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Sleep Related Breathing Disorders: Surgical Management

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Related Policies (if applicable)
SUR706.001: Nasal and Sinus Surgery
MED204.005 Diagnosis of Obstructive Sleep Apnea Syndrome
MED204.006 Medical Management of Sleep Related Breathing Disorders

Disclaimer

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Coverage

Palatopharyngoplasty (e.g., uvulopalatopharyngoplasty, uvulopharyngoplasty, uvulopalatal flap, expansion sphincter pharyngoplasty, lateral pharyngoplasty, palatal advancement pharyngoplasty, relocation pharyngoplasty) **may be considered medically necessary** for the treatment of clinically significant obstructive sleep apnea (OSA) (see **NOTE 1** below) syndrome in appropriately selected adults who have failed an adequate trial of continuous positive airway pressure (CPAP) or failed an adequate trial of an oral appliance.

Hyoid suspension, surgical modification of the tongue, and/or maxillofacial surgery, including mandibular-maxillary advancement (MMA), **may be considered medically necessary** in appropriately selected adults with clinically significant OSA (see **NOTE 1** below) and objective documentation of hypopharyngeal obstruction who have failed an adequate trial of CPAP or failed an adequate trial of an oral appliance.

NOTE 1: Clinically significant OSA is defined as those adult individuals who have:

- Apnea Hypopnea Index (AHI) or Respiratory Disturbance Index (RDI) greater than or equal to 15 events per hour, **OR**
- AHI or RDI greater than or equal to 5 events and less than or equal to 14 events per hour with documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders or insomnia, or documented hypertension, ischemic heart disease, or stroke.

NOTE 2: Documentation of attempts at weight loss; or provider/patient discussion regarding importance of weight loss in morbidly obese individuals should be considered.

Hypoglossal nerve stimulation used in accordance with the U.S. FDA approved indications **may be considered medically necessary** in adults with OSA under the following conditions:
- Age ≥ 18 years; **AND**
- AHI ≥ 15 with <25% central apneas; **AND**
- CPAP failure (residual AHI ≥ 15 or failure to use CPAP ≥ 4 hours per night for ≥ 5 nights per week) or inability to tolerate CPAP; **AND**
- Body mass index ≤ 40 kg/m^2; **AND**
- Non-concentric retropalatal obstruction on drug-induced sleep endoscopy (See **NOTE 3**).

Hypoglossal nerve stimulation used in accordance with the U.S. FDA approved indications **may be considered medically necessary** in adolescents or young adults with Down syndrome and OSA under the following conditions:
- Age 13 to 18 years; **AND**
- AHI > 10 and < 50 with <25% central apneas after prior adenotonsillectomy; **AND**
- Have either tracheotomy or be ineffectively treated with CPAP due to noncompliance, discomfort, un-desirable side effects, persistent symptoms despite compliance use, or refusal to use the device; **AND**
- Body mass index ≤ 95th percentile for age; **AND**
- Non-concentric retropalatal obstruction on drug-induced sleep endoscopy (See **NOTE 3**).

NOTE 3: Drug-induced sleep endoscopy (DISE) replicates sleep with an infusion of propofol. DISE will suggest either a flat, anterior-posterior collapse or complete circumferential oropharyngeal collapse. Concentric collapse decreases the success of hypoglossal nerve stimulation and is an exclusion criterion from the Food and Drug Administration.

Implantable hypoglossal nerve stimulators **are considered experimental, investigational and/or unproven** for all indications other than listed above.

Surgical treatment of OSA that does not meet the criteria **above is considered not medically necessary.**

The following minimally-invasive surgical procedures **are considered experimental, investigational and/or unproven** for the sole or adjunctive treatment of OSA:

- Radiofrequency volumetric tissue reduction of the tongue, the palatal tissues (including the uvula), or the inferior turbinates;
- Laser-assisted uvulopalatoplasty (LAUP), laser-assisted palatoplasty or radiofrequency volumetric tissue reduction of the palatal tissues;
- Palatal stiffening procedures including, but not limited to, cautery-assisted palatal stiffening operation (CAPSO), injection of a sclerosing agent, and the implantation of palatal implants;
- Tongue base suspension;
- All other minimally-invasive surgical procedures not described above.

NOTE 4: This medical policy addresses surgical treatment of the inferior turbinates as it relates to the management of obstructive sleep apnea. The surgical treatment of inferior turbinates may be appropriate in other medical conditions not addressed in this medical policy.

Uvulectomy as a stand-alone procedure for the treatment of **OSA is considered experimental, investigational and/or unproven**. (**NOTE 5**: Uvulectomy performed for other indications e.g., acute inflammation/angioedema of the uvula is not addressed in this medical policy).

All interventions **are considered not medically necessary** for the treatment of snoring in the absence of documented OSA; snoring alone is not considered a medical condition.

Genioplasty performed alone or in conjunction with other orthognathic surgical procedures **is considered cosmetic.**

Tracheostomy **may be considered medically necessary** for individuals with documented sleep apnea, particularly for individuals whose oxygen desaturations are frequently below 50%, and who have failed conservative treatment.

NOTE 6: For information on Rhinoplasty see Medical Policy SUR706.001 Nasal and Sinus Surgery.

Policy Guidelines

None.

Description

Obstructive sleep apnea (OSA) syndrome is characterized by repetitive episodes of upper airway obstruction due to the collapse of the upper airway during sleep. For individuals who have failed conservative therapy, established surgical approaches may be indicated. This medical policy addresses surgical procedures used to treat OSA.

Obstructive Sleep Apnea

Obstructive sleep apnea is characterized by repetitive episodes of upper airway obstruction due to the collapse and obstruction of the upper airway during sleep. The hallmark symptom of OSA is excessive daytime sleepiness, and the typical clinical sign of OSA is snoring, which can abruptly cease and be followed by gasping associated with a brief arousal from sleep. The snoring resumes when the patient falls back to sleep, and the cycle of snoring/apnea/arousal may be repeated as frequently as every minute throughout the night. Sleep fragmentation associated with the repeated arousal during sleep can impair daytime activity. For example, adults with OSA-associated daytime somnolence are thought to be at higher risk for accidents involving motorized vehicles (i.e., cars, trucks, heavy equipment). OSA in children may result in neurocognitive impairment and behavioral problems. In addition, OSA affects the cardiovascular and pulmonary systems. For example, apnea leads to periods of hypoxia, alveolar hypoventilation, hypercapnia, and acidosis. This, in turn, can cause systemic hypertension, cardiac arrhythmias, and cor pulmonale. Systemic hypertension is common in individuals with OSA. Severe OSA is associated with decreased survival, presumably related to severe hypoxemia, hypertension, or an increase in automobile accidents related to overwhelming sleepiness.

There are racial and ethnic health disparities seen for OSA, impacting the prevalence of disease and accessibility to treatment options, particularly affecting children. Black children are 4 to 6 times more likely to have OSA than white children. (1) Among young adults 26 years of age or younger, African American individuals are 88% more likely to have OSA compared to white individuals. Another study found that African American individuals 65 years of age and older were 2.1 times more likely to have severe OSA than white individuals of the same age group. These health disparities may affect accessibility to treatment for OSA and impact health outcomes. One analysis of insurance claims data, including over 500,000 patients with a diagnosis of OSA, found that increased age above the 18- to 29- year range ($p<.001$) and Black race ($p=.020$) were independently associated with a decreased likelihood of receiving surgery for sleep apnea. (2) Lee et al. (2022) found that Black men had a continuous mortality increase specifically related to OSA over the study period (1999 to 2019; annual percentage change 2.7%; 95% confidence interval, 1.2 to 4.2) compared to any other racial group. (3)

Terminology and diagnostic criteria for OSA are shown in Table 1.

Table 1. Terminology and Definitions for Obstructive Sleep Apnea

Terms	Definitions
Respiratory Event	
Apnea	The frequency of apneas and hypopneas is measured from channels assessing oxygen desaturation, respiratory airflow, and respiratory effort. In adults, apnea is defined as a drop in airflow by ≥90% of pre-event baseline for at least 10 seconds. Due to faster respiratory rates in children, pediatric scoring criteria define an apnea as ≥2 missed breaths, regardless of its duration in seconds.
Hypopnea	Hypopnea in adults is scored when the peak airflow drops by at least 30% of pre-event baseline for at least 10 seconds in association with

	either at least 3% or 4% decrease in arterial oxygen desaturation (depending on the scoring criteria) or an arousal. Hypopneas in children are scored by a ≥50% drop in nasal pressure and either a ≥3% decrease in oxygen saturation or an associated arousal.
Respiratory event-related arousal (RERA)	Respiratory event-related arousal is defined as an event lasting at least 10 seconds associated with flattening of the nasal pressure waveform and/or evidence of increasing respiratory effort, terminating in an arousal but not otherwise meeting criteria for apnea or hypopnea.
Respiratory Event Reporting	
Apnea/Hypopnea Index (AHI)	The average number of apneas or hypopneas per hour of sleep.
Respiratory Disturbance Index (RDI)	The respiratory disturbance index is the number of apneas, hypopneas, or respiratory event-related arousals per hour of sleep time. RDI is often used synonymously with the AHI.
Respiratory event index (REI)	The respiratory event index is the number of events per hour of monitoring time. Used as an alternative to AHI or RDI in home sleep studies when actual sleep time from EEG is not available.
Diagnosis	
Obstructive sleep apnea (OSA)	Repetitive episodes of upper airway obstruction due to the collapse and obstruction of the upper airway during sleep.
Mild OSA	In adults: AHI of 5 to <15. In children: AHI ≥1 to 5.
Moderate OSA	AHI of 15 to < 30. Children: AHI of > 5 to 10.
Severe OSA	Adults: AHI ≥30. Children: AHI of >10.
Treatment	
Positive airway pressure (PAP)	CPAP (continuous positive airway pressure), APAP (auto-adjusting positive airway pressure), Bi-PAP (Bi-level positive airway pressure).
PAP Failure	Usually defined as an AHI greater than 20 events per hour while using PAP.
PAP Intolerance	PAP use for less than 4 hours per night for 5 nights or more per week, or refusal to use CPAP. CPAP intolerance may be observed in patients with mild, moderate, or severe OSA.

EEG: electroencephalogram; OSA: obstructive sleep apnea; RERA: respiratory event-related arousal

Treatment

Continuous positive airway pressure (CPAP) is the preferred first-line treatment for most individuals. A smaller number of individuals may use oral appliances as a first-line treatment. The Apnea/Hypopnea Index is the total number events (apnea or hypopnea) per hour of recorded sleep. The Respiratory Disturbance Index is the total number events (apnea or hypopnea) per hour of recording time. An obstructive apnea is defined as at least a 10-second cessation of respiration associated with ongoing ventilatory effort. Hypopnea is defined as an abnormal respiratory event lasting at least 10 seconds with at least a 30% reduction in thoracoabdominal movement or airflow compared with baseline, and with at least a 4% oxygen desaturation.

Hypoglossal Nerve Stimulation
The hypoglossal nerve (cranial nerve XII) innervates the genioglossus muscle. Stimulation of the nerve causes anterior movement and stiffening of the tongue and dilation of the pharynx. Hypoglossal nerve stimulation reduces airway collapsibility and alleviates obstruction at both the level of the soft palate and tongue base.

Tracheostomy
Tracheostomy is the formation of an opening into the trachea. Tracheostomy was used as an effective treatment of sleep apnea before the disease was fully recognized as an entity. While newer methods have displaced tracheostomy as the primary treatment for the disease, tracheostomy is not obsolete.

Regulatory Status
The regulatory status of minimally invasive surgical interventions is shown in Table 2.

Table 2. Minimally Invasive Surgical Interventions for Obstructive Sleep Apnea

Interventions	Devices (predicate or prior name)	Manufacturer (previously owner)	Indication	PMA/ 510(k)	Year	FDA Product Code
LAUP	Various					
Radio-frequency ablation	Somnoplasty®		Simple snoring and for the base of the tongue for OSA	K982717	1998	GEI
Palatal Implant	Pillar® Palatal Implant	Pillar Palatal (Restore Medical/ Medtronic)	Stiffening the soft palate which may reduce the severity of snoring and incidence of airway obstruction in patients with mild-to-moderate OSA	K040417	2004	LRK
Tongue base suspension	AIRvance® (Repose)	Medtronic	OSA and/or snoring. The AIRvance ™ Bone Screw System is also suitable for the performance	K122391	1999	LRK

			of a hyoid suspension			
Tongue base suspension	Encore™ (PRELUDE III)	Siesta Medical	Treatment of mild or moderate OSA and/or snoring	K111179	2011	ORY
Hypoglossal Nerve stimulation	Inspire II Upper Airway Stimulation	Inspire Medical Systems	Patients ≥ 18 years with AHI ≥15 and ≤100 who have failed (AHI >15 despite CPAP usage) or cannot tolerate (<4-hour use per night for ≥5 nights per week) CPAP and do not have complete concentric collapse at the soft palate level. Patients between ages 18 and 21 should also be contraindicated for or not effectively treated by adeno-tonsillectomy. Inspire is also indicated in pediatric patients ages 13 to 18 years with Down Syndrome and severe sleep apnea (AHI >10 and <50).	P130008/S039	2014	MNQ

Hypoglossal Nerve stimulation	aura6000®	LivaNova (ImThera Medical)		IDE	2014	
Hypoglossal Nerve stimulation	Genio™	Nyxoah		Euro-pean CE Mark	2019	

AHI: Apnea/Hypopnea Index; CPAP: continuous positive airway pressure; IDE: investigational device exemption; LAUP: Laser-assisted uvulopalatoplasty; OSA: obstructive sleep apnea

The expanded indication for hypoglossal nerve stimulation in patients aged 18 to 21 was based on patients with Down syndrome and is contingent on a post-approval study of the Inspire® UAS in this age group. The post-approval study will be a multicenter, single-arm, prospective registry with 60 pediatric patients aged 18 to 21. Visits will be scheduled at pre-implant, post-implant, 6 months, and yearly thereafter through 5 years.

Rationale

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are the length of life, quality of life, and ability to function, including benefits and harms. Every clinical condition has specific outcomes that are important to patients and managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) is associated with a heterogeneous group of anatomic variants producing obstruction. The normal pharyngeal narrowing may be accentuated by anatomic factors, such as a short, fat “bull” neck, elongated palate and uvula, and large tonsillar pillars with redundant lateral pharyngeal wall mucosa. In addition, OSA is associated with obesity. OSA may also be associated with craniofacial abnormalities, including micrognathia, retrognathia, or maxillary hypoplasia. Obstruction anywhere along the upper airway can result in apnea. The

severity and type of obstruction may be described with the Friedman staging system. (4) Nonsurgical treatment for OSA or upper airway resistance syndrome includes continuous positive airway pressure (CPAP) or mandibular repositioning devices, which are addressed in medical policy MED204.006. Patients who fail conservative therapy may be evaluated for surgical treatment of OSA.

Traditional surgeries for OSA include uvulopalatopharyngoplasty (UPPP) and a variety of maxillofacial surgeries such as mandibular-maxillary advancement. UPPP involves surgical resection of the mucosa and submucosa of the soft palate, tonsillar fossa, and the lateral aspect of the uvula. The amount of tissue removed is individualized for each patient, as determined by the potential space and width of the tonsillar pillar mucosa between the 2 palatal arches. UPPP enlarges the oropharynx but cannot correct obstructions in the hypopharynx. Patients who have minimal hypoglossal obstruction have greater success with UPPP. Patients who fail UPPP may be candidates for additional procedures, depending on the site of obstruction. Additional procedures include hyoid suspensions, maxillary and mandibular osteotomies, or modification of the tongue. Drug-induced sleep endoscopy and/or cephalometric measurements have been used as methods to identify hypopharyngeal obstruction in these patients. The first-line treatment in children is usually adenotonsillectomy. Minimally invasive surgical approaches are being evaluated for OSA in adults.

Clinical Context and Therapy Purpose

The purpose of minimally invasive surgery in individuals who have OSA is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this policy.

Populations

The population of interest is individuals with OSA who have failed or are intolerant of positive airway pressure (PAP). Indications for the various procedures are described in Table 3 and in the Regulatory Status section.

Interventions

The interventions addressed in this policy are laser-assisted uvulopalatoplasty (LAUP), radiofrequency (RF) volumetric reduction of palatal tissues and base of tongue, palatal stiffening procedures, tongue base suspension, and hypoglossal nerve stimulation (HNS) (see Table 3).

Table 3. Minimally Invasive Surgical Interventions for OSA

Interventions	Devices	Description	Key Features	Indications
LAUP	Various	Superficial palatal tissues are sequentially reshaped over 3 to 7	• Part of the uvula and associated soft-palate tissues are reshaped	Snoring with or without OSA

		sessions using a carbon dioxide laser	• Does not alter tonsils or lateral pharyngeal wall tissues	
RF volumetric reduction of palatal tissues and base of tongue	Somnoplasty	Radiofrequency is used to produce thermal lesions within the tissues	• Similar to LAUP • Can include soft palate and base of tongue	Simple snoring and base of tongue OSA
Palatal Implant	Pillar Palatal Implant	Braided polyester filaments that are implanted submucosally in the soft palate	Up to 5 implants may be used	Snoring
Tongue base suspension	AIRvance Encore	A suture is passed through the tongue and fixated with a screw to the inner side of the mandible, below the tooth roots	The aim of the suspension is to make it less likely for the base of the tongue to prolapse during sleep	Snoring and/or OSA
Hypoglossal nerve stimulation (HNS)	Inspire II Upper Airway Stimulation	Stimulation of the hypoglossal nerve which contracts the tongue and some palatal tissue	The device includes an implanted stimulator and a sensor implanted in the ribs to detect respiration.	A subset of patients with moderate-to-severe OSA who have failed or cannot tolerate CPAP (see Regulatory Status section)

CPAP: positive airway pressure; LAUP: laser-assisted uvulopalatoplasty; OSA: obstructive sleep apnea; RF: radiofrequency.

Comparators

The following therapies and practices are currently being used to treat OSA:

For individuals with mild OSA who are intolerant of CPAP, the comparator would be oral appliances (see Medical Policy MED204.006 on Medical Management of Sleep Related Breathing Disorders) or an established upper airway surgical procedure.

For individuals with moderate-to-severe OSA who have failed CPAP or are intolerant of CPAP, the comparator would be conventional surgical procedures such as maxillofacial surgeries that may include UPPP, hyoid suspensions, maxillary and mandibular osteotomies, and modification of the tongue. UPPP may be modified or combined with a tongue base procedure such as UPPP, depending on the location of the obstruction. It is uncertain whether UPPP variants without tongue volume reduction are the most appropriate comparator for HNS, since the procedures may address different sources of obstruction.

Outcomes
Established surgical procedures are associated with adverse events such as dysphagia. In addition, the surgical procedures are irreversible should an adverse event occur. Therefore, an improvement in effectiveness and/or a decrease in adverse events compared with standard surgical procedures would be the most important outcomes.

The outcomes measure used to evaluate treatment success are a decrease in Apnea/Hypopnea Index (AHI) and Oxygen Desaturation Index on polysomnography (PSG) and improvement in a measure of sleepiness such as the Epworth Sleepiness Scale (ESS) or Functional Outcomes of Sleep Questionnaire (FOSQ) (see Table 4).

Table 4. Health Outcome Measures Relevant to OSA

Outcome	Measure (Units)	Description	Clinically Meaningful Difference (If Known)
Change in AHI	AHI	Mean change in AHI from baseline to post-treatment	Change from severe to moderate or mild OSA
AHI Success	Percentage of patients achieving success	Studies may use different definitions of success; the most common definition of AHI success is the Sher criteria	Sher criteria is a decrease in AHI ≥50% and an AHI <20 Alternative measures of success may be AHI <15, <10, or <5
Oxygen Desaturation Index	Oxygen levels in blood during sleep	The number of times per hour of sleep that the blood oxygen level drops by ≥4 percentage points	More than 5 events per hour
Snoring	10-point visual analog score	Filled out by the bed partner to assess snoring intensity or frequency	There is no standard for a good outcome. Studies have used 50% decrease in VAS (4) or final VAS of <5 or <3 (5)

Epworth Sleepiness Score (ESS)	Scale from 0 to 24	The ESS is a short, self-administered questionnaire that asks patients how likely they are to fall asleep in 8 different situations such as watching TV, sitting quietly in a car, or sitting and talking to someone	An ESS of ≥10 is considered excessively sleepy. The MCID has been estimated at -2 to -3. (6)
Functional Outcomes of Sleep Questionnaire (FOSQ)	30 questions	Disease-specific quality of life questionnaire that evaluates functional status related to excessive sleepiness	A score of ≥18 is the threshold for normal sleep-related functioning, and a change of ≥2 points is considered to be a clinically meaningful improvement
OSA-18	18 item survey graded from 1 to 7	Validated survey to assess quality of life in children	Change score of 0.5 to 0.9 is a small change, 1.0 to 1.4 a moderate change, and 1.5 a large change

AHI: Apnea/Hypopnea Index; ESS: Epworth Sleepiness Score; MCID: minimum clinically import difference; OSA; obstructive sleep apnea; VAS: visual analog score.

The effect of surgical treatment of OSA should be observed on follow-up PSG that would be performed from weeks to months after the surgery. Longer term follow-up over 2 years is also needed to determine whether the effects of the procedure are durable or change over time.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs.
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

Laser-Assisted Uvulopalatoplasty (LAUP)

LAUP is proposed as a treatment of snoring with or without associated OSA. LAUP cannot be considered an equivalent procedure to the standard UPPP, with the laser simply representing a surgical tool that the physician may opt to use. LAUP is considered a unique procedure, which raises its own issues of safety and, in particular, effectiveness.

One RCT (Ferguson et al. [2003]) on LAUP has been identified. (7) This trial compared LAUP with no treatment, finding treatment success (AHI <10) to be similar between LAUP (24%) and no treatment controls (17%) (see Tables 5 and 6). The primary benefit of LAUP was on snoring as rated by the bed partner. Subjective improvements in ESS and quality of life were not greater in the LAUP group in this nonblinded study. Adverse events of the treatment included moderate-to-severe pain and bleeding in the first week and difficulty swallowing at follow-up.

Table 5. Summary of Key Randomized Controlled Trial Characteristics

Study	Countries	Sites	Participants	Interventions[1]	
				Active	**Comparator**
Ferguson et al. (2003) (7)	Canada	1	46 patients with mild-to-moderate symptomatic OSA (AHI of 10 to 25) and loud snoring	21 patients treated with LAUP ever 1-2 mo[1]	25 patients received no treatment

AHI: Apnea/Hypopnea Index; LAUP: laser-assisted uvulopalatoplasty; OSA: obstructive sleep apnea.
[1] The LAUP procedure was repeated at 1- to 2-month intervals until either the snoring was significantly reduced, no more tissue could safely be removed, or the patient refused further procedures. There was a mean of 2.4 procedures (range, 1-4).

Table 6. Summary of Key Randomized Controlled Trial Results

Study	Treatment Success (AHI <10)	Change in Snoring (10-point VAS)	Change in ESS	Change in SAQLI Quality of Life	Moderate-to-Severe Pain in First Week	Bleeding in First Week	Difficulty Swallowing at Follow-up
Ferguson et al. (2003) (7)							
N	45	45	45	45	45	45	45
LAUP	24%	-4.4	-1.4	+0.4	81%	19%	19%
No treatment	17%	-0.4	+0.8	+0.2			
P	NR	<0.001	*NS*	*NS*			

AHI: Apnea/Hypopnea Index; ESS: Epworth Sleepiness Scale (maximum of 24); LAUP: laser-assisted uvulopalatoplasty; *NS:* not significant; NR: not reported; SAQLI: Sleep Apnea Quality of Life Index (maximum of 7); VAS: visual analog scale.

Study limitations are described in Tables 7 and 8. The major flaw is the uncertain clinical significance of the outcome measure.

Table 7. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Ferguson et al. (2003) (7)	1. Entry criteria includes populations with mild OSA (AHI between 10 and 15) for whom an improvement to AHI <10 is not clinically significant		2. Controls had no treatment	6. The definition of success (AHI <10) combined with the eligibility criteria (AHI >10) can lead to clinically insignificant improvements being labeled success	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
AHI: Apnea/Hypopnea Index; OSA: obstructive sleep apnea.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 8. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Ferguson et al. (2003) (7)		1-3. No blinding				4. Comparison of primary outcome not reported

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Follow-Up key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Subsection Summary: Laser-Assisted Uvulopalatoplasty

A single RCT has been identified on LAUP for the treatment of mild-to-moderate OSA. LAUP improved snoring as reported by the bed partner but did not improve treatment success in terms of AHI when compared with no treatment controls. Patients in this nonblinded study did not report an improvement in ESS or quality of life after LAUP.

Radiofrequency (RF) Volumetric Reduction of Palatal Tissues and Base of Tongue

RF is used to produce thermal lesions within the tissues rather than using a laser to ablate the tissue surface. In some situations, RF of the soft palate and base of tongue are performed together as a multilevel procedure.

Randomized Controlled Trials

Two RCTs have been identified on RF volumetric reduction of the palate and tongue. One of the trials (Back et al. [2009]) gave a single RF treatment to palatal tissues and found no statistical difference in scores on the AHI, visual analog scale (VAS) for snoring, ESS, or FOSQ between RF and sham (see Tables 9-11). (8) The second trial (Woodson et al. [2003]), provided a mean of 4.8 sessions of RF to the tongue and palate. This trial found a statistically significant improvement from baseline to posttreatment for ESS and FOSQ. (9) However, the improvement in the FOSQ score (1.2; standard deviation [SD], 1.6) was below the threshold of 2.0 for clinical significance and the final mean score in ESS was 9.8, just below the threshold for excessive sleepiness. AHI decreased by 4.5 events per hour, which was not statistically or clinically significant. The statistical significance of between-group differences was not reported (see Tables 10 and 12).

Table 9. Summary of Key Randomized Controlled Trial Characteristics

Study	Countries	Sites	Participants	Interventions	
				Active	**Comparator**
Back et al. (2009) (8)	Finland	1	32 patients with symptomatic mild OSA and habitual snoring with	Single-stage RF to palatal tissues	Sham control with local anesthetic and multiple insertions of an applicator needle without the RF

			only velopharyngeal obstruction		
Woodson et al. (2003) (9)	U.S.	2	90 patients with symptomatic mild-to-moderate OSA randomized to RF, sham, or CPAP	30 subjects received up to 7 sessions (mean, 4.8) of RF to tongue base and palate	30 Subjects received sham procedure to tongue for 3 sessions, including local anesthetic and multiple insertions of an applicator needle without the RF

CPAP: continuous positive airway pressure; OSA: obstructive sleep apnea; RF: radiofrequency; U.S. United States.

Table 10. Summary of Key Randomized Controlled Trial Results

Study	AHI	Snoring	ESS	Function	Adverse Events
	Median (Range)	**Snoring Median (Range)**	**Median (Range)**	**Compound end Point Score[a] Median (Range)**	
Back et al. (2009) (8)					
N	32	30	32	32	32
RF	13.0 (2.0-26.0)	5.0 (2.0-8.0)	7.0 (0-20.0)	6 (3-9)	
Sham	11.0 (1.0-29.0)	6.0 (3.0-8.0)	5.0 (2.0-15.0)	7 (4-10)	
P	0.628	0.064	0.941	0.746	No significant differences after 6 days
	Change Score (SD)		Change Score (SD)	FOSQ Score (SD)	
Woodson et al. (2003) (9)					
N	52		54	54	54
RF	-4.5 (13.8)		-2.1 (3.9)[b]	1.2 (1.6)[b]	
Sham	-1.8 (11.5)		-1.0 (3.1)	0.4 (2.0)	
Effect size[c]	0.34		0.50	0.66	No significant differences after 1 week

AHI: Apnea/Hypopnea Index; ESS: Epworth Sleepiness Scale (maximum of 24); FOSQ: Functional Outcomes of Sleep Questionnaire; MCS: Mental Component Summary score; PCS: Physical Component Summary score; RF: radiofrequency; SD: standard deviation; SF-36: 36-Item Short-Form Health Survey.
[a] The compound end point scored added points derived from AHI, ESS, SF-36 PCS, and SF-36 MCS;
[b] p=0.005 for baseline to posttreatment.
[c] Effect size=post-treatment mean-baseline mean.

Tables 11 and 12 display notable limitations identified in each study.

Table 11. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcome[d]	Follow-up[e]
Back et al. (2009) (8)	4. Included patients with mild OSA and snoring	4. Single treatment with RFA			
Woodson et al. (2003) (9)					

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
OSA: obstructive sleep apnea; RFA: radiofrequency ablation.
[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 12. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Complete-ness[d]	Power[e]	Statistical[f]
Back et al. (2009) (8)		2. Surgeons also performed follow-up assessments				
Woodson et al. (2003) (9)						3. Comparative treatment effects not reported

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness Key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Observational Studies

Herman et al. (2023) published a prospective, open-label, single-arm, nonrandomized trial that investigated multilevel RFA as an alternative therapy for patients with mild-to-moderate OSA (AHI 10 to 30) with intolerance or inadequate adherence to CPAP. (10) Patients were treated with 3 sessions of office based RFA to the soft palate and tongue base. Of the 56 patients recruited for the study, 43 completed the protocol. Overall, 22/43 (51%) were considered complete responders with a ≥50% reduction in baseline AHI and an overall AHI <20 at study completion. A statistically significant reduction in mean and median AHI was observed at 6 months follow-up (p=.001 for both); the mean AHI decreased from 19.7 to 9.86 and the median AHI decreased from 17.8 to 7.5. Likewise, ODI scores were significantly reduced at 6 months follow-up; the mean ODI score decreased from 12.79 to 8.36 (p=.006) and the median ODI score decreased from 11.65 to 6.23 (p=.008).

Subsection Summary: Radiofrequency Volumetric Reduction of Palatal Tissues and Base of Tongue

The evidence on RF volume reduction includes 2 randomized trials, both sham-controlled and a prospective, single-arm cohort study. Single-stage RF to palatal tissues did not improve outcomes compared with sham. Multiple sessions of RF to the palate and base of tongue did not significantly (statistically or clinically) improve AHI, while the improvement in functional outcomes did not achieve a level of clinical significance. The prospective cohort study included 56 patients with mild-to-moderate OSA who received 3 sessions of office-based multilevel RFA. Results demonstrated improvement in AHI and Oxygen Desaturation Index (ODI) at the 6-month follow up.

Palatal Stiffening Procedures

Palatal stiffening procedures include insertion of palatal implants, injection of a sclerosing agent (snoreplasty), or a cautery-assisted palatal stiffening operation. Snoreplasty and cautery-assisted palatal stiffening operations are intended for snoring and are not discussed here. Palatal implants are cylindrically shaped devices that are implanted in the soft palate.

Randomized Controlled Trials

Two double-blind, sham-controlled randomized trials with over 50 patients have evaluated the efficacy of palatal implants to improve snoring and OSA (see Table 13). AHI success by the Sher criteria ranged from 26% to 45% at 3-month follow-up. AHI success was observed in 0% to 10%

of the sham control patients (see Table 14). In 1 study (Steward et al. [2008]), the statistical significance of AHI success was marginal and there was no statistical difference in snoring or change in ESS between the 2 groups. (11) In the study by Friedman et al. (2008), there was greater success in AHI (45% vs 0%, p<0.001), improvement in snoring (-4.7 vs -0.7 on a 10-point VAS, p<0.001), and improvement in ESS (-2.4 vs -0.5, p<0.001) with palatal implants compared with sham controls. (4) Patient selection criteria were different in the 2 studies. In the trial by Friedman et al. (2008), patients with a Friedman tongue position of IV and palate of 3.5 cm or longer were excluded, whereas, in the trial by Steward et al. (2008), selection criteria included patients with primarily retropalatal pharyngeal obstruction.

Table 13. Summary of Key Randomized Controlled Trial Characteristics

Study	Countries	Sites	Participants	Interventions	
				Active	**Comparator**
Steward et al. (2008) (11)	U.S.	3	100 patients with mild-to-moderate OSA (AHI ≥5 and ≤40), and primarily retropalatal pharyngeal obstruction, BMI ≤32 kg/m^2	50 received the office-based insertion of 3 palatal implants	50 received the sham procedure
Friedman et al. (2008) (4)	U.S.	1	62 patients with mild-to-moderate OSA (AHI ≥5 and ≤40), soft palate ≥2 cm and <3.5 cm, Friedman tongue position I, II, or III, BMI ≤32 kg/m^2	31 received the office-based insertion of 3 palatal implants	31 received the sham procedure

AHI: Apnea/Hypopnea Index, BMI: body mass index; OSA: obstructive sleep apnea.

Table 14. Summary of Key Randomized Controlled Trial Results

Study	AHI Success (Sher criteria)	Snoring (10-point VAS)	Change in ESS (95% CI) or (SD)	Change in FOSQ Score (95% CI)	Foreign Body sensation /Extrusion
Steward et al. (2008) (11)					
N	97	43	96	98	100
Palatal implants	26%	6.7	-1.8 (-0.8 to -2.9)	1.43 (0.84 to 2.03)	18% / 4 extruded
Sham control	10%	7.0	-1.5 (-.04 to -2.5)	0.6 (0.01 to 1.20)	2%
P	0.04	0.052	*NS*	0.05	
Friedman et al. (2008) (4)		Change in VAS			
N	55	62	62		

Palatal implants (SD)	44.8%	-4.7 (2.1)	-2.4 (2.2)		2 extruded
Sham control (SD)	0%	-0.7 (0.9)	-0.5 (1.5)		
MD (95%CI)		4.0 (3.2 to 4.9)	1.9 (1.0 to 2.9)		
p	<0.001	<0.001	<0.001		
Summary: Range	26% to 44.8%				

AHI: Apnea/Hypopnea Index; CI: confidence interval; ESS: Epworth Sleepiness Score; FOSQ: Functional Outcomes of Sleep Questionnaire; MD: mean difference; NS: not significant; SD: standard deviation; VAS: visual analog scale.

Case Series

Uncontrolled series have provided longer follow-up data on patients treated with palatal implants. Using criteria of 50% improvement in AHI and final AHI of less than 10 events hour, Neruntarat et al. (2011) (12) reported a success rate of 52% at a minimum of 24 months (see Tables 15 and 16). Compared with nonresponders, responders had lower body mass index, lower baseline AHI and a lower percentage of patients with a modified Mallampati classification of III or IV (obscured visualization of the soft palate by the tongue). Tables 17 and 18 summarize the limitations of the studies described above.

Table 15. Summary of Key Case Series Characteristics

Study	Country	Participants	Follow-Up
Neruntarat et al. (2011) (12)	Thailand	92 patients with mild-to-moderate symptomatic OSA and palate >2 cm.	Minimum 24 mo

OSA: obstructive sleep apnea; mo: months.

Table 16. Summary of Key Case Series Results

Study	N	AHI (SD)	Snoring (SD) (10-point VAS)	ESS (SD)	Implant Extrusion
Neruntarat et al. (2011) (12)	92				
Baseline		21.7 (6.8)	8.2 (1.2)	12.3 (2.6)	
29 months		10.8 (4.8)	3.8 (2.3)	7.9 (1.8)	7 (7.6%)
P		<0.001	<0.001	<0.001	

AHI: Apnea/Hypopnea Index; ESS: Epworth Sleepiness Score; SD: standard deviation; VAS: visual analog scale.

Table 17. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]

Neruntarat et al. (2011) (12)			2. No comparator		
Steward et al. (2008) (11)	4. Out of 968 patients assessed for eligibility, 100 were enrolled				1, 2: 3 months
Friedman et al. (2008) (4)	4. Number screened was not reported. Soft palate was at least 2 cm but less than 3.5 cm.				1, 2: 3 months

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 18. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Complete-ness[d]	Power[e]	Statistical[f]
Neruntarat et al. (2011) (12)	1. Retrospective	1. None (case series)				
Steward et al. (2008) (11)						
Friedman et al. (2008) (4)						

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Subsection Summary: Palatal Stiffening Procedures

Two sham-controlled trials and several case series have assessed palatal implants for the treatment of snoring and OSA. The sham-controlled studies differed in the inclusion criteria, with the study that excluded patients with Friedman tongue position of IV and palate of 3.5 cm or longer reporting greater improvement in AHI (45% success) and snoring (change of -4.7 on a 10-point VAS) than the second trial.

Tongue Base Suspension

In this procedure, the base of the tongue is suspended with a suture that is passed through the tongue and fixated with a screw to the inner side of the mandible, below the tooth roots. The suspension aims to make it less likely for the base of the tongue to prolapse during sleep.

One preliminary RCT with 17 patients was identified that compared UPPP plus tongue suspension with UPPP plus tongue advancement (see Table 19). (13) Success rates using the Sher criteria ranged from 50% to 57% (see Table 20). Both treatments improved snoring and reduced ESS to below 10. The major limitations of the trial were the number of subjects (N=17) in this feasibility study and the lack of blinding (see Tables 21 and 22). In addition, there was no follow-up after 16 weeks.

Table 19. Summary of Key Randomized Controlled Trial Characteristics

Study	Countries	Sites	Participants	Interventions	
				Active	**Comparator**
Thomas et al. (2003) (14)	U.S.	1	17 Patients with moderate-to-severe OSA who failed conservative treatment	• UPPP with tongue suspension • Mean AHI=46 (n=9)	• UPPP with tongue advancement • Mean AHI=37.4 (n=8)

AHI: Apnea/Hypopnea Index; OSA: obstructive sleep apnea; UPPP: uvulopalatopharyngoplasty.

Table 20. Summary of Key Randomized Controlled Trial Results

Study	AHI Success (Sher Criteria)	Snoring (SD)	ESS (SD)	Pain, Speech, Swallowing
Thomas et al. (2003) (14)				
N	11	17	17	17
UPPP plus tongue suspension	57%	3.3 (2.1) [a]	4.1 (3.4) [b]	
UPPP plus tongue advancement	50%	5.0 (0.6) [c]	5.4 (3.5) [d]	No significant differences between groups

AHI: Apnea/Hypopnea Index; ESS: Epworth Sleepiness Score; SD: standard deviation; UPPP: uvulopalatopharyngoplasty.

[a] Baseline to posttreatment p=0.02.

[b] Baseline to posttreatment p=0.007.

[c] Baseline to posttreatment p=0.04.

[d] Baseline to posttreatment p=0.004.

Table 21. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes [d]	Follow-Up[e]
Thomas et al. (2003) (14)					1, 2. Follow-up was to 16 weeks

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms**.**

Table 22. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Complete-ness[d]	Power[e]	Statistical[f]
Thomas et al. (2003) (14)	3. Alloca-tion conceal-ment unclear	1-3. Not blinded			1. Feasibility study	2. Compara-tive treatment effects not calculated

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.
[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Subsection Summary: Tongue Base Suspension

One feasibility study with 17 patients was identified on tongue suspension. This study compared tongue suspension plus UPPP with tongue advancement plus UPPP and reported 50% to 57% success rates for the 2 procedures. Additional RCTs with a larger number of subjects are needed to determine whether tongue suspension alone or added to UPPP improves the net health outcome.

Hypoglossal Nerve Stimulation

Stimulation of the hypoglossal nerve causes tongue protrusion and stiffening of the anterior pharyngeal wall, potentially decreasing apneic events. For individuals with moderate-to-severe sleep apnea who have failed or are intolerant of CPAP, the alternative would be an established surgical procedure, as described above.

Systematic Reviews

A summary of systematic reviews is included in Tables 23 and 24.

Costantino et al. (2020) conducted a systematic review and meta-analysis of 6- to 60-month outcomes following HNS (15) They identified 12 studies with a total of 350 patients with OSA who were treated with the Inspire, ImThera, or Apnex HNS systems. Only the Inspire device has obtained FDA approval as of May 2022 and contributed the largest number of patients to the meta-analysis. In addition to the trials described below by Steffen et al. (2015, 2018) (16, 17) and Strollo et al. (Stimulation Therapy for Apnea Reduction [STAR] Trial, 2014, 2018) (18, 19), several other trials with the Inspire system were included in the meta-analysis. At 6-month follow-up, the overall change in AHI was -17.74 with an improvement in ESS of -5.36. At 12-month follow-up, the change in AHI was -17.50 with an improvement in ESS of -5.27. Sixty-month data were provided only by the STAR trial as reported by Woodson et al. (2018) and are described below. (20)

Kim et al. (2023) compared HNS to other OSA treatments in a systematic review and meta-analysis. (21) A total of 10 studies with 2209 patients (mean BMI ≤30 kg/m^2 in every study) who were treated with HNS or alternative interventions were included. HNS improved post-treatment AHI <10 and <15 events/hour compared with other surgical options including uvulopalatopharyngoplasty, expansion sphincterpharyngoplasty, or tongue-based surgery (odds ratio [OR]; 5.33; 95% CI, 1.21 to 23.42). Other results are summarized in Table 24.

Table 23. Meta-analysis Characteristics

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Constantino et al. (2020) (15)	Through 2018	12	Adult patients with moderate to severe OSA	350 (8-124)	Cohort	6, 12, and 60 mo
Kim et al. (2023) (21)	Through March 2023	10	Adults with moderate to severe OSA with inadequate CPAP adherence	2209 (23-698)	RCT (n=2)/cohort (n=8)	NR

CPAP: continuous positive airway pressure; mo: months;NR: not reported, OSA: obstructive sleep apnea; RCT: randomized controlled trial.

Table 24. Meta-analysis Results

Study	AHI Change at 6 mo (95% CI)	AHI Change at 12 mo (95% CI)	ESS Change at 6 mo (95% CI)	ESS Change at 12 mo (95% CI)	AHI Success n (%) Sher Criteria[a]
Constantino et al. (2020) (15)					
Total N	210	255	210	255	
Inspire	-17.74 (-24.73 to -10.74)	-17.50 (-20.01 to -14.98)	-5.36 (-6.64 to -4.08)	-5.27 (-6.18 to -4.35)	115 (70%)
ImThera	-9.50 (-19.14 to 0.14)	-24.20 (-37.39 to -11.01)	-3.70 (-5.65 to -1.75)	-2.90 (-6.97 to 1.17)	46 (35%)
Apnex	-24.20 (-30.94 to -17.45)	-20.10 (-29.62 to -10.58)	3.87 (-5.53 to-2.21)	-4.20 (-6.30 to -2.10)	115 (59.8%)
I^2 (p)	*68%* (.004)	*0%* (.77)	*25%* (.25)	*27%* (.24)	
Range of N	8 to 56	13 to 124	21 to 56	13 to 124	
Kim et al. (2023) (21)					
	AHI MD	**ESS MD**	**ODI (95% CI)**		

	(95% CI)	(95% CI)			
HNS vs all other airway surgeries	-8.0 (95% CI, -12.0344 to -3.9656)	0.3968 (95% CI, -1.5231 to 2.3167)			
HNS vs no treatment	-12.8394 (95% CI, -16.1475 to -9.5312)	-5.3929 (95% CI, -6.6078 to -4.1781)	-11.8384 (95% CI, -17.4476 to -6.2292)		
HNS vs CPAP	1.5000 (95% CI, -1.0145 to 4.0145)	-1.8236 (95% CI, -4.5634 to 0.9163)			

AHI: Apnea/Hypopnea Index; CI: confidence interval; CPAP: continuous positive airway pressure; ESS: Epworth Sleepiness Score; ESS: Epworth Sleepiness Score; HNS: hypoglossal nerve stimulation; MD: mean difference; ODI: oxygen desaturation index.

[a] Surgical success according to Sher criteria is defined as a 50% reduction in AHI and overall AHI <20.

Randomized Controlled Trials

Two RCTs have been identified on the effect of HNS in patients with OSA. Study characteristics and a summary of results are described in Tables 25 and 26, respectively.

Schwartz et al. (2023) published results from the ImThera Medical Targeted Hypoglossal Neurostimulation Study #3 (THN3), which investigated the efficacy and safety of targeted HNS of the proximal hypoglossal nerve in patients with moderate-to-severe OSA (AHI 20-60 events per hour) and a BMI of 35 kg/m2 or less. (22) This was a multicenter, randomized trial where all patients (N=138) were implanted with the HNS system (aura6000; ImThera Medical), and randomly assigned 2:1 to HNS device activation at 1 or 4 months after implant for the treatment and control groups, respectively. Efficacy was measured at month 4, as well as after 11 months of therapy (study months 12 and 15 for treatment and control groups, respectively). The study included mostly males (86.2%) and White individuals (91.3%). The results demonstrated that at month 4, the treatment group had significantly better outcomes compared to the control group for AHI and ODI scores. However, after 11 months of active therapy, the difference between the treatment and control groups was not statistically significant for AHI (RR, -7.5; 95% CI, -16 to 1.4) but remained significant for ODI (RR, 10.4; 95% CI, 1.6 to 18.8).

Heiser et al. (2021) conducted The Effect of Upper Airway Stimulation in Patients With Obstructive Sleep Apnea (EFFECT) trial, a multicenter, randomized, double-blind, crossover design study in adult patients with moderate-to-severe OSA (defined as AHI ≥15) who were intolerant to CPAP. (23) All individuals included in the study were White. All patients received implantation of HNS device (Inspire Medical Solutions) at least 6 months prior to enrollment. Baseline AHI before implantation was 32.2 events/h; after implantation, baseline AHI was approximately 8.3 events/h. All participants received therapeutic stimulation during the baseline visit. Patients were then randomized to 1 of 2 treatment groups: HNS-Sham (n=45) or Sham-HNS (n=44). After randomization, the HNS-Sham group received therapeutic stimulation

and the Sham-HNS received sham stimulation for 1 week. During the second week, the HNS-Sham group received sham stimulation while the Sham-HNS group received therapeutic stimulation. Changes in AHI over time showed a statistically significant decrease in AHI with stimulation compared to sham stimulation during the baseline, week 1, and week 2 visits. This meant that during week 1 when the HNS-Sham group received stimulation, they had significantly lower AHI; during week 2, when the Sham-HNS group received stimulation, they had significantly lower AHI. Similarly, participants reported a lower ESS with stimulation compared to sham stimulation during all visits. The change of AHI and ESS from baseline to the 1-week and 2-week visits was analyzed between the groups and investigators found no evidence of a carryover effect for AHI or ESS.

Dedhia et al. (2024) conducted a double-blind, randomized, crossover study comparing cardiovascular outcomes in patients (N=60) with severe OSA who had an HNS device implanted. (24) Patients were randomized to a 4-week period of active HNS and a 4-week period of sham HNS. The primary endpoint was mean 24- hour systolic blood pressure. In patients with a BMI of 30 kg/2 or more, the decrease in SBP (+0.5 mmHg vs. -0.64 mmHg) and DBP (-0.17 mmHg vs. -0.25 mmHg) measurements were numerically smaller than those who had a lower BMI; however, the clinical importance of this is unclear).

Table 25. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	**Comparator**
Schwartz et al. (2023); (22) THN3	US, Belgium, Israel, Germany, France, Portugal	20	2015-2018	Adults with moderate-to-severe OSA (AHI 20 to 65 events/hr), intolerant to CPAP; 91.3% of participants were White; mean BMI, 29.84 kg/m2 (SD, 3.03)	HNS (aura6000 device) starting at 1 month post implant with follow up at 12 months (n=92)	HNS (aura6000 device) starting at 4 months post implant with follow up at 15 months (n=46)
Heiser et al. (2021); (23) EFFECT	Germany	3	2018-2019	Adults with moderate-to-severe OSA (AHI	HNS (Inspire device) for week 1 followed by	Sham stimulation for week 1 followed by crossover to

				≥15), intolerant to CPAP; 100% of participants were White; mean BMI, 29.2 kg/m2 (SD, 4.4)	crossover to sham in week 2 (n=45)	HNS (Inspire device) in week 2 (n=44)
Dedhia et al. (2024) (24) CARDIOSA-12	US	3	2018-2022	Adults with severe OSA who had an HNS device; mean BMI, 28.7 kg/m^2 (SD, 4.6)	HNS (Inspire device) for 4 weeks before crossover (n=29 received active treatment first)	Sham for 4 weeks (n=31 received sham first)

AHI: Apnea/Hypopnea Index; CPAP: continuous positive airway pressure; HNS: hypoglossal nerve stimulation; OSA: obstructive sleep apnea; RCT: randomized controlled trial; SD: standard deviation.

Table 26. Summary of Key RCT Results

Study			
	AHI response at month 4 (≥50% reduction to 20 or fewer events/hr)	**ODI response at month 4 (≥25% reduction)**	
Schwartz et al. (2023); (22) THN3	N=138	N=138	
HNS therapy starting at 1-month post implant (treatment)	72/138 (52.3%)	86/138 (62.5%)	
HNS therapy starting at 4 months post-implant (control)	27/138 (19.6%)	57/138 (41.3%)	
RR (95% CI)	32.7 (15.2 to 49.0)	21.2 (3.3 to 38.1)	
	AHI response after 1 week (AHI ≤15 events/h)	**Change in ESS after 1 week**	**Overall change from baseline in FOSQ across treatment modalities**

Heiser et al. (2021); (23) EFFECT	N=89	N=89	N=86
HNS	73.3%	0.4 ± 2.3	0.2 (-0.5 to 0.9)
Sham	29.5%	5.0 ± 4.6	-1.9 (-2.6 to -1.2)
Difference (95% CI)	43.8% (25.1 to 62.5)	4.6 (3.1 to 6.1)	2.1 (1.4 to 2.8)
p-value	<.001	.001	<.001
	AHI events per hour (SD)	**24 hour SBP, mean (SD)**	**24 hour DBP, mean (SD)**
Dedhia et al. (2024); (24) CARDIOSA-12			
HNS	18.1 (14.8)	122.8 mmHg (11.8)	71.9 mmHg (7.8)
Sham	23.0 (15.6)	123.0 mmHg (10.8)	72.1 mmHg (7.0)
Difference (95% CI)	-4.9 (-8.8 to -1.0)	-0.18 (-2.21 to 1.84)	−0.22 (−1.27 to 0.83)
p-value	NR	NR	NR

AHI: Apnea/Hypopnea Index; CI: confidence interval; ESS: Epworth Sleepiness Scale; FOSQ: Functional Outcomes of Sleep Questionnaire; HNS: hypoglossal nerve stimulation; HR: hazard ratio; NNT: number needed to treat; ODI: oxygen desaturation index; OR: odds ratio; RCT: randomized controlled trial; RR: relative risk.

Notable study limitations are described in Tables 27 and 28.

Table 27. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Schwartz et al. (2023); (22) THN3	4. Study population was predominantly male and exclusively White		2. Both groups received treatment but at different starting points		
Heiser et al. (2021); (23) EFFECT	4. Study population was predominantly male and exclusively White				1, 2. Limited follow-up period precluded long-term evaluation of safety and efficacy
Dedhia et al. (2024); (24) CARDIOSA-12	4. Study population was predominantly			1. Primary outcomes were	1. Total duration of 10 weeks

	male and White			cardiovascular focused	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 28. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Schwartz et al. (2023) (22)		1. Open-label trial				
Heiser et al. (2021); (23) EFFECT		4. Most participants randomized to sham stimulation became aware of the group allocation, possibly impacting subjective outcomes				
Dedhia et al. (2024); (24) CARDIOSA-12						

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.

[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Comparative Studies

Study characteristics and results are described in Tables 29 and 30. Limitations in relevance and design and conduct, including comparative studies and 2 single-arm studies, are described in Tables 31 and 32.

Besides the RCT described above, comparative evidence consists of 3 studies that compared HNS with historical controls treated with UPPP or a variant of UPPP (expansion sphincter pharyngoplasty) and a study that compared HNS with transoral robotic surgery. AHI success by the Sher criteria ranged from 87% to 100% in the HNS group compared with 40% to 64% in the UPPP group. Post-treatment ESS was below 10 in both groups. It is not clear from some studies whether the patients in the historical control group were similar to the subset of patients in the HNS group, particularly in regards to the pattern of palatal collapse and from patients who did not return for postoperative PSG.

Several comparative studies have addressed these concerns by only including patients who meet the criteria for HNS in the control group. Yu et al. (2019) compared outcomes for patients who met the criteria for both HNS (non-concentric collapse on drug-induced sleep endoscopy) and transoral robotic surgery (retroglossal obstruction). (25) When patients with similar anatomic criteria were compared, HNS led to significantly better improvements in AHI, cure rate (defined as AHI <5), and the percentage of time that oxygen saturation fell below 90%. Huntley et al. (2021) selected patients in the control group who met the criteria for HNS (non-concentric collapse on drug-induced sleep endoscopy and BMI criteria) but had been treated at their institutions by single or multi-level palatal and lingual surgery. (26) There was no explanation of why the different treatments were given during the overlap period of 2010 to 2019, but the HNS patients were older and heavier. HNS resulted in a modestly greater decrease in AHI (HNS: -21.4 vs -15.9; p<.001), but not in ESS (HNS: -4.7 vs -5.8; p=.06). More patients in the HNS group achieved success by the Sher criteria (70% vs 48 to 49%) suggesting that there might be a clinical benefit for some patients.

Another report from Adherence and Outcome of Upper Airway Stimulation for OSA International Registry (ADHERE) registry investigators (Mehra et al., 2020) compared outcomes from HNS patients with patients who met the criteria but had been denied insurance coverage.

(27) In a post-hoc multivariate analysis, previous use of PAP and prior surgical procedures were predictors of insurance approval. In the group of patients who received HNS, the average use downloaded from the device was 5.6 h/night and 92% of patients had usage greater than 20 h/week. A majority of the comparator group (86%) were not using any therapy at follow-up. The remaining 14% were using PAP, an oral appliance, or underwent OSA surgery. The AHI decreased to 15 events/h (moderate OSA) on the night of the sleep test in patients with HNS, with only a modest improvement in patients who did not receive HNS. The hours of use on the night of the post-operative sleep study were not reported, and the HNS patients may have been more likely to use their device on the test night. In addition, the use of a home sleep test for follow-up may underestimate the AHI. The ESS improved in the HNS group but worsened in the controls. This suggests the possibility of bias in this subjective measure in patients who were denied coverage.

Additional non-comparative reports from the ADHERE registry are described below.

Table 29. Summary of Observational Comparative Study Characteristics

Study	Study type	Country	Dates	Participants	HNS	Tradition-al surgery	Follow Up
Shah et al. (2018) (28)	Retro-spective series with historical controls	U.S.	HNS 2015-2016 UPPP 2003-2012	40 OSA patients with AHI >20 and <65, BMI ≤32 kg mg/m^2, failed CPAP, favorable pattern of palatal collapse [a]	35% had previous-ly had surgery for OSA	UPPP 50% of patients had additional surgical procedures	2-13 months
Huntley et al. (2018) (29)	Retro-spective series with historical controls	U.S.	HNS 2014-2016 Modified UPPP 2011-2016	Retro-spective review included treated patients who had a post-operative PSG	75 patients age 61.67 y with a favor-able pattern of palatal collapse	33 patients age 43.48 y treated by ESP	To post-opera-tive PSG
Yu et al. (2019) (25)	Retro-spective series with historical controls	U.S.	HNS 2014-2016 TORS	OSA patients with AHI >20 and	27 patients age 62 with	20 patients age 53 y who	NR

			2011-NR	<65, BMI ≤32 kg mg/m^2, failed CPAP, favorable pattern of palatal collapse[a]	Retro-glossal collapse amen-able to TORS	would have qualified for HNS and were treated by TORS	
Huntley et al. (2020) (26)	ADHERE registry compared to retro-spective controls	U.S., EU	• HNS 2010-2019 • Modified UPPP 2003-2019	OSA patients who were intolerant to CPAP and met HNS criteria of AHI 15 to 65, BMI ≤ 35, and favorable pattern of palatal collapse[a]	465 registry patients treated with HNS who had 12 mo follow-up	233 patients who would have qualified for HNS and were treated by single level (68%) or multilevel (31%) surgery	173 days after surgery 383 days after HNS
Mehra et al. (2020) (27)	ADHERE registry	U.S., EU	2017-2019	OSA patients who were intolerant to CPAP and met HNS criteria of AHI 15 to 65, BMI ≤ 35, and favorable pattern of palatal collapse [a]	250 registry patients treated with HNS	100 patients who qualified for HNS but were denied insurance coverage	6 to 24 months

AHI: Apnea/Hypopnea Index; BMI: body mass index; CPAP: continuous positive airway pressure; ESP: expansion sphincter pharyngoplasty; HNS: hypoglossal nerve stimulation; NR: not reported; OSA: obstructive sleep apnea; PSG: polysomnography; TORS: transoral robotic surgery; UPPP: uvulopalatopharyngoplasty.

[a] A favorable pattern of palatal collapse is not concentric retropalatal obstruction on drug-induced sleep endoscopy.

Table 30. Summary of Key Observational Comparative Study Results

Study	Baseline AHI (SD)	Post-treatment AHI (SD)	AHI Success n (%) Sher Criteria	Baseline ESS (SD)	Post-treatment ESS (SD)
Shah et al. (2018) (28)					
HNS	38.9 (12.5)	4.5 (4.8) [b]	20 (100%)	13 (4.7)	8 (5.0) [b]
UPPP	40.3 (12.4)	28.8 (25.4) [a]	8 (40%)	11 (4.9)	7 (3.4) [b]
Huntley et al. (2018) (29)					
HNS	36.8 (20.7)	7.3 (11.2)	86.7	11.2 (4.2)	5.4 (3.4)
ESP	26.7 (20.3)	13.5 (19.0)	63.6	10.7 (4.5)	7.0 (6.0)
p-value	0.003	0.003	0.008	0.565	*NS*
Yu et al. (2018) (25)		Average AHI Reduction	% Cure Rate	Change in SaO_2 <90%	
HNS		33.3	70.4%	14.1	
TORS		12.7	10.0%	1.3	
p-value		0.002	<0.001	0.02	
Huntley et al. (2020) (26)					
HNS	35.5 (15.0)	14.1 (14.4)	70	11.9 (5.5)	7.3 (4.7)
Single or multi-level UPPP	35.0 (13.1)	19.3 (16.3)	48 to 49	11.3 (5.1)	5.9 (4.0)
p-Value	0.88	<0.001	<0.001	0.22	0.06
Mehra et al. (2020) (27)					
HNS	33.7 (13.4)	14.7 (13.8)		12.3 (5.5)	7.2 (4.8)
No HNS	34.9 (16.4)	26.8 (17.6)		10.9 (5.4)	12.8 (5.2)
p-Value	0.95	<0.001		0.06	<0.001

AHI: Apnea/Hypopnea Index; ESP: expansion sphincter pharyngoplasty; ESS: Epworth Sleepiness Score; HNS: hypoglossal nerve stimulation; NS: not significant; Sher criteria: 50% decrease in AHI and final AHI <20; SD; standard deviation; SaO_2: oxygen saturation; TORS: transoral robotic surgery; UPPP: uvulopalatopharyngoplasty.

[a] Baseline vs posttreatment p<0.05.

[b] Baseline vs posttreatment p<0.001.

Table 31. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Out-comes[d]	Follow-Up[e]
Shah et al. (2018) (28)			2. UPPP may not be preferred treatment for patients with primarily lingual obstruction		

Huntley et al. (2018) (29)	4. Study populations not comparable		1. Not clearly defined, few ESP patients had follow-up PSG		
Yu et al. (2018) (25)					1,2. Duration of follow-up unclear
Huntley et al. (2020) (26)	4. Study populations not comparable				1. The timing of follow-up was different (173 days after surgery and 383 days after HNS)
Mehra et al. (2020) (27)	4. Study populations not comparable		3. Hours of use on the test night was not reported. This may not represent the normal use of the device.		1. The timing of follow-up was different
Steffen et al. (2018) (16)			2. No comparator		
STAR trial (18, 19, 30-33)			2. No comparator		

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

ESP: expansion sphincter pharyngoplasty; HNS: hypoglossal nerve stimulation; PSG: polysomnography; STAR: Stimulation Therapy for Apnea Reduction; UPPP: uvulopalatopharyngoplasty.

[a] Population key: 1. Intended use population unclear; 2. Clinical context is unclear; 3. Study population is unclear; 4. Study population not representative of intended use.

[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest.

[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively.

[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. No CONSORT reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported.

[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms.

Table 32. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Complete-ness[d]	Power[e]	Statisitical[f]
Shah et al. (2018) (28)	1. Not randomized (retrospect-tive) 4. Inadequate control for selection bias	1-3. No blinding				4. Compara-tive treatment effects not calculated
Huntley et al. (2018) (29)	1. Not randomized (retrospect-tive)	1-3. No blinding				
Yu et al. (2018) (25)	1. Not randomized (retrospect-tive)					
Huntley et al. (2020) (26)	1. Not randomized (retrospect-tive)	1-3. No blinding				
Mehra et al. (2020) (27)	1. Not randomized	1-3. No blinding			1. Power calculations not reported	
Steffen et al. (2018) (16)	1. Not randomized	1-3. No blinding				
STAR trial (18, 19, 30-33)	1. Not randomized	1-3. No blinding				

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.

STAR: Stimulation Therapy for Apnea Reduction.

[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias.

[b] Blinding key: 1. Not blinded to treatment assignment; 2. Not blinded outcome assessment; 3. Outcome assessed by treating physician.

[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication.

[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials).
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference.
[f] Statistical key: 1. Intervention is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Intervention is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated.

Single-Arm Studies
Characteristics and results of single-arm studies are described in Tables 33 to 35. Limitations are mentioned in Tables 31 and 32, above.

Results of prospective single-arm studies show AHI success rates in 66% to 68% of patients who had moderate-to-severe sleep apnea and a favorable pattern of palatal collapse. Mean AHI was 31 to 32 at baseline, decreasing to 14 to 15 at 12 months. ESS scores decreased to 6.5 to 7.0. All improvements were maintained through 5 years of follow-up. Discomfort due to the electrical stimulation and tongue abrasion were initially common but were decreased when stimulation levels were reduced (see Table 35). In the post-market study, a normal ESS score (≤ 10) was obtained in 73% of patients. A FOSQ score of at least 19 was observed in 59% of patients compared to 13% at baseline. At the 12-month follow-up, 8% of bed partners regularly left the room due to snoring, compared to 75% of bed partners at baseline. The average use was 5.6 + 2.1 h per night. Use was correlated with the subjective outcomes, but not with AHI response. Two- and 3-year follow-up of this study were reported by Steffen et al. (2020) (17), but the percentage of patients at follow-up was only 68% at 2 years and 63% at 3 years, limiting conclusions about the longer-term efficacy of the procedure. A comparison of the populations who had 12-month versus 2- or 3-year results showed several differences between the patients who followed up and those who dropped out, including higher baseline AHI, higher baseline Oxygen Desaturation Index (ODI), and trends towards lower usage per night and a lower responder rate at 12 months.

Table 33. Summary of Prospective Single-Arm Study Characteristics

Study	Country	Participants	Treatment Delivery	Follow-Up
STAR trial (18, 19, 30-33)	EU, U.S.	126 Patients with AHI >20 and <50, BMI ≤32 kg/m^2, failed CPAP, favorable pattern of palatal collapse [a]	Stimulation parameters titrated with full PSG	5 years
Postmarket studies:	3 sites in Germany	60 patients with AHI ≥15 and ≤65 on home sleep		12 months, 2 years, and 3 years

Heiser et al. (2017) (35) Steffen et al. (2018) (16) Hasselbacher et al. (2018) (36) Steffen et al. (2020) (17)		study, BMI ≤35 kg/m^2, failed CPAP; favorable pattern of palatal collapse [a]		

AHI: apnea/hypopnea index; BMI: body mass index; CPAP: continuous positive airway pressure; EU: European Union; PSG: polysomnography; U.S.: United States; STAR: Stimulation Therapy for Apnea Reduction.

[a] A favorable pattern of palatal collapse is non-concentric retropalatal obstruction on drug-induced sleep endoscopy.

Table 34. Summary of Prospective Single-Arm Study Results

Study	N	Percent of Patients With AHI Success (Sher Criteria)	Mean AHI Score (SD)	Mean ODI Score (SD)	FOSQ Score (SD)	ESS Score (SD)
STAR trial (18, 19, 30-33)						
Baseline	126		32.0 (11.8)	28.9 (12.0)	14.3 (3.2)	11.6 (5.0)
12 months	124	66%	15.3 (16.1) [d]	13.9 (15.7) [d]	17.3 (2.9) [d]	7.0 (4.2) [d]
3 years	116[a]	65%	14.2 (15.9)	9.1 (11.7)	17.4 (3.5)[b]	7.0 (5.0)[b]
5 years	97[c]	63%	12.4 (16.3)	9.9 (14.5)	18.0 (2.2)	6.9 (4.7)
Postmarket studies: **Heiser et al. (2017) (35)** **Steffen et al. (2018) (16)** **Hasselbacher et al. (2018) (36)** **Steffen et al. (2020) (17)**						
Baseline	60		31.2 (13.2)	27.6 (16.4)	13.7 (3.6)	12.8 (5.3)
6 months					17.5 (2.8)[d]	7.0 (4.5)[d]
12 months	56[f]	68%	13.8 (14.8) [e]	13.7 (14.9) [e]	17.5 (3)[e]	6.5 (4.5)[e]
Normalized at 12 months					59%	73%

AHI: Apnea/Hypopnea Index; ESS: Epworth Sleepiness Scale; FOSQ: Functional Outcomes of Sleep Questionnaire; ODI: Oxygen Desaturation Index; PSG: polysomnography; SD: standard deviation; STAR: Stimulation Therapy for Apnea Reduction.

[a] Ninety-eight participants agreed to undergo PSG at 36 months, of the 17 participants who did not undergo PSG at 36 months, 54% were nonresponders and their PSG results at 12 or 18 months were carried forward.
[b] The change from baseline was significant at p <.001.
[c] Seventy-one participants agreed to a PSG.
[d] p<.001.
[e] p< .05.
[f] Four patients lost to follow-up were analyzed as treatment failures.

Table 35. Device-Related Adverse Events From Prospective Single-Arm Studies

Study	N	Discomfort due to Electrical Stimulation[a]	Tongue Abrasion	Dry Mouth	Mechanical Pain From Device	Internal Device Usability	External Device Usability
STAR trial (20)							
0 to 12 months	126	81	28	10	7	12	11
12 to 24 months	124	23	12	5	2	8	11
24 to 36 months	116	26	4	2	3	1	8
36 to 48 months	97	7	3	0	1	3	9
>48 months		5	3	3	1	1	6
Participants with event, n of 126 (%)		76 (60.3)	34 (27.0)	19 (15.1)	14 (11.1)	21 (16.7)	33 (26.2)

N: number; STAR: Stimulation Therapy for Apnea Reduction.
[a] Stimulation levels were adjusted to reduce discomfort.

Down Syndrome

Liu et al. (2022) published a systematic review investigating HNS in adolescents with Down Syndrome and OSA. (37) A total of 9 studies were included with a follow up period ranging from 2 to 58 months; 6 studies had sample sizes fewer than 10 patients. The largest of the included studies was a prospective cohort study published by Yu et al. (2022), which is summarized below. In an analysis that included 104 patients, AHI scores were significantly reduced in patients after HNS (mean AHI reduction, 17.43 events/h; 95% CI, 13.98 to 20.88 events/h; p<.001). Similarly, in an analysis that included 88 patients, OSA-18 survey scores were significantly reduced after HNS (mean OSA-18 reduction, 1.67; 95% CI, 1.27 to 2.08; p<.001).

Yu et al. (2022) reported on the safety and effectiveness of HNS in 42 adolescents with Down Syndrome and severe OSA (AHI of 10 events/h or greater). (38) This was a single-group, multicenter, cohort study with a 1-year follow-up that included non-obese (BMI <95%) children and adolescents aged 10 to 21 years who were refractory to adenotonsillectomy and unable to

tolerate CPAP. Patients who were included had an AHI between 10 and 50 on baseline PSG; the mean baseline AHI was 23.5 (SD, 9.7). All patients included tolerated HNS without any intraoperative complications. The most common complication was tongue or oral discomfort or pain, which occurred in 5 (11.9%) patients and was temporary, lasting weeks or rarely, months. Four patients (9.5%) had device extrusion resulting in readmissions to replace the extruded device. At 12 months, there was a mean decrease in AHI of 12.9 (SD, 13.2) events per hour (95% CI, -17.0 to -8.7 events/h). At the 12-month PSG, 30 of 41 patients (73.2%) had an AHI of less than 10 events/h, 14/41 patients (34.1%) had an AHI of less than 5 events/h, and 3/41 patients (7.3%) had an AHI of less than 2 events/h. There was also a significant improvement in quality-of-life outcomes. The mean improvement in the OSA-18 total score was 34.8 (SD, 20.3; 95% CI, -42.1 to -27.5) and the ESS improved by 5.1 (SD, 6.9; 95% CI, -7.4 to -2.8).

Registry

Boon et al. (2018) reported results from 301 patients in the multicenter Adherence and Outcome of Upper Airway Stimulation for OSA International Registry (ADHERE). (39) The ADHERE registry included both retrospective and prospectively collected data from the U.S. and Germany between October 2016 and September 2017. Data were collected from PSG prior to implantation and between 2 and 6 months after implantation, or from home sleep tests which were often performed at 6 and 12 months after implantation as part of routine care. Mean AHI decreased from 35.6 (SD: 15.3) to 10.2 (SD: 12.9) post-titration with 48% of patients achieving an AHI of 5 or less. ESS decreased from 11.9 (5.5) to 7.5 (4.7) (P<.001).

Kent et al. (2019) pooled data from the ADHERE registry plus data from 3 other studies to evaluate factors predicting success. (40) Over 80% of the 584 patients were men, and most were overweight. Seventy seven percent of patients achieved treatment success, defined as a decrease in AHI by at least 50% and below 20 events/per hour. AHI decreased to below 5 in 41.8% of patients. Greater efficacy was observed in patients with a higher preoperative AHI, older patient age, and lower BMI. A report of data from the ADHERE registry by Thaler et al. (2020) included 640 patients with 6-month follow-up and 382 with 12-month follow-up. (41) AHI was reduced from 35.8 at baseline to 14.2 at 12 months (p<.001), although the number of hours of use during the sleep test was not reported and home sleep studies may underestimate AHI. ESS was reduced from 11.4 at baseline to 7.2 at 12 months (p<.001), and patient satisfaction was high. In a multivariate model, only female sex (odds ratio: 3.634; p=.004) and lower BMI (odds ratio: 0.913; p=.011) were significant predictors of response according to the Sher criteria. In sensitivity analysis, higher baseline AHI was also found to be a negative predictor of success.

Suurna et al. (2021) evaluated the impact of BMI on HNS using the ADHERE registry (N=1849). (42) The mean BMI of all patients in the registry was 29.3 kg/m^2. All patients had a BMI of 35 kg/m^2 or lower and were categorized as those with BMI of 32 kg/m^2 or less and those with a BMI greater than 32 kg/m^2 and less than or equal to 35 kg/m^2. At 12 months, both groups had reduced AHI events/hour compared with baseline, although the mean change was greater in the lower BMI group (-21.4) compared with the higher BMI group (-20.3; mean difference 1.05

with the upper 97.5% CI at 4.5 which fell within the noninferiority margin). The difference in ESS scores between groups was also noninferior.

In a retrospective analysis by Huntley et al. (2018) of procedures at 2 academic institutions, patients with a body mass index (BMI) of greater than 32 did not have lower success rates than patients with a BMI less than 32. (43) However, only patients who had palpable cervical landmarks and carried most of their weight in the waist and hips were offered HNS. Therefore, findings from this study are limited to this select group of patients with BMI greater than 32.

Patel et al. (2024) conducted a retrospective cohort study at a single academic institution evaluating the effects of BMI on response to HNS. (44) A total of 76 patients with an average age of 61 years and a median BMI of 28.9 kg/m^2 were identified. Patients with a BMI of 32 to 35 kg/m^2 had 75% lower odds of a response to HNS (OR, 0.25; 95% CI, 0.07 to 0.90). Further analysis revealed an approximate 17% decrease in odds of being a responder for each 1-unit BMI increase.

Subsection Summary: Hypoglossal Nerve Stimulation

The evidence on HNS for the treatment of OSA includes systematic reviews, 3 RCTs, nonrandomized prospective studies, nonrandomized studies with historical controls, and prospective single-arm studies. An RCT of 89 adults with moderate-to-severe OSA who did not tolerate CPAP found significant short-term improvement in AHI, ESS, and quality of life measures with HNS compared to sham stimulation. The study was limited by short duration of follow-up and lack of diverse individuals included in the trial. Another RCT including 138 patients with moderate-to-severe OSA who did not tolerate CPAP compared outcomes for patients who received HNS therapy at 1 or 4 months after implant for the treatment and control groups, respectively. Results demonstrated significant short-term improvement in AHI and ODI when comparing HNS to no HNS at month 4. However, after 11 months of active therapy, the difference between the treatment and control groups was not statistically significant for AHI but remained significant for ODI in favor of the treatment group. This trial was also limited by a lack of diverse individuals, as well as a lack of a true control group for long-term outcomes. In nonrandomized studies, about two-thirds of patients with moderate-to-severe OSA who had failed conservative therapy (CPAP) and had a favorable pattern of palatal collapse met the study definition of success. Results observed at the 12-month follow-up were maintained at 5 years in the pivotal study. A prospective study that compared outcomes in patients who had received HNS to patients who were denied insurance coverage reported significant differences in both objective and subjective measures of OSA. However, there is a high potential for performance bias in this non-blinded study. For children and adolescents with OSA and Down Syndrome who are unable to tolerate CPAP, the evidence includes a systematic review and a prospective study of 42 individuals. The systematic review investigated HNS in adolescents with Down Syndrome and OSA and demonstrated significant improvement in AHI and OSA-18 after HNS. The study of 42 individuals with Down Syndrome and OSA found a success rate of 73.2% with 4 device extrusions corrected with replacement surgery.

Summary of Evidence

For individuals who have obstructive sleep apnea (OSA) who receive laser-assisted uvulopalatoplasty, the evidence includes a single randomized controlled trial (RCT). Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The trial indicates reductions in snoring, but limited efficacy on the Apnea/Hypopnea Index (AHI) or symptoms in patients with mild-to-moderate OSA. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have OSA who receive radiofrequency volumetric reduction of palatal tissues and base of tongue, the evidence includes 2 sham-controlled randomized trials and a prospective, single-arm cohort study. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. Single-stage radiofrequency to palatal tissues did not improve outcomes compared with sham. Multiple sessions of radiofrequency to the palate and base of tongue did not significantly (statistically or clinically) improve AHI, and the improvement in functional outcomes was not clinically significant. The prospective cohort study included 56 patients with mild-to-moderate OSA who received 3 sessions of office-based multilevel RFA. Results demonstrated improvement in AHI and Oxygen Desaturation Index (ODI) at the 6-month follow up. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have OSA who receive palatal stiffening procedures, the evidence includes 2 sham-controlled randomized trials and several case series. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The 2 RCTs differed in their inclusion criteria, with the study that excluded patients with Friedman tongue position of IV and palate of 3.5 cm or longer reporting greater improvement in AHI (45% success) and snoring (change of -4.7 on a 10-point visual analog scale) than the second trial. Additional studies are needed to corroborate the results of the more successful trial and, if successful, define the appropriate selection criteria. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have OSA who receive tongue base suspension, the evidence includes a feasibility RCT with 17 patients. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The single RCT compared tongue suspension plus uvulopalatopharyngoplasty (UPPP) with tongue advancement plus UPPP and showed success rates of 50% to 57% for both procedures. Additional RCTs with a larger number of subjects are needed to determine whether tongue suspension alone or added to UPPP improves the net health outcome. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have OSA who receive hypoglossal nerve stimulation (HNS), the evidence includes systematic reviews, 3 RCTs, nonrandomized prospective studies, nonrandomized studies with historical controls, and prospective single-arm studies. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. A double-blind, multicenter RCT of 89 adults with moderate-to-severe OSA who did not tolerate CPAP found significant short-term improvement in AHI, Epworth Sleepiness Score (ESS), and quality

of life measures with HNS compared to sham stimulation. The study was limited by short duration of follow-up and lack of diversity among included participants. Another RCT including 138 patients with moderate-to-severe OSA who did not tolerate CPAP compared outcomes for patients who received HNS therapy at 1 or 4 months after implant for the treatment and control groups, respectively. Results demonstrated significant short-term improvement in AHI and ODI when comparing HNS to no HNS at month 4. However, after 11 months of active therapy, the difference between the treatment and control groups was not statistically significant for AHI but remained significant for ODI in favor of the treatment group. This trial was also limited by a lack of diverse individuals, as well as a lack of a true control group for long-term outcomes. Hypoglossal nerve stimulation has shown success rates for about two-thirds of a subset of patients who met selection criteria that included AHI, BMI, and favorable pattern of palatal collapse across nonrandomized trials. These results were maintained out to 5 years in the pivotal single-arm study. The single prospective comparative study of patients who received HNS versus patients who were denied insurance coverage for the procedure has a high potential for performance bias. For children and adolescents with OSA and Down Syndrome who are unable to tolerate CPAP, the evidence includes a systematic review and a prospective study of 42 individuals. The systematic review investigated HNS in adolescents with Down Syndrome and OSA and demonstrated significant improvement in AHI and OSA-18 survey scores after HNS. The study of 42 individuals with Down Syndrome and OSA found a success rate of 73.2% with 4 device extrusions corrected with replacement surgery. Limitations of the current evidence base preclude determination of who is most likely to benefit from this invasive procedure. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Clinical Input From Physician Specialty Societies and Academic Medical Centers

For individuals who have OSA who receive HNS, clinical input supports that this use provides a clinically meaningful improvement in net health outcome and indicates this use is consistent with generally accepted medical practice in subgroups of appropriately selected patients. One subgroup includes adult patients with a favorable pattern of non-concentric palatal collapse. The alternative treatment for this anatomical endotype is maxillo-mandibular advancement (MMA), which is associated with greater morbidity and lower patient acceptance than HNS. The improvement in Apnea/Hypopnea Index (AHI) with HNS, as shown in the Stimulation Therapy for Apnea Reduction (STAR) trial, is similar to the improvement in AHI following MMA. Another subgroup includes appropriately selected adolescents with OSA and Down's syndrome who have difficulty in using continuous positive airway pressure (CPAP). The following patient selection criteria are based on information from clinical study populations and clinical expert opinion.

- Age ≥22 years in adults or adolescents with Down's syndrome age 10 to 21; AND
- Diagnosed moderate to severe OSA (with less than 25% central apneas); AND
- CPAP failure or inability to tolerate CPAP; AND
- Body mass index ≤ 32 kg/m^2 in adults; AND
- Favorable pattern of palatal collapse.

Practice Guidelines and Position Statements

American Academy of Sleep Medicine (AASM)

The AASM (2021) published practice guidelines on when to refer patients for surgical modifications of the upper airway for OSA. (45) These guidelines replaced the 2010 practice parameters for surgical modifications. (46) The AASM guidelines note that positive airway pressure (PAP) is the most efficacious treatment for OSA, but effectiveness can be compromised when patients are unable to adhere to therapy or obtain an adequate benefit, which is when surgical management may be indicated. The AASM guideline recommendations are based on a systematic review and meta-analysis of 274 studies of surgical interventions, including procedures such as uvulopalatopharyngoplasty (UPPP), modified UPPP, MMA, tongue base suspension, and hypoglossal nerve stimulation. (47) The systematic review deemed most included data of low quality, consisting of mostly observational data. The AASM strongly recommends that clinicians discuss referral to a sleep surgeon with adults with OSA and body mass index (BMI) <40 kg/m^2 who are intolerant or unaccepting of PAP. Clinically meaningful and beneficial differences in nearly all critical outcomes, including a decrease in excessive sleepiness, improved quality of life (QOL), improved Apnea/Hypopnea Index (AHI) or respiratory disturbance index (RDI), and sleep quality, were demonstrated with surgical management in patients who are intolerant or unaccepting of PAP. The AASM makes a conditional recommendation that clinicians discuss referral to a sleep surgeon with adults with OSA, BMI <40 kg/m^2, and persistent inadequate PAP adherence due to pressure-related side effects, as available data (very low-quality), suggests that upper airway surgery has a moderate effect in reducing minimum therapeutic PAP level and increasing PAP adherence. In adults with OSA and obesity (class II/III, BMI ≥ 35) who are intolerant or unaccepting of PAP, the AASM strongly recommends discussion of referral to a bariatric surgeon, along with other weight-loss strategies.

American Academy of Otolaryngology - Head and Neck Surgery

The American Academy of Otolaryngology - Head and Neck Surgery (AAO-HNS; 2021) has a position statement on surgical management of OSA. (48) Procedures AAO-HNS supported as effective and not considered investigational when part of a comprehensive approach in the medical and surgical management of adults with OSA include:

- Tracheotomy,
- Nasal and pharyngeal airway surgery,
- Tonsillectomy and adenoidectomy,
- Palatal advancement,
- UPPP,
- Genioglossal advancement,
- Hyoid myotomy,
- Midline glossectomy,
- Tongue suspension,
- Maxillary and mandibular advancement.

In a 2021 position statement, AAO-HNS supported hypoglossal nerve stimulation as an effective second-line treatment of moderate-to-severe OSA. (49)

American Society for Metabolic and Bariatric Surgery

The American Society for Metabolic and Bariatric Surgery (2012) published guidelines on the perioperative management of OSA. (50) The guideline indicated that OSA is strongly associated with obesity, with the incidence of OSA in the morbidly obese population reported as between 38% and 88%. The Society recommended bariatric surgery as the initial treatment of choice for OSA in this population, besides CPAP, as opposed to surgical procedures directed at the mandible or tissues of the palate. The updated 2017 guidelines reaffirmed these recommendations. (51)

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence 2017 guidance concluded that evidence on the safety and efficacy of hypoglossal nerve stimulation is limited in quantity and quality, and the procedure should only be used in the context of a clinical trial. (52)

Ongoing and Unpublished Clinical Trials

Some currently ongoing and unpublished trials that might influence this policy are listed in Table 36.

Table 36. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05592002	A Multicenter Study to Assess the Safety and Effectiveness of the Genio® Dual-sided Hypoglossal Nerve Stimulation System for the Treatment of Obstructive Sleep Apnea in Subjects With Complete Concentric Collapse of the Soft Palate	124	Oct 2027
NCT02413970[a]	Inspire® Upper Airway Stimulation System (UAS): Post-Approval Study Protocol Number 2014-001	127	Jan 2025
NCT03868618[a]	A Multicenter Study to Assess the Safety and Effectiveness of the Genio Dual-sided Hypoglossal Nerve Stimulation System for the Treatment of Obstructive Sleep Apnea in Adults Subjects	115	Feb 2028
NCT03763682[a]	A Multicentre, Prospective, Open-label, 2 Groups Study to Assess the	42	Dec 2023 (status unknown)

	Safety and Performance of the Genio™ Bilateral Hypoglossal Nerve Stimulation System for the Treatment of Obstructive Sleep Apnoea in Adult Patients With and Without Complete Concentric Collapse of the Soft Palate		
NCT04801771[a]	Effects of Hypoglossal Nerve Stimulation on Cognition and Language in Down Syndrome and Obstructive Sleep Apnea	57	Mar 2025
NCT04031040[a]	A Post-market Clinical Follow up of the Genio™ System for the Treatment of Obstructive Sleep Apnea in Adults. (EliSA)	110	Oct 2025
NCT02907398[a]	Adherence and Outcome of Upper Airway Stimulation (UAS) for OSA International Registry	5000	Dec 2025
NCT04950894[a]	Treating Obstructive Sleep Apnea Using Targeted Hypoglossal Neurostimulation	150	Apr 2024
Unpublished			
NCT04928404	Barbed Suspension of the Tongue Base for Treatment of Obstructive Sleep Apnea Patients	13	Dec 2022 (unknown status)

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	21083, 21085, 21120, 21121, 21122, 21123, 21127, 21141, 21142, 21143, 21193, 21194, 21195, 21196, 21198, 21199, 21210, 21215, 21244, 21245, 21246, 21685, 30801, 30802, 31600, 41120, 41512, 41530, 42140, 42145, 42299, 42950, 64568, 64582, 64583, 64584,
HCPCS Codes	C1767, C1778, C9727, L8680, L8688, S2080

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

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Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
02/01/2025	Document updated with literature review. Coverage unchanged. References 21, 24, 42 and 44 added; others updated.
03/15/2024	Document updated with literature review. The following changes were made to the Coverage section addressing hypoglossal nerve stimulation: 1) Added the phrase "used in accordance with the U.S. FDA approved indications" to the statements that address hypoglossal nerve stimulation for both adults with OSA and adolescents or young adults with Down syndrome: 2) Changed the age criteria for adults with OSA from 22yrs to 18 yrs; 3) Changed BMI criteria for adults with OSA from ≤ 32 kg/m^2 to ≤ 40 kg/m^2; 4) Changed age criteria for hypoglossal nerve stimulation in adolescents or young adults with Down syndrome and OSA from 10 to 21 yrs to Age 13 to 18 yrs. References 10, 21, 35 and 50 were added, other references updated, and one reference removed.
01/15/2023	Document updated with literature review. Coverage unchanged. References 1-3, 12, 14, 16, 20, 22-23, 34, 37, 39, 41, 45, 47 were added; some references were updated and others removed.
01/01/2022	Reviewed. No changes.
11/01/2020	Document updated with literature review. The following changes were made to the Coverage: 1) Examples of interventions were removed from the following statement: All interventions are considered not medically necessary for the treatment of snoring in the absence of documented OSA; snoring alone is not considered a medical condition; 2) Hypoglossal nerve stimulation for adults with OSA had the second and third bullet criteria changed to: AHI ≥ 15 with less than 25% central apneas; AND CPAP failure (residual AHI ≥ 15 or failure to use CPAP ≥ 4 hours per night for ≥ 5 nights per week) or inability to tolerate CPAP; 3) Removed Coverage addressing an implantable stimulation device delivering electrical pulses to the phrenic nerve in patients with central sleep apnea (CSA). Coverage addressing an implantable stimulation device delivering electrical pulses to the phrenic nerve in patients with central sleep apnea (CSA) has been moved to medical policy SUR701.042 Phrenic Nerve Stimulation for Central Sleep Apnea. References 5, 13, 21-22, 26-30, 32, and 35 added.
04/15/2020	Document updated with the following Coverage changes: 1) Removed: Rhinoplasty may be considered medically necessary when performed to correct significant deformity in individuals with documented obstructive sleep apnea or breathing difficulty, or chronic rhinosinusitis as a result of external nasal pyramid deformity following documented trauma or injury. 2) Renumbered NOTEs; 3) Changed: NOTE 6 To: For information on Rhinoplasty

	see Medical Policy SUR706.001 Nasal and Sinus Surgery. No references added or removed.
09/01/2019	Document updated with literature review. The following Coverage changes were made: 1) Added conditional coverage for implantable hypoglossal nerve stimulation; 2) Removed the following Coverage statement: Implantable hypoglossal nerve stimulators are considered experimental, investigational and/or unproven for all indications, including but not limited to the treatment of OSA.; 3) Removed NOTE 6; See related eviCore Clinical Guidelines for Sleep Apnea. References added: 3, 6, 9, 12-15, 20-22, 27, and 34.
04/15/2018	Document updated with literature review. The following changes were made to Coverage: 1) variants of palatopharyngoplasty have been added to the medically necessary statement when criteria have been met. 2) Criteria for the variants of palatopharyngoplasty and Hyoid suspension replaced adult patients who have not responded to or do not tolerate continuous positive airway pressure (CPAP); with who have failed an adequate trial of continuous positive airway pressure (CPAP) or failed an adequate trial of an oral appliance. 3) Uvulopalatal flap has been removed from the following statement: Uvulopalatal flap or uvulectomy as stand-alone procedures for the treatment of OSA are considered experimental, investigational and/or unproven. 4) The following Coverage statement was clarified by adding the word “obstructive” and replacing “and chronic rhinosinusitis” with “or chronic rhinosinusitis”: Rhinoplasty may be considered medically necessary when performed to correct significant deformity in individuals with documented obstructive sleep apnea or breathing difficulty, or chronic rhinosinusitis as a result of external nasal pyramid deformity following documented trauma or injury. The following coverage has been added: Surgical treatment of OSA that does not meet the criteria above would be considered not medically necessary. The following statement has been removed: Uvulopalatopharyngoplasty (UPPP) is considered not medically necessary for the treatment of respiratory conditions, including but not limited to snoring, other than clinically significant obstructive sleep apnea syndrome (OSA). The following Note was added: Documentation of attempts at weight loss; or provider/patient discussion regarding importance of weight loss in morbidly obese patients should be considered. The word palatoplasty was added to the following Coverage statement under the minimally-invasive surgical procedures: Laser-assisted uvulopalatoplasty (LAUP), palatoplasty or radiofrequency volumetric tissue reduction of the palatal tissues.
01/01/2017	Reviewed. No changes.
01/01/2016	Document updated with literature review. The following statements were added to the Coverage section: 1) Implantable hypoglossal nerve stimulators are considered experimental, investigational and/or unproven for all indications, including but not limited to the treatment of OSA. 2) NOTE: This

	medical policy addresses surgical treatment of the inferior turbinates as it relates to the management of obstructive sleep apnea. The surgical treatment of inferior turbinates may be appropriate in other medical conditions not addressed in medical policy. 3) Uvulopalatal flap or uvulectomy as stand-alone procedures for the treatment of OSA are considered experimental, investigational and/or unproven. (NOTE: Uvulectomy performed for other indications e.g., acute inflammation/angioedema of the uvula are not addressed in this medical policy). The following clarification was added to the minimally-invasive surgical procedures to include the uvula in the following statement for Radiofrequency volumetric tissue reduction of the tongue, the palatal tissues; (including the uvula), or the inferior turbinates. 4) Respicardia remede® System, an implantable stimulation device delivering electrical pulses to the phrenic nerve in patients with central sleep apnea (CSA) is considered experimental, investigational and/or unproven.
03/15/2014	The following was added to the coverage section: 1) Uvulopalatopharyngoplasty (UPPP) is considered not medically necessary for the treatment of respiratory conditions, including but not limited to snoring, other than clinically significant obstructive sleep apnea syndrome (OSA). 2) The following statement changed from: The following minimally-invasive surgical procedures are considered experimental, investigational and/or unproven for the sole or adjunctive treatment of OSA: Radiofrequency volumetric tissue reduction of the tongue, with or without radiofrequency reduction of the palatal tissues to: The following minimally-invasive surgical procedures are considered experimental, investigational and/or unproven for the sole or adjunctive treatment of OSA: Radiofrequency volumetric tissue reduction of the tongue, the palatal tissues, or the inferior turbinates.
10/01/2013	Document updated with literature review. Title changed from Sleep Related Breathing Disorders, Medical and Surgical Management. Medical Management coverage has been moved to medical policy MED205.001 Diagnosis and Medical Management of Sleep Related Breathing Disorders. The diagnosis and treatment related to Upper Airway Resistance Syndrome (UARS) was removed. The definition of clinically significant Obstructive Sleep Apnea (OSA) has changed – 1) Uvulopalatopharyngoplasty (UPPP), Hyoid suspension, surgical modification of the tongue, and/or maxillofacial surgery, including mandibular-maxillary advancement (MMA), Tracheostomy, and Rhinoplasty may be considered medically necessary when all applicable criteria has been met. 2) Minimally-invasive surgical procedures are considered experimental, investigational and unproven, examples provided under coverage. 3) All interventions, including LAUP, radiofrequency volumetric tissue reduction of the palate, glossectomy, or palatal stiffening procedures, are considered not medically necessary for the treatment of snoring in the absence of documented OSA; snoring alone is not considered

	a medical condition. 4) Genioplasty performed alone or in conjunction with other orthognathic surgical procedures is considered cosmetic.
01/15/2013	Document updated with literature review. The following was added: A nasal expiratory positive airway pressure (EPAP) device (e.g. PROVENT) is considered experimental, investigational and unproven.
08/15/2009	Policy updated to acknowledge conditional coverage of home sleep studies addressed on MED205.001.
11/01/2008	Revised/updated entire document. This policy is no longer scheduled for routine literature review and update.
05/15/2008	Coverage revised
01/01/2008	Codes added/deleted
11/01/2007	Revised/updated entire document
12/15/2006	Revised/updated entire document
10/01/2006	Revised/updated entire document
07/01/1999	Revised/updated entire document
05/01/1996	Revised/updated entire document
10/01/1995	Revised/updated entire document
07/01/1995	Revised/updated entire document
09/01/1990	New medical document