* **2024**, *28*, 859–867. [CrossRef]
22. Malhotra, A.; Grunstein, R.R.; Fietze, I.; et al. Tirzepatide for the treatment of obstructive sleep apnea and

obesity. *N. Engl. J. Med.* **2024**, *391*, 1193–1205. [CrossRef]
23. Kapur, V.K.; Auckley, D.H.; Chowdhuri, S.; et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: An American Academy of Sleep Medicine clinical practice guideline. *J. Clin. Sleep Med.* **2017**, *13*, 479–504. [CrossRef]
24. Caples, S.M.; Anderson, W.M.; Calero, K.; et al. Use of polysomnography and home sleep apnea tests for the longitudinal management of obstructive sleep apnea in adults: An American Academy of Sleep Medicine clinical guidance statement. *J. Clin. Sleep Med.* **2021**, *17*, 1287–1293. [CrossRef]
25. Kent, D.; Stanley, J.; Aurora, R.N.; et al. Referral of adults with obstructive sleep apnea for surgical consultation: An American Academy of Sleep Medicine clinical practice guideline. *J. Clin. Sleep Med.* **2021**, *17*, 2499–2505. [CrossRef]
26. Strollo Jr., P.J.; Soose, R.J.; Maurer, J.T.; et al. Upper-airway stimulation for obstructive sleep apnea. *N. Engl. J. Med.* **2014**, *370*, 139–149. [CrossRef]
27. Inspire Upper Airway Stimulation - P130008/S090. Available online: https://www.fda.gov/medical-devices/recently-approved-devices/inspire-upper-airway-stimulation-p130008s090 (accessed on 21 August 2026).
28. Bonsignore, M.R.; Mazzuca, E.; Baiamonte, P.; et al. REM sleep obstructive sleep apnoea. *Eur. Respir. Rev.* **2024**, *33*, 230166. [CrossRef]
29. Pengo, M.F.; Martinez Garcia, M.A.; Vitiello, M.V.; et al. OSA in the aging population: Diagnostic and therapeutic considerations. *Sleep Med. Rev.* **2026**, *86*, 102247. [CrossRef]
30. Sunwoo, B.Y.; Raphelson, J.R.; Malhotra, A. Chronic obstructive pulmonary disease and obstructive sleep apnea overlap: Who to treat and how? *Expert Rev. Respir. Med.* **2024**, *18*, 527–537. [CrossRef]
31. Nguyen, B.H.M.; Murphy, P.B.; Yee, B.J. Chronic obstructive pulmonary disease and obstructive sleep apnea overlap syndrome: An update on the epidemiology, pathophysiology, and management. *Sleep Med. Clin.* **2024**, *19*, 405–417. [CrossRef]
32. Fabozzi, A.; Bouloukaki, I.; Bonini, M.; et al. Asthma-OSA overlap syndrome: A distinct endophenotype? *Respir. Med.* **2025**, *248*, 108344. [CrossRef]
33. Hack, S.; Alsleibi, S.; Shemesh, S.; et al. AI meets sleep surgery: Assessing drug-induced sleep endoscopy interpretation with a large language model. *Sleep* **2026**, *49*, zsaf338. [CrossRef]
34. BaHammam, A.S. Phenotyping obstructive sleep apnea: A pathway to precision medicine. *Sleep Breath.* **2026**, *30*, 125. [CrossRef]
35. Patil, S.P.; Ayappa, I.A.; Caples, S.M.; et al. Treatment of adult obstructive sleep apnea with positive airway pressure: An American Academy of Sleep Medicine clinical practice guideline. *J. Clin. Sleep Med.* **2019**, *15*, 335–343. [CrossRef]

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