7.01.101 Surgical Treatment of Snoring and Obstructive Sleep Apnea Syndrome			
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Policy Statement

I. Palatopharyngoplasty (e.g., uvulopalatopharyngoplasty, uvulopharyngoplasty, uvulopalatal flap, expansion sphincter pharyngoplasty, lateral pharyngoplasty, palatal advancement pharyngoplasty, relocation pharyngoplasty) may be considered **medically necessary** in appropriately selected individuals when **all** of the following criteria are met:
   A. Individuals who are diagnosed with clinically significant obstructive sleep apnea (OSA) syndrome
   B. Individuals who have failed an adequate[a] trial of **all** of the following:
      1. Continuous positive airway pressure (CPAP)
      2. Oral appliance (OA)[b,c]

II. Hyoid suspension, surgical modification of the tongue, and/or maxillofacial surgery, including mandibular-maxillary advancement (MMA), may be considered **medically necessary** in appropriately selected individuals when **all** of the following criteria are met:
   A. Individuals who are diagnosed with clinically significant OSA syndrome
   B. There is objective documentation of hypopharyngeal obstruction
   C. Individuals who have failed an adequate[a] trial of **all** of the following:
      1. Continuous positive airway pressure (CPAP)
      2. Oral appliance (OA)[b,c]

III. Adenotonsillectomy may be considered **medically necessary** in pediatric individuals when **all** of the following criteria are met:
   A. An individual is diagnosed with clinically significant OSA syndrome
   B. An individual has hypertrophic tonsils

IV. Hypoglossal nerve stimulation may be considered **medically necessary** for an adult individual when **all** of the following criteria are met:
   A. An individual is diagnosed with clinically significant OSA syndrome
   B. Age is 18 years or older
   C. Apnea/Hypopnea Index (AHI) is greater than or equal to 15 and less than or equal to 100 with less than or equal to 25% central apneas
   D. Failed CPAP (residual AHI greater than or equal to 15 or failure to use CPAP greater than or equal to 4 hours or more per night for at least 5 nights per week) or inability to tolerate CPAP
   E. Body mass index is less than or equal to 35 kg/m^2
   F. Absence of complete concentric collapse at the soft palate level

V. Hypoglossal nerve stimulation may be considered **medically necessary** in an adolescent or young individual when **all** of the following criteria are met:
   A. An individual is diagnosed with Down syndrome and clinically significant OSA syndrome
   B. Age 13 to 18 years
   C. AHI greater than 10 and less than 50 with less than or equal to 25% central apneas after prior adenotonsillectomy
   D. Documentation of **one or more** of the following:
      1. Tracheotomy
      2. Was ineffectively treated with CPAP due to noncompliance, discomfort, undesirable side effects, persistent symptoms despite compliance use, or refusal to use the device
   E. Body mass index less than or equal to 95th percentile for age

F. Absence of complete concentric collapse at the soft palate level

VI. Surgical treatment of OSA using the techniques addressed above that do not meet the required criteria is considered **not medically necessary**.

VII. The following are considered **investigational** for the sole or adjunctive treatment of OSA or upper airway resistance syndrome:
A. Laser-assisted palatoplasty or radiofrequency volumetric tissue reduction of the palatal tissues
B. Radiofrequency volumetric tissue reduction of the tongue, with or without radiofrequency reduction of the palatal tissues
C. Palatal stiffening procedures including, but not limited to, cautery-assisted palatal stiffening operation, injection of a sclerosing agent, and the implantation of palatal implants
D. Tongue base suspension

VIII. Implantable hypoglossal nerve stimulators are considered **investigational** for all indications other than listed above.

IX. All interventions, (e.g., laser-assisted palatoplasty, radiofrequency volumetric tissue reduction of the palate, or palatal stiffening procedures,) are considered **investigational** for the treatment of snoring alone (there is no clinically significant in OSA).

NOTE: Refer to Appendix A to see the policy statement changes (if any) from the previous version.

Policy Guidelines

Notes and Clarifications:

a. An "adequate trial" of an oral appliance may extend over a length of time because the known side effects (drooling, sore jaw muscles, sore jaw joints, etc.) of using an oral appliance are generally self-limiting and subside-resolve themselves after using the device for several months. An adequate trial of CPAP would include documented attempts to resolve issues with masks, fit, pressure, etc.
b. An oral appliance for obstructive sleep apnea must meet the same criteria as delineated in the Blue Shield of California Medical Policy "Medical Management of Obstructive Sleep Apnea:" Specifically, the appliance must be approved by the Federal Drug Administration (FDA) and be custom made by a dentist trained in making oral appliances for obstructive sleep apnea (OSA).
c. If a patient indicates they cannot use an oral appliance, **clinical** documentation must be provided by an independent dentist trained in making oral appliances for OSA, stating an oral appliance cannot adequately manage the patient's OSA symptoms. An oral appliance is deemed successful when the AHI is reduced to what is considered "mild" sleep apnea levels.

Clinically Significant Obstructive Sleep Apnea Syndrome in Adults
Clinically significant OSA in adults is defined as patients who have **either** of the following:

- An Apnea/Hypopnea Index (AHI) or Respiratory Disturbance Index (RDI) of 15 or more events per hour
- An AHI or RDI of more than 5 (but 14 or less) events per hour with documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders or insomnia, or documented hypertension, ischemic heart disease, or history of stroke

Clinically Significant Obstructive Sleep Apnea Syndrome in Pediatrics
Clinically significant OSA is defined as those pediatric patients who have **either** of the following:

- An AHI or RDI of at least 5 per hour
- An AHI or RDI of at least 1.5 per hour in a patient with excessive daytime sleepiness, behavioral problems, or hyperactivity

Continuous positive airway pressure is the preferred first-line treatment for obstructive sleep apnea for most individuals. A smaller number of individuals may use oral appliances as a first-line treatment (see Blue Shield of California Medical Policy: Medical Management of Obstructive Sleep Apnea Syndrome).

The Apnea/Hypopnea Index is the total number of events (apnea or hypopnea) per hour of recorded sleep. The Respiratory Disturbance Index is the total number of 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.

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.

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 U.S. Food and Drug Administration.

Coding
See the Codes table for details.

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 evidence review addresses minimally invasive surgical procedures for the treatment of OSA. They include laser-assisted uvuloplasty, tongue base suspension, radiofrequency volumetric reduction of palatal tissues and base of tongue, palatal stiffening procedures, and hypoglossal nerve stimulation (HNS). This evidence review does not address conventional surgical procedures such as uvulopalatopharyngoplasty (UPPP), hyoid suspension, surgical modification of the tongue, maxillofacial surgery, or adenotonsillectomy.

Related Policies

- Diagnosis of Obstructive Sleep Apnea Syndrome

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program [FEP]) prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

The regulatory status of minimally invasive surgical interventions is shown in Table 1.

Table 1. Minimally Invasive Surgical Interventions for Obstructive Sleep Apnea

Interventions	Devices (predicate or prior name)	Manufacturer (previous owner)	Indication	PMA/ 510(k)	Year	FDA Product Code
LAUP	Various					
Radiofrequency 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 obstructions in patients with mild-to-moderate OSA	K040417	2004	LRK
Tongue base suspension	AIRvance® (Repose)	Medtronic	OSA and/or snoring. The AIRvance TM Bone Screw System is also suitable for the performance of a hyoid suspension.	K122391	1999	LRK
Tongue base suspension	Encore™ (PRELUDE III)	Siesta Medical	Treatment of mild or moderate OSA and/or snoring	K111179	2011	ORY
Hypoglossal nerve stimulation	Inspire® (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 h 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 adenotonsillectomy. 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		European 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 age 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 age 18 to 21. Visits will be scheduled at pre-implant, post-implant, 6 months, and yearly thereafter through 5 years.

Rationale

Background

Obstructive Sleep Apnea

Obstructive sleep apnea (OSA) 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 2.

Table 2. 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 the pre-event baseline for at least 10 seconds. Due to faster respiratory rates in children, pediatric scoring criteria define 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 the 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 arousal. Hypopneas in children are scored by a ≥50% drop in nasal pressure and either a ≥3% decrease in oxygen saturation or associated arousal.

Terms	Definitions
RERA	RERA is defined as an event lasting at least 10 seconds associated with flattening of the nasal pressure waveform and/or evidence of increased respiratory effort, terminating in arousal but not otherwise meeting criteria for apnea or hypopnea.
Respiratory event reporting	
AHI	The average number of apneas or hypopneas per hour of sleep.
RDI	The RDI is the number of apneas, hypopneas, or respiratory event-related arousals per hour of sleep time. RDI is often used synonymously with the AHI.
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	
OSA	Repetitive episodes of upper airway obstruction due to the collapse and obstruction of the upper airway during sleep.
Mild OSA	Adults: AHI 5 to <15; Children: AHI ≥1 to 5
Moderate OSA	Adults: AHI 15 to <30; Children: AHI >5 to 10
Severe OSA	Adults: AHI ≥30; Children: AHI >10
Treatment	
PAP	CPAP, APAP, or Bi-PAP
PAP Failure	Usually defined as an AHI greater than 20 events per hour while using PAP.
PAP Intolerance	PAP use for less than 4 h 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

AHI: Apnea/Hypopnea Index; APAP:auto-adjusting positive airway pressure; Bi-PAP: Bi-level positive airway pressure; CPAP: continuous positive airway pressure; EEG: electroencephalogram; OSA: obstructive sleep apnea; PAP: positive airway pressure; RDI: Respiratory Disturbance Index; REI: Respiratory Event Index; RERA: respiratory event-related arousal.

Literature Review

This review was informed by TEC Assessments on surgical management and radiofrequency volumetric tissue reduction for obstructive sleep apnea (OSA).[4,]

Evidence reviews 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 1 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.

Promotion of greater diversity and inclusion in clinical research of historically marginalized groups (e.g., People of Color [African-American, Asian, Black, Latino and Native American]; LGBTQIA (Lesbian, Gay, Bisexual, Transgender, Queer, Intersex, Asexual); Women; and People with Disabilities [Physical and Invisible]) allows policy populations to be more reflective of and findings more applicable to our diverse members. While we also strive to use inclusive language related to these

groups in our policies, use of gender-specific nouns (e.g., women, men, sisters, etc.) will continue when reflective of language used in publications describing study populations.

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.[5,] Nonsurgical treatment for OSA or upper airway resistance syndrome includes continuous positive airway pressure (CPAP) or mandibular repositioning devices, which are addressed in Blue Shield of California Medical Policy: Medical Management of Obstructive Sleep Apnea Syndrome. Patients who fail conservative therapy may be evaluated for surgical treatment of OSA.

Traditional surgeries for OSA or upper airway resistance syndrome include 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 review.

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 review 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 Obstructive Sleep Apnea

Interventions	Devices	Description	Key Features	Indications
LAUP	Various	Superficial palatal tissues are sequentially reshaped over 3 to 7 sessions using a carbon dioxide laser	• Part of the uvula and associated soft-palate tissues are reshaped • Does not alter tonsils or lateral pharyngeal wall tissues	Snoring with or without OSA

Interventions	Devices	Description	Key Features	Indications
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 suspension aims to make it less likely for the base of the tongue to prolapse during sleep	Snoring and/or OSA
Hypoglossal nerve stimulation	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 Blue Shield of California Medical Policy: Medical Management of Obstructive Sleep Apnea Syndrome on diagnosis and medical management of OSA) 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 Obstructive Sleep Apnea

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 the 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 a 50% decrease in VAS[5], or final VAS of <5 or <3[6],
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 television, 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.[7],
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 the 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; FOSQ: Functional Outcomes of Sleep Questionnaire; 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.

Review of Evidence

Laser-Assisted Uvulopalatoplasty

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.[8,] 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)[8,]	Canada	1	46 patients with mild-to-moderate symptomatic OSA (AHI of 10 to 25) and loud snoring	21 patients treated with LAUP every 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 the First Week	Difficulty Swallowing at Follow-up
Ferguson et al (2003)[8,]							
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	<.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)[8,]	1. Entry criteria include populations with mild OSA (AHI between 10 and 15) for whom an improvement to AHI <10 is not clinically significant		3. 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 established and validated measurements; 5. Clinical significant difference

not prespecified; 6. Clinical 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)[8,]		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] 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.
[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.

Section 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 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.

The analysis of RF volumetric tissue reduction was informed by a TEC Assessment (2000) that evaluated 4 primary studies on palatal radiofrequency ablation (RFA) and 1 study on tongue base RFA.[9,] All studies were nonrandomized.

Review of Evidence

Randomized Controlled Trials

Two RCTs have subsequently 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 through 11).[10,] 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 post-treatment for ESS and FOSQ.[11,] 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

Study	Countries	Sites	Participants	Interventions	
Back et al (2009)[10,]	Finland	1	32 patients with symptomatic mild OSA and habitual snoring with only velopharyngeal obstruction	Single-stage RF to palatal tissues	Sham control with local anesthetic and multiple insertions of an applicator needle without the RF
Woodson et al (2003)[11,]	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 a sham procedure to the 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.

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)[10,]					
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	.628	.064	.941	.746	No significant differences after 6 d
	Change Score (SD)		Change Score (SD)	FOSQ Score (SD)	
Woodson et al (2003)[11,]					
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 wk

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=.005 for baseline to post-treatment.
[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]	Outcomes[d]	Follow-Up[e]
Back et al (2009)[10,]	4. Included patients with mild OSA and snoring	4. Single treatment with RFA			
Woodson et al (2003)[11,]					

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. Clinical significant difference not prespecified; 6. Clinical 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 Completeness[d]	Power[e]	Statistical[f]
Back et al (2009)[10,]		2. Surgeons also performed follow-up assessments				.
Woodson et al (2003)[11,]						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.[12,] 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).

Section 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 the 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.

Review of Evidence

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.[13,] In the study by Friedman et al (2008), there was greater success in AHI (45% vs 0%, p<.001), improvement in snoring (-4.7 vs -0.7 on a 10-point VAS, p<.001), and improvement in ESS (-2.4 vs -0.5, p<.001) with palatal implants compared with sham controls.[5,] 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. 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)[13,]	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)[5,]	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)[13,]					
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	.04	.052	*NS*	.05	
Friedman et al (2008)[5,]		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	<.001	<.001	<.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) reported a success rate of 52% at a minimum of 24 months (see Tables 15 and 16).[14,] Compared with nonresponders, responders had lower body mass index (BMI), 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 case series and the RCTs described above.

Table 15. Summary of Key Case Series Characteristics

Study	Country	Participants	Follow-Up
Neruntarat et al (2011)[14,]	Thailand	92 patients with mild-to-moderate symptomatic OSA and palate >2 cm	Minimum 24 mo

OSA: obstructive sleep apnea.

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)[14,]	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		<.001	<.001	<.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)[14,]			2. No comparator		
Steward et al (2008)[13,]	4. Out of 968 patients assessed for eligibility, 100 were enrolled				1,2: 3 mo
Friedman et al (2008)[5,]	4. Number screened was not reported. Soft palate was at least 2 cm but less than 3.5 cm.				1,2: 3 mo

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 established and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical 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 Completeness[d]	Power[e]	Statistical[f]
Neruntarat et al (2011)[14,]	1. Retrospective	1. None (case series)				
Steward et al (2008)[13,]						

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Friedman et al (2008)[5,]						

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.

Section 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.

Review of Evidence

One preliminary RCT with 17 patients was identified that compared UPPP plus tongue suspension with UPPP plus tongue advancement (see Table 19).[15,] 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)[16,]	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)[16,]				
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 post-treatment p=.02.
[b] Baseline to post-treatment p=.007.
[c] Baseline to post-treatment p=.04.
[d] Baseline to post-treatment p=.004.

Table 21. Study Relevance Limitations

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

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 established and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical 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 Completeness[d]	Power[e]	Statistical[f]
Thomas et al (2003)[16,]	3. Allocation concealment unclear	1-3. Not blinded			1. Feasibility study	4. Comparative 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.

Section 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.

Review of Evidence

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.[17,] They identified 12 studies with a total of 350 patients (median BMI, 29.8 [IQR, 28.8 to 31.6 kg/m^2] with OSA who were treated with the Inspire, ImThera, or Apnex HNS systems. The Inspire device contributed the largest number of patients to the meta-analysis. In addition to the trials described below by Steffen et al (2015, 2018)[18,19,] and Strollo et al (Stimulation Therapy for Apnea Reduction [STAR] Trial, 2014, 2018)[20,21,], several other trials with the Inspire system were included in the meta-analysis. At 6 mo follow-up, the overall change in AHI was -17.74 with an improvement in ESS of -5.36. At 12 mo 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.[22,]

Kim et al (2023) compared HNS to other OSA treatments in a systematic review and meta-analysis.[23,] 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)[17,]	Through 2018	12	Adult patients with moderate to severe OSA	350 (8-124)	Cohort	6, 12, and 60 mo
Kim et al (2023)[23,]	Through March 2023	10	Adults with moderate to severe OSA with inadequate CPAP adherence	2209 (23-698)	RCT (n=2)/cohort (n=8)	NR

OSA: obstructive sleep apnea

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)[17,]					
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)[23,]	**AHI MD (95% CI)**	**ESS MD (95% CI)**	**ODI (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; HNS: hypoglossal nerve stimulation; MD: mean difference; ODI: oxygen desaturation index.
[a]Surgical success according to Sher criteria is defined as a 50% recution 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 hypoglosal nerve in patients with moderate-to-severe OSA (AHI 20-60 events per hour) and a BMI of 35 kg/m^2 or less.[24,] 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). The authors noted that the results should only be applied to patients with moderate-to-severe OSA and a BMI of 35 kg/m^2 or less.

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 $\geq$15) who were intolerant to CPAP.[25,] 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.[26,] 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

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
Schwartz et al (2023);[24] THN3	US, Belgim, 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/m^2 (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);[25] EFFECT	Germany	3	2018-2019	Adults with moderate-to-severe OSA (AHI ≥15), intolerant to CPAP; 100% of participants were White; mean BMI, 29.2 kg/m^2 (SD, 4.4)	HNS (Inspire device) for week 1 followed by crossover to sham in week 2 (n=45)	Sham stimulation for week 1 followed by crossover to HNS (Inspire device) in week 2 (n=44)
Dedhia et al (2024);[26] 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);[24] 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);[25] 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);[26] 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; NR: not reported; 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);[24,]THN3	4. Study population was predominantly male and exclusively White		2. Both groups received treatment but at different starting points		
Heiser et al (2021);[25,] 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);[26,] CARDIOSA-12	4. Study population was predominantly male and White			1. Primary outcomes were cardiovascular focused	1. Total duration of 10 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. 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)[24,]		1. Open-label trial				
Heiser et al (2021);[25,] EFFECT		4. Most participants randomized to sham stimulation became aware of the group allocation, possibly impacting subjective outcomes				
Dedhia et al (2024);[26,] 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 groups compared with 40% to 64% in the UPPP groups. 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 regard 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).[27,] 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.[28,] 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.[29,] 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	Traditional Surgery	Follow-Up
Shah et al (2018)[30,]	Retrospective series with	US	• HNS 2015-2016	40 OSA patients with AHI >20 and <65, BMI ≤32 kg	35% had previously had	UPPP 50% of patients had additional	2-13 mo

Study	Study Type	Country	Dates	Participants	HNS	Traditional Surgery	Follow-Up
	historical controls		• UPPP 2003-2012	mg/m^2, failed CPAP, favorable pattern of palatal collapse[a]	surgery for OSA	surgical procedures	
Huntley et al (2018)[31,]	Retrospective series with historical controls	US	• HNS 2014-2016 • Modified UPPP 2011-2016	Retrospective review included treated patients who had a postoperative PSG	75 patients age 61.67 y with a favorable pattern of palatal collapse	33 patients age 43.48 y treated by ESP	To post-operative PSG
Yu et al (2019)[27,]	Retrospective series with historical controls	US	• HNS 2014-2016 • TORS 2011-NR	OSA patients with AHI >20 and <65, BMI ≤32 kg mg/m^2, failed CPAP, favorable pattern of palatal collapse[a]	27 patients age 62 with retroglossal collapse amenable to TORS	20 patients age 53 y who would have qualified for HNS and were treated by TORS	NR
Huntley et al (2020)[28,]	ADHERE registry compared to retrospective controls	US, 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)[29,]	ADHERE registry	US, 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)[30,]					
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)[31,]					
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	.003	.003	.008	.565	*NS*
Yu et al (2018) [27,]		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		.002	<.001	.02	
Huntley et al (2020)[28,]					

Study	Baseline AHI (SD)	Post-treatment AHI (SD)	AHI Success n(%) Sher Criteria	Baseline ESS (SD)	Post-treatment ESS (SD)
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	.88	<.001	<.001	.22	.06
Mehra et al (2020)[29,]					
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	.95	<.001		.06	<.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 post-treatment p<.05.
[b] Baseline vs post-treatment p<.001.

Table 31. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Follow-Up[e]
Shah et al (2018)[30,]			2. UPPP may not be the preferred treatment for patients with primarily lingual obstruction		
Huntley et al (2018)[31,]	4. Study populations not comparable		1. Not clearly defined, few ESP patients had follow-up PSG		
Yu et al (2018) [27,]					1, 2. Duration of follow-up unclear
Huntley et al (2020)[28,]	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)[29,]	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)[18,]			2. No comparator		
STAR trial[20,21,32,33,34,35,]			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 established and validated measurements; 5. Clinical significant difference not prespecified; 6. Clinical 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 Completeness[d]	Power[e]	Statistical[f]
Shah et al (2018)[30],	1. Not randomized (retrospective) 4. Inadequate control for selection bias	1-3. No blinding				4. Comparative treatment effects not calculated
Huntley et al (2018)[31],	1. Not randomized (retrospective)	1-3. No blinding				
Yu et al (2018) [27],	1. Not randomized (retrospective)					
Huntley et al (2020)[28],	1. Not randomized (retrospective)	1-3. No blinding				
Mehra et al (2020)[29],	1. Not randomized	1-3. No blinding			1. Power calculations not reported	
Steffen et al (2018)[18],	1. Not randomized	1-3. No blinding				
STAR trial[20,21,32,33,34,35],	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] 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.

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 from 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 hours 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)[19], 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[20,21,32,33,36,22,]	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 y
Postmarket studies: Heiser et al (2017);[37,] Steffen et al (2018);[18,] Hasselbacher et al (2018);[38,] Steffen et al (2020)[19,]	3 sites in Germany	60 patients with AHI ≥15 and ≤65 on home sleep study, BMI ≤35 kg/m^2, failed CPAP; favorable pattern of palatal collapse[a]		12 mo, 2 yr, and 3 yr

AHI: apnea/hypopnea index; BMI: body mass index; CPAP: continuous positive airway pressure; PSG: polysomnography; 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[20,21,32,33,36,22,]						
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);[37,] Steffen et al (2018)[18,] Hasselbacher et al (2018);[38,] Steffen et al (2020)[19,]						
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 non-responders 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[22,]							
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 an event, n of 126 (%)		76 (60.3)	34 (27.0)	19 (15.1)	14 (11.1)	21 (16.7)	33 (26.2)

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.[39,] 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).[40,] 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).[41,] 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.[42,] 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.[43,] 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 (OR, 3.634; p=.004) and lower BMI (OR, 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).[44,] 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 32kg/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 BMI of greater than 32 did not have lower success rates than patients with a BMI less than 32.[45,] 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.[46,] 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.

Section 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. The efficacy of HNS in obese patients is limited with recent clinical trials only enrolling patients who have a BMI of 35 kg/m^2 or lower.

Supplemental Information

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2018 Input

Clinical input was sought to help determine whether the use of hypoglossal nerve stimulation (HNS) for individuals with obstructive sleep apnea (OSA) would provide a clinically meaningful improvement in net health outcome and whether the use is consistent with generally accepted medical practice. In response to requests, clinical input was received from 2 respondents, including 1 specialty society-level response and physicians with academic medical center affiliation.

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 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

Further details from clinical input are included in the Appendix.

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to

guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Academy of Sleep Medicine

The American Academy of Sleep Medicine (AASM, 2021) published practice guidelines on when to refer patients for surgical modifications of the upper airway for OSA.[47,] These guidelines replaced the 2010 practice parameters for surgical modifications.[48,] 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.[49,] 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/m2 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/m2, 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 $\geq$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 Pediatrics

The American Academy of Pediatrics (2012) published a clinical practice guideline on the diagnosis and management of childhood OSA.[50,] The Academy indicated that if a child has OSA, a clinical examination consistent with adenotonsillar hypertrophy, and does not have a contraindication to surgery, the clinician should recommend adenotonsillectomy as first-line treatment. The Academy recommended that patients should be referred for CPAP management if symptoms/signs or objective evidence of OSA persist after adenotonsillectomy or if adenotonsillectomy is not performed. Weight loss was recommended in addition to other therapy if a child or adolescent with OSA is overweight or obese (defined as BMI >95th percentile).

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.[51,] 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:

- tracheostomy,
- 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.[52,]

American Society for Metabolic and Bariatric Surgery

The American Society for Metabolic and Bariatric Surgery (2012) published guidelines on the perioperative management of OSA.[53,] 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.[54,]

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (NICE) 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.[55,]

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

The Centers for Medicare & Medicaid Services (CMS; 2001) published a decision memorandum that addressed how to define moderate-to-severe OSA as a guide for a coverage policy on CPAP.[56,] Because surgical approaches are considered when CPAP fails, CMS policy was adapted to this evidence review on the surgical management of OSA. The CMS review of the literature suggested there is a risk of hypertension with an AHI or RDI of at least 15 events per hour, and thus treatment is warranted for patients without any additional signs and symptoms. For patients with an AHI or RDI between 5 and 14 and associated symptoms, CMS concluded that the data from randomized controlled trials have demonstrated improved daytime somnolence and functioning in those treated with CPAP.

There is no national coverage determination for hypoglossal nerve stimulation. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review 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	Jun 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 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	42	Dec 2023 (status unknown)

NCT No.	Trial Name	Planned Enrollment	Completion Date
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	Jul 2024
Unpublished			

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

Appendix 1

2018 Clinical Input

Objective

Clinical input was sought to help determine whether the use of hypoglossal nerve stimulation for individuals with obstructive sleep apnea would provide a clinically meaningful improvement in net health outcome and whether the use is consistent with generally accepted medical practice.

Respondents

Clinical input was provided by the following specialty societies and physician members identified by a specialty society or clinical health system:

- American Academy of Otolaryngology - Head and Neck Surgery (AAO-HNS)
- Anonymous, MD, Otolaryngology, identified by American Academy of Pediatrics (AAP)[a]

[a] Indicates that conflicts of interest related to the topic where clinical input is being sought were identified by this respondent.

Clinical input provided by the specialty society at an aggregate level is attributed to the specialty society. Clinical input provided by a physician member designated by a specialty society or health system is attributed to the individual physician and is not a statement from the specialty society or health system. Specialty society and physician respondents participating in the Evidence Street® clinical input process provide review, input, and feedback on topics being evaluated by Evidence Street. However, participation in the clinical input process by a specialty society and/or physician member designated by a specialty society or health system does not imply an endorsement or explicit agreement with the Evidence Opinion published by BCBSA or any Blue Plan.

Ratings

			Confidence Level That Clinical Use Expected to Provide Clinically Meaningful Improvement in Net Health Outcome										Confidence Level that Clinical Use is Consistent with Generally Accepted Medical Practice									
			NO					YES					NO					YES				
			High	Intermediate			Low	Low	Intermediate			High	High	Intermediate			Low	Low	Intermediate			High
Clinical Indication	Respondent	Identified by	Yes or No	5	4	3	2	1	1	2	3	4	5	Yes or No	5	4	3	2	1	1	2	3	4	5
Individuals with mild obstructive sleep apnea who have failed an adequate trial of (or are unable to tolerate) continuous positive airway pressure (CPAP) who receive hypoglossal nerve stimulation	AAO-HNS		NO			■								NO			■						
	Anonymous**	AAP	NO			■								NO			■						
Individuals with moderate to severe obstructive sleep apnea who have failed an adequate trial of (or are unable to tolerate) continuous positive airway pressure (CPAP) who receive hypoglossal nerve stimulation	AAO-HNS		YES									■		YES									■
	Anonymous**	AAP	YES									■		YES									■

** Indicates that conflicts of interest related to the topic where clinical input is being sought were identified by this respondent (see Appendix).

Respondent Profile

	Specialty Society	
No.	*Name of Organization*	*Clinical Specialty*
1	American Academy of Otolaryngology - Head and Neck Surgery (AAO-HNS)	Otolaryngology

	Physician				
No.	*Name*	*Degree*	*Institutional Affiliation*	*Clinical Specialty*	*Board Certification and Fellowship Training*
Identified by American Academy of Pediatrics					
2	Anonymous	MD	Academic medical center	Otolaryngology	Otolaryngology and Sleep Medicine

Respondent Conflict of Interest Disclosure

No.	1. Research support related to the topic where clinical input is being sought		2. Positions, paid or unpaid, related to the topic where clinical input is being sought		3. Reportable, morethan$1000,healthcare-related assets or sources of income for myself, my spouse, or my dependent children related to the topic where clinical input is being sought		4. Reportable, more than $350, gifts or travel reimbursements for myself, my spouse, or my dependent children related to the topic where clinical input is being sought	
	Yes/No	*Explanation*	*Yes/No*	*Explanation*	*Yes/No*	*Explanation*	*Yes/No*	*Explanation*
1	No		No		No		No	
2	Yes	Participating in pediatric hypoglossal nerve stimulator implantation trial for children with OSA and Down Syndrome	No		No		No	

No.	*Conflict of Interest Policy Statement*
1	Sleep Disorders Committee, Physician Payment Policy Workgroup provided input to the response.

Individual physician respondents answered at individual level. Specialty Society respondents provided aggregate information that may be relevant to the group of clinicians who provided input to the Society-level response.

Responses

- We are seeking your opinion on whether using hypoglossal nerve stimulation for individuals with obstructive sleep apnea provides a clinically meaningful improvement in net health outcome. Please respond based on the evidence and your clinical experience. Please address these points in your response:
    a. Relevant clinical scenarios (e.g., a chain of evidence) where the technology is expected to provide a clinically meaningful improvement in net health outcome;
    b. Any relevant patient inclusion/exclusion criteria or clinical context important to consider in identifying individuals for this indication;
    c. Supporting evidence from the authoritative scientific literature (please include PMID).

No.	Rationale
1	The technological basis of hypoglossal nerve stimulation (HNS) originated with pilot studies in the early 1990s. Since that time a number of companies: Apnex, Inspire, ImThera, and Nyxoah, have and continued to develop this technology to produce a clinically meaningful device. The only product which is approved by the FDA is the Inspire Medical Systems HNS, on which the vast majority of the published data is based.

No.	Rationale
	The only HNS to achieve FDA approval achieved this status in 2014. Since that time, thousands of patients have undergone treatment of this device and dozens of publications have shown clinically meaningful benefit in both polysomnographic (PSG) parameters and quality of life indices. There is no question that this technology is no longer investigational and has the potential to benefit patients unable to tolerate conservative therapy and mitigate health risks associated with obstructive sleep apnea (OSA). The current CMS indications for HNS include adult patients (greater than 22 years old), with moderate to severe OSA (AHI between 15-65), whose central apnea index is less than 25% of the overall AHI, with BMI less than 32, who have been unable to tolerate conservative therapy with positive pressure ventilation, and have specific anatomic findings on sedated endoscopy. The Stimulation Therapy for Apnea Reduction trial (STAR) was published in 2014 in the New England Journal of Medicine. This study and its follow-up publications showed significant improvement in PSG indices of apnea-hypopnea index (AHI) and oxygen desaturation nadir (nadir) along with quality of life improvement after one year of use. The findings were confirmed with the withdrawal cohort of the original STAR trail and have shown lasting benefit through 5 years of use with follow-up publication. It is becoming increasingly well recognized that OSA does not represent a single phenotype or more accurately stated, endotype. Anatomic endotypes certainly exist with sub-populations of patients with craniofacial abnormalities, obesity, soft tissue hypertrophy, and/or redundancy treated appropriately with conventional surgery. However, we are now understanding that ineffective upper airway dilator muscles (genioglossus muscle supplied by the hypoglossal nerve) are a key contributor to OSA pathogenesis (Subramani et al, Anesth Analg 2017; 124:179-91, PMID - 27861433). This requires a treatment targeted to that pathology. • Subramani Y, Singh M, Wong J, et al, Understanding Phenotypes of Obstructive Sleep Apnea: Applications in Anesthesia, Surgery, and Perioperative Medicine. Anesth Analg Jan 2017; 124(1):179-91. PMID 27861433 In our opinion, BCBS approval of upper airway stimulation (UAS) therapy will advance the care of properly selected patients with OSA due to airway collapsibility who are intolerant of CPAP. The option to not approve UAS is a financial decision on the part of BCBS and not based on the growing evidence which is overwhelmingly in favor of UAS therapy. The evidence for UAS will continue to be produced, and at some point, BCBS will have to approve the therapy based on that evidence. Instead of advocating for comparator trials of questionable ethical soundness, BCBS should advocate for better trials in what constitutes a CPAP failure. Currently, there is little guidance of what is meant by CPAP failure which can range from a mere dislike of the device to severe claustrophobia. Better guidance on what constitutes a reasonable CPAP trial and what constitutes a "true" failure would help better select patients for downstream second-line therapy like UAS. • Boyd SB, Upender R, Walter AS, et al. Effective Apnea-Hypopnea Index ("Effective AHI"): A Measure of Effectiveness for Positive Airway Pressure Therapy. *Sleep*. Nov 2016;39(11):1961-1972. PMID 27568799 When making comparisons between the benefit of PAP and hypoglossal neurostimulation, we would argue that the PAP failure intolerant population is different and may be more difficult to treat than the treatment-naive population often assigned to PAP. In addition, PAP must be held to the same standard of effectiveness as surgery. That is, residual AHI on PAP should be computed based on pre-treatment AHI as a function of the fraction of hours used over total hours of sleep for fairness. This comparison should be made at similar time points that are advocated in the review for all treatments, including surgery. PAP is known to have a major drop-off in adherence and effectiveness measures must include the failure rate due to drop-off long term. Institutional Review Boards would not approve a randomized controlled study of the HGN.
2	There is now a substantial body of evidence that describes the safety and efficacy of hypoglossal nerve stimulator in adults with moderate to severe sleep apnea that have failed CPAP. Most recently 5-year follow-up data was published demonstrating sustained improvement in PSG parameters such as AHI, QOL measures, and daytime sleepiness following hypoglossal nerve stimulator utilization. The criteria for adults with OSA that would benefit from hypoglossal nerve stimulation have been well established and include: 1) 22 years of age and older; 2) Diagnosed OSA with an AHI range of 15-65 per hour (Less 25% Central Apneas); 3)CPAP failure or inability to tolerate CPAP treatment; 4) Appropriate airway anatomy on Drug-Induced Sleep Endoscopy; 5) BMI <32.

No.	Rationale
	• Woodson BT, Strohl KP, Soose RJ, et al. Upper Airway Stimulation for Obstructive Sleep Apnea: 5-Year Outcomes. *Otolaryngol Head Neck Surg*. Jul 2018;159(1):194-202. PMID: 29582703 Recent data has also emerged on the efficacy and safety of hypoglossal nerve simulator therapy in children with Down Syndrome that have persistent severe OSA following T&A. The inclusion criteria for these children is as follows: 1) Adolescents with Down syndrome age 10 to 21 years with prior T&A; 2) BMI <95th percentile; 3) Severe OSA with AHI between 10 and 50 (<25% central events); 4) Unable to tolerate CPAP or tracheostomy dependent at night; 5) need for future head MRI Children with Down Syndrome that have persistent OSA after adenotonsillectomy are very difficult to treat. They often are unable to tolerate CPAP and outside of a tracheostomy there were limited options available to cure their obstruction outside of the hypoglossal nerve stimulator. • Diercks GR, Wentland C, Keamy D, et al. Hypoglossal Nerve Stimulation in Adolescents with Down Syndrome and Obstructive Sleep Apnea. *JAMA Otolaryngol Head Neck Surg*. Nov 2 2017. PMID: 29098288

- Are conventional surgical procedures the appropriate and clinically relevant comparator for hypoglossal nerve stimulation for individuals with obstructive sleep apnea? If not, please describe the appropriate and clinically relevant comparator(s). For purposes of this question, conventional surgical procedures are palatopharyngoplasty (e.g., uvulopalatopharyngoplasty, uvulopharyngoplasty, uvulopalatal flap, expansion sphincter pharyngoplasty, lateral pharyngoplasty, palatal advancement pharyngoplasty, relocation pharyngoplasty) or hyoid suspension, surgical modification of the tongue, and/or maxillofacial surgery (e.g., osteotomies), including mandibular-maxillary advancement.

No.	Yes/No	Comments
1	No	With the advent of drug-induced sleep endoscopy, surgical interventions can now be tailored based on an individual's OSA severity and type and site of airway collapse. Uvulopalatopharyngoplasty (UPPP) would not be a good comparator for HNS therapy as these surgeries address 2 different sites of collapse. This procedure is technically different in 2 important aspects when compared to conventional surgical procedures as listed in the question above. First, all of the above-mentioned procedures involve various surgical approaches to anatomical restructuring. Hypoglossal nerve stimulation (HNS) is a unique approach that involves a meticulous nerve dissection and nerve stimulator placement for improving upper airway functional tone via consistent, targeted stimulation of airway muscles. Conventional surgical procedures are not the most clinically relevant comparator to consider in the average patient being evaluated for HNS therapy. The majority of patients have typically undergone a series of prior failed treatments, many times surgical (17% of patients in the STAR trial had prior failed UPPP surgery) and are now at a decision point of either proceeding with HNS or continuing without any treatment for their OSA. The appropriate clinical comparator would therefore be no treatment in this circumstance and its accordant health outcomes for patients with untreated moderate to severe OSA (e.g., elevated long-term risk of mortality and adverse cardiovascular outcomes). The only appropriate surgical comparator would need to meet the following criteria: • Address collapsibility of upper airway musculature • Treat moderate to severe OSA With regard to currently available treatment options, the only one that fit these criteriais maxillofacial surgery (MMA). The success rate of MMA is high, as noted in the review, but its acceptance rate among patients, especially older patients is low. The surgery is invasive, may alter bite or facial contour, and may not be available since many qualified maxillofacial surgeons refuse to accept medical insurance. In addition, although you accept the effectiveness of MMA, this evidence is not based on randomized control trials (RCTs). The data for UAS is very favorable when compared to historic MMA outcomes.
2	No	With the advent of Drug-induced sleep endoscopy, surgical interventions can now be tailored based on an individual's OSA severity and type and site of airway collapse. UPPP would not be a

No.	Yes/No	Comments
		good comparator for hypoglossal nerve stimulator therapy as these surgeries address 2 different sites of collapse. However, there was one recent study that did suggest that hypoglossal nerve stimulator therapy offered similar or even improved efficacy to expansion palatopharyngoplasty (UPPP variant). • Huntley C, Chou DW, Doghramji K, et al. Comparing Upper Airway Stimulation to Expansion Sphincter Pharyngoplasty: A Single University Experience. Ann Otol Rhinol Laryngol. Jun 2018;127(6):379-383. PMID 29707958 The ideal comparator would be CPAP or mandibular-maxillary advancement (MMF). Unfortunately, MMF is invasive and can have significant morbidity including changes in facial appearance. In addition, as oral surgeons perform this procedure, patients without dental insurance are not able to qualify for this treatment. As noted above, patients who are candidates for hypoglossal nerve stimulation have already failed CPAP therapy so a trial comparing these 2 treatments is not feasible. In addition, CPAP therapy should be held to the same standards as surgery when considering outcomes. For example, adherence to CPAP often wanes with time. When comparing CPAP to surgical interventions, residual AHI on PAP should be computed based on pre-treatment AHI as a function of the fraction of hours used over total hours of sleep.

- Based on the evidence and your clinical experience for each of the clinical indications described below:
  a. Respond Yes or No for each clinical indication whether the intervention would be expected to provide a clinically meaningful improvement in net health outcome; AND
  b. Rate your level of confidence in your Yes or No response using the 1 to 5 scale outlined below.

No.	Indications	Yes/No	Low Confidence		Intermediate Confidence		High Confidence
			1	2	3	4	5
1	Individuals with mild obstructive sleep apnea who have failed an adequate trial of (or are unable to tolerate) continuous positive airway pressure (CPAP) who receive hypoglossal nerve stimulation	No			X		
	Individuals with moderate to severe obstructive sleep apnea who have failed an adequate trial of (or are unable to tolerate) continuous positive airway pressure (CPAP) who receive hypoglossal nerve stimulation	Yes					X
2	Individuals with mild obstructive sleep apnea who have failed an adequate trial of (or are unable to tolerate) continuous positive airway pressure (CPAP) who receive hypoglossal nerve stimulation	No			X		
	Individuals with moderate to severe obstructive sleep apnea who have failed an adequate trial of (or are unable to tolerate) continuous positive airway pressure (CPAP) who receive hypoglossal nerve stimulation	Yes					X

- Based on the evidence and your clinical experience for each of the clinical indications described below:
  a. Respond Yes or No for each clinical indication whether this intervention is consistent with generally accepted medical practice; AND
  b. Rate your level of confidence in your Yes or No response using the 1 to 5 scale outlined below.

No.	Indications	Yes/No	Low Confidence		Intermediate Confidence		High Confidence
			1	2	3	4	5
1	Individuals with mild obstructive sleep apnea who have failed an adequate trial of (or are unable to tolerate) continuous positive airway pressure (CPAP) who receive hypoglossal nerve stimulation	No			X		
	Individuals with moderate to severe obstructive sleep apnea who have failed an adequate trial of (or are unable to tolerate) continuous positive airway pressure (CPAP) who receive hypoglossal nerve stimulation	Yes					X
2	Individuals with mild obstructive sleep apnea who have failed an adequate trial of (or are unable to tolerate) continuous positive airway pressure (CPAP) who receive hypoglossal nerve stimulation	No			X		
	Individuals with moderate to severe obstructive sleep apnea who have failed an adequate trial of (or are unable to tolerate) continuous positive airway pressure (CPAP) who receive hypoglossal nerve stimulation	Yes					X

- Additional narrative rationale or comments regarding clinical pathway and/or any relevant scientific citations (including the PMID) supporting your clinical input on this topic.

No.	Additional Comments
1	1. Please note in Background, under clinical context and Therapy Purpose (pg 2) that oral appliances are not orthodontic repositioning devices and for some, result in malocclusion. The proper term is mandibular repositioning devices. Likewise in the Background section, current upper airway surgery is not traditional UPPP but a variety of lateral wall procedures involving muscle and other soft tissue repositioning and little resection of tissue other than tonsils. 2. Please note under comparators (Pg 5), that for patients with moderate to severe OSA, maxillofacial surgeries are not required as soft-tissue lateral wall procedures may be used alone. 3. ODI clinically meaningful difference is not known (pg 5). Please provide a reference to why ODI >5 is significant in table 3. 4. FOS-Q change > 2 points (pg 5) implies a large effect but please provide evidence that this is an absolute threshold for a clinically meaningful difference. 5. Under Timing (pg 6), "Longer follow-up over 2 years is also needed" for procedures. The same should apply to PAP and oral appliance therapy who suffer significant drop-off rates when calculating effectiveness. 6. With respect to RFA treatment of palate and tongue base (pg 9), please note that snoring VAS and FOS-Q are subjective outcome tools, whereas, in the Woodson 2003 study, it was not noted in the current review that objective, slowest reaction time was improved by RFA. 7. Alternative to CPAP for severe OSA can also be oral appliance therapy, although not as predictable in AHI reduction as CPAP. Evidence is below for AHI and clinical measures o Doff MH, Hoekema A, Wijkstra PJ, van der Hoeven JH, Huddleston Slater JJ, de Bont LG, Stegenga B. Oral appliance versus continuous positive airway pressure in obstructive sleep apnea syndrome: a 2-year follow-up. Sleep. 2013 Sep 1;36(9):1289-96. doi: 10.5665/sleep.2948. PubMed PMID: 23997361; PubMed Central PMCID: PMC3738037. o Holley AB, Lettieri CJ, Shah AA. Efficacy of an adjustable oral appliance and comparison with continuous positive airway pressure for the treatment of obstructive sleep apnea syndrome. Chest. 2011 Dec;140(6):1511-1516. doi: 10.1378/chest.10-2851. Epub 2011 Jun 2. PubMed PMID: 21636666. o Anandam A, Patil M, Akinnusi M, Jaoude P, El-Solh AA. Cardiovascular mortality in obstructive sleep apnoea treated with continuous positive airway pressure or oral

No.	Additional Comments
	appliance: an observational study. Respirology. 2013 Nov;18(8):1184-90. doi:10.1111/resp.12140. PubMed PMID: 23731062. 8. The Huntley 2018 and Shah 2018 control groups have additional problems as comparators. Traditional UPPP in Shah 2018 is not a good comparator. A lateral pharyngeal wall surgery eg ESP is appropriate. In Huntley 2018, it appears that patients with complete circular collapse on DISE were included in the ESP group and thus patients with considerably greater anatomical collapse were present in the ESP group. 9. HNS is now accepted on policy both by the US Dept of Veterans Affairs and now health insurer Aetna, as of July 2018. The AAO-HNS agrees with Aetna's criteria for coverage. 10. Laser-assisted uvuloplasty (LAUP)- agree that the evidence is lacking for this therapy, and the evidence is not recent reflecting loss of interest in this procedure by practicing clinicians. The therapy is painful, not very effective, and carries significant potential for long-term dysphagia. This therapy is not recommended. 11. Upper airway radiofrequency ablation (RFA), including palate and base of tongue- Upper airway radiofrequency ablation results in volumetric tissue reduction and stiffening that reduces airway collapsibility. The effects reduce over 18 to 24 months due to natural softening and remodeling of the scar tissue produced by the procedure. In order to be an effective therapy, RFA must be applied to appropriate sites of collapse (palate and/or tongue); be repeated to effect (once is not enough); and often combined with other traditional approaches (nasal surgery; oral appliance; tonsillectomy). Advantages of the procedure include AHI reduction of a mean of 10 with repeated application; ability to perform in-office under local anesthesia; and relatively low cost (no general anesthesia; cost being the handpiece applicator ($200-300)); low morbidity with minimal pain or swallowing difficulty compared to traditional tissue removal surgery. RFA is likely an acceptable, cost-effective, office-based option for appropriately selected patients: AHI<30; failed CPAP trial; BMI<32; few medical co-morbidities. A logical approach would be a fee with a global period that covers the primary treatment and repeated applications, or a reduced fee with no global to allow a sufficient number of applications (typically three) titrated to effect. More evidence is needed but may be addressed by an ongoing trial of the Olympus company with which I am involved. 12. Tongue Suspension- Tongue suspension technique is designed to advance and support base of tongue to reduce tongue collapsibility during sleep. The evidence supports that this therapy is an acceptable alternative to genioplasty techniques. In my practice, the clinical utility of this technique is limited. The best patients for this therapy are patients with mild-moderate OSA (AHI<30); BMI<32; intolerance of CPAP therapy; with evidence of tongue collapse on drug-induced sleep endoscopy. The therapy does not work for bulky tongue (acquired macroglossia) associated with obesity. It does not work sufficiently for severe OSA. It is associated with temporary dysphagia in almost all patients. The inclusion criteria overlap with patients who are expected to do well with oral appliance therapy, therefore you may refer most patients in this group to a sleep dentist for an oral appliance. Then when it can occasionally be performed: they are edentulous patients who meet the above criteria but do not have dentition to support an oral appliance or sufficient bone stock to support osteotomy. 13. Pillar Implant- Your review includes 2 randomized controlled trials of Pillar which show an overall reduction in AHI compared to sham control. Both of these trials utilized 3 implants, which is fewer than the current recommendation of 4 or 5 implants. Pillar improves snoring (average 50% reduction), sleep quality, and AHI (average 10 point reduction). The morbidity of the procedure is minimal. It is performed under local anesthesia; the patient does not require a post-treatment narcotic; and the patient can start an oral diet immediately after the procedure. For patients with base of tongue collapse, it can be combined with a well-fitted oral appliance for effective multi-level treatment. Pillar works best for mild-moderate OSA (AHI<30); BMI <32; modified Mallampati 1-2; Tonsil 0,1,2; who are intolerant of CPAP. Pillar has the theoretical advantage over upper airway RFA in that the scar capsule produced by the implant should be more stable due to the permanent presence of the scar inciting implant. Pillar would produce equal value at a much lower cost to UPPP for people with mild-moderate OSA who meet the above criteria.
2	Under Timing (pg 6), "Longer follow-up over 2 years is also needed" for procedures. The same should apply to PAP and oral appliance therapy for those who suffer significant drop-off rates when calculating effectiveness.

- Is there any evidence missing from the attached draft review of evidence that demonstrates clinically meaningful improvement in net health outcome? If Yes, please share any relevant scientific citations of missing evidence (including PMID).

No.	Yes/No	Citations of Missing Evidence
1	Yes	A complete list of additional citations is attached for BCBSA review. • Baptista P, Garaycochea O, Alvarez-Gomez L, et al. Hypoglossal nerve stimulation surgery for obstructive sleep apnea: Our preliminary experience. *Acta Otorrinolaringol* Esp. Jan-Feb 2018;69(1):42-47. PMID 28755767 • Bender B. Upper airway stimulation in OSA. *Laryhnorhinoologie*. Nov 2016; 95(11):795-807 (article in German). PMID 27829262 • Boon M, Huntley C, Steffen A, et al. Upper Airway Stimulation for Obstructive Sleep Apnea: Results from the ADHERE Registry. *Otolaryngol Head Neck Surg*. Aug 2018;159(2):379-385. PMID 29557280. • Boon M et al. Upper Airway Stimulation for Obstructive Sleep Apnea: Results from the ADHERE Registry. *Otolaryngol Head Neck Surg*. 2018 Mar 1. (Epub ahead of print). • Bowe SN, Diercks GR, Hartnick CJ. Modified surgical approach to hypoglossal nerve stimulator implantation in the pediatric population. *Laryngoscope*. June 2018;128(6):1490-1492. PMID 28771734 • Bowen AJ, Nowacki AS, Kominsky AH, et al. Voice and swallowing outcomes following hypoglossal nerve stimulation for obstructive sleep apnea. *Am J Otolaryngol*. Mar-Apr 2018;39(2):122-126. PMID 29277289 • Carroll W, Wilhoit CS, Intaphan J, et al. Snoring management with nasal surgery and upper airway radiofrequency ablation. *Otolaryngol Head Neck Surg*. Jun 2012;146(6):1023-7. PMID 22323433 • Certal VF, Zaghi S, Riaz M, et al. Hypoglossal nerve stimulation in the treatment of obstructive sleep apnea: A systematic review and meta-analysis. *Laryngoscope*. May 2015;125(5):1254-64. PMID 25389029 • Dedhia RC, Strollo PJ, Soose RJ. Upper Airway Stimulation for Obstructive Sleep Apnea: Past, Present, and Future. *Sleep*. Jun 2015;38(6):899-906. PMID 25409109 • Diercks GR, Wentland C, Keamy D, et al. Hypoglossal Nerve Stimulation in Adolescents with Down Syndrome and Obstructive Sleep Apnea. *JAMA Otolaryngol Head Neck Surg*. Jan 2018;144(1):37-42. PMID 29098288 • Diercks GR et al. Hypoglossal nerve stimulator implantation in an adolescent with Down Syndrome and sleep apnea. Pediatrics. 2016 May; 137(5). • Doghramji K, Boon M. The role of upper airway stimulation therapy in the multidisciplinary management approach of obstructive sleep apnea in the adult patient. *Laryngoscope*. Sep 2016;126: S9-S11. PMID 27572121 • Eisele DW et al. Direct hypoglossal nerve stimulation in obstructive sleep apnea. *Arch Otolaryngol Head Neck Surg*. 1997 Jan;123(1):57-61. • Eisele DW et al. Tongue neuromuscular and direct hypoglossal nerve stimulation for obstructive sleep apnea. *Otolaryngol Clin North Am*. 2003 Jun;36(3):501-10. Review. • Elshebiny T et al. Airway evaluation in response to hypoglossal nerve stimulation a case report. *J Dental Sleep Med*. 2017;4(1)15-17. • ElShebiny T et al. Hyoid arch displacement with hypoglossal nerve stimulation. *Am J Respir Crit Care Med*. 2017 May (online). • Fairbanks DW et al. Neurostimulation for obstructive sleep apnea: investigations. *Ear Nose Throat J*. 1993 Jan;72(1):52-4, 57. • Farrar J, Ryan J, Oliver E, Gillespie MB. Radiofrequency ablation for the treatment of obstructive sleep apnea: a meta-analysis. *Laryngoscope*. 2008 Oct;118(10):1878-83. doi: 10.1097/MLG.0b013e31817d9cc1. PMID: 18806478 • Fibbi A et al. Tongue base suspension and radiofrequency volume reduction: a comparison between 2 techniques for the treatment of sleep-disordered breathing. *Am J Otolaryngol*. 2009 Nov-Dec;30(6):401-6. doi: 10.1016/j.amjoto.2008.08.006. Epub 2009 Mar 6. PubMed PMID: 19880029.

No.	Yes/No	Citations of Missing Evidence
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2	Yes	Children with moderate to severe persistent sleep apnea following adenotonsillectomy are difficult to treat. Children often have difficulty tolerating CPAP therapy and treatment options are limited, especially in children with craniofacial anomalies such as Down Syndrome. There are reports of improvement in sleep study and quality of life parameters in children treated with tongue base suspension and radiofrequency ablation. Randomized trials of these interventions comparing them to CPAP would not be feasible as the children are often unable to tolerate CPAP. • Wootten CT, Shott SR. Evolving therapies to treat retroglossal and base-of-tongue obstruction in pediatric obstructive sleep apnea. *Arch Otolaryngol Head Neck Surg*. Oct 2010;136(10):983-7. PMID: 20956744

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Documentation for Clinical Review

Please provide the following documentation:

- History and physical and/or consultation notes including:
  - Type of procedure requested
  - Documentation of obstructive sleep apnea including:
    - AHI/RDI
    - Symptoms
    - Comorbidities
  - Clinical findings (i.e., diagnosis of Down syndrome; if applicable)
  - Documentation of age and Body Mass Index; when applicable
  - Documentation of hypertrophic tonsils; if applicable
- Drug-induced sleep endoscopy result; if applicable
- Prior treatment and response (including documented failed trial of both CPAP and oral appliance; if applicable)

Post Service (in addition to the above, please include the following):

- Procedure report(s)

Coding

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contract language should be reviewed before applying the terms of the Policy.

The following codes are included below for informational purposes. Inclusion or exclusion of a code(s) does not constitute or imply member coverage or provider reimbursement policy. Policy Statements are intended to provide member coverage information and may include the use of some codes for clarity. The Policy Guidelines section may also provide additional information for how to interpret the Policy Statements and to provide coding guidance in some cases.

Type	Code	Description
CPT®	21199	Osteotomy, mandible, segmental; with genioglossus advancement
	21685	Hyoid myotomy and suspension
	41512	Tongue base suspension, permanent suture technique
	41530	Submucosal ablation of the tongue base, radiofrequency, 1 or more sites, per session
	42145	Palatopharyngoplasty (e.g., uvulopalatopharyngoplasty, uvulopharyngoplasty)
	42299	Unlisted procedure, palate, uvula
	42820	Tonsillectomy and adenoidectomy; younger than age 12
	42821	Tonsillectomy and adenoidectomy; age 12 or over
	42825	Tonsillectomy, primary or secondary; younger than age 12
	42826	Tonsillectomy, primary or secondary; age 12 or over
	42830	Adenoidectomy, primary; younger than age 12
	42831	Adenoidectomy, primary; age 12 or over
	42835	Adenoidectomy, secondary; younger than age 12
	42836	Adenoidectomy, secondary; age 12 or over
	42950	Pharyngoplasty (plastic or reconstructive operation on pharynx)
	42975	Drug-induced sleep endoscopy, with dynamic evaluation of velum, pharynx, tongue base, and larynx for evaluation of sleep-disordered breathing, flexible, diagnostic

Type	Code	Description
	64568	Open implantation of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator
	64582	Open implantation of hypoglossal nerve neurostimulator array, pulse generator, and distal respiratory sensor electrode or electrode array
	64583	Revision or replacement of hypoglossal nerve neurostimulator array and distal respiratory sensor electrode or electrode array, including connection to existing pulse generator
	64584	Removal of hypoglossal nerve neurostimulator array, pulse generator, and distal respiratory sensor electrode or electrode array
HCPCS	C1767	Generator, neurostimulator (implantable), nonrechargeable
	C1778	Lead, neurostimulator (implantable)
	C9727	Insertion of implants into the soft palate; minimum of three implants
	E0492	Power source and control electronics unit for oral device/appliance for neuromuscular electrical stimulation of the tongue muscle, controlled by phone application ***(Code effective 1/1/2024)***
	E0493	Oral device/appliance for neuromuscular electrical stimulation of the tongue muscle, used in conjunction with the power source and control electronics unit, controlled by phone application, 90-day supply ***(Code effective 1/1/2024)***
	K1028	Power source and control electronics unit for oral device/appliance for neuromuscular electrical stimulation of the tongue muscle, controlled by phone application ***(Deleted code effective 1/1/2024)***
	K1029	Oral device/appliance for neuromuscular electrical stimulation of the tongue muscle, used in conjunction with the power source and control electronics unit, controlled by phone application, 90-day supply ***(Deleted code effective 1/1/2024)***
	S2080	Laser-assisted uvulopalatoplasty (LAUP)

Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

Effective Date	Action
01/30/2015	New policy. Policy title changed from Obstructive Sleep Apnea - Diagnosis and Management to current one. Policy statement updated.
02/01/2017	Annual review. Policy statement, guidelines and literature review updated. Coding update.
11/01/2017	Annual review. Policy statement, guidelines and literature review updated.
11/01/2018	Annual review. Policy statement, guidelines and literature review updated.
05/01/2019	Annual review. Policy statement, guidelines and literature review updated.
10/01/2019	Annual review. Policy statement, guidelines and literature review updated.
05/01/2020	Admin update
09/01/2020	Annual review. No change to policy statement. Literature review updated.
11/01/2020	Administrative update. Policy statement updated.
08/01/2021	Annual review. No change to policy statement. Literature review updated.
03/01/2022	Coding update.
07/01/2022	Coding and Administrative update.
08/01/2022	Annual review. Policy statement, guidelines and literature review updated.
08/01/2023	Annual review. No change to policy statement. Policy guidelines and literature review updated. Coding update.

Effective Date	Action
12/01/2023	Coding update.
03/01/2024	Coding update.
08/01/2024	Annual review. No change to policy statement and literature review. Policy guidelines updated.
09/01/2024	Annual review. Policy statement, guidelines and literature review updated.

Definitions of Decision Determinations

Medically Necessary: Services that are Medically Necessary include only those which have been established as safe and effective, are furnished under generally accepted professional standards to treat illness, injury or medical condition, and which, as determined by Blue Shield, are: (a) consistent with Blue Shield medical policy; (b) consistent with the symptoms or diagnosis; (c) not furnished primarily for the convenience of the patient, the attending Physician or other provider; (d) furnished at the most appropriate level which can be provided safely and effectively to the patient; and (e) not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of the Member's illness, injury, or disease.

Investigational/Experimental: A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

Split Evaluation: Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements and Feedback (as applicable to your plan)

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department at (800) 541-6652, or the Transplant Case Management Department at (800) 637-2066 ext. 3507708 or visit the provider portal at www.blueshieldca.com/provider.

We are interested in receiving feedback relative to developing, adopting, and reviewing criteria for medical policy. Any licensed practitioner who is contracted with Blue Shield of California or Blue Shield of California Promise Health Plan is welcome to provide comments, suggestions, or concerns. Our internal policy committees will receive and take your comments into consideration.

For utilization and medical policy feedback, please send comments to: MedPolicy@blueshieldca.com

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must

be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.

Appendix A

POLICY STATEMENT	
BEFORE Red font: Verbiage removed	**AFTER** Blue font: Verbiage Changes/Additions
Surgical Treatment of Snoring and Obstructive Sleep Apnea Syndrome 7.01.101 **Policy Statement:** I. Palatopharyngoplasty (e.g., uvulopalatopharyngoplasty, uvulopharyngoplasty, uvulopalatal flap, expansion sphincter pharyngoplasty, lateral pharyngoplasty, palatal advancement pharyngoplasty, relocation pharyngoplasty) may be considered **medically necessary** in appropriately selected individuals when **all** of the following criteria are met: A. Individuals who are diagnosed with clinically significant obstructive sleep apnea (OSA) syndrome B. Individuals who have failed an adequate[a] trial of **all** of the following: 1. Continuous positive airway pressure (CPAP) 2. Oral appliance (OA)[b,c] II. Hyoid suspension, surgical modification of the tongue, and/or maxillofacial surgery, including mandibular-maxillary advancement (MMA), may be considered **medically necessary** in appropriately selected individuals when **all** of the following criteria are met: A. Individuals who are diagnosed with clinically significant OSA syndrome B. There is objective documentation of hypopharyngeal obstruction C. Individuals who have failed an adequate[a] trial of **all** of the following: 1. Continuous positive airway pressure (CPAP) 2. Oral appliance (OA)[b,c] III. Adenotonsillectomy may be considered **medically necessary** in pediatric individuals when **all** of the following criteria are met: A. An individual is diagnosed with clinically significant OSA syndrome	**Surgical Treatment of Snoring and Obstructive Sleep Apnea Syndrome 7.01.101** **Policy Statement:** I. Palatopharyngoplasty (e.g., uvulopalatopharyngoplasty, uvulopharyngoplasty, uvulopalatal flap, expansion sphincter pharyngoplasty, lateral pharyngoplasty, palatal advancement pharyngoplasty, relocation pharyngoplasty) may be considered **medically necessary** in appropriately selected individuals when **all** of the following criteria are met: A. Individuals who are diagnosed with clinically significant obstructive sleep apnea (OSA) syndrome B. Individuals who have failed an adequate[a] trial of **all** of the following: 1. Continuous positive airway pressure (CPAP) 2. Oral appliance (OA)[b,c] II. Hyoid suspension, surgical modification of the tongue, and/or maxillofacial surgery, including mandibular-maxillary advancement (MMA), may be considered **medically necessary** in appropriately selected individuals when **all** of the following criteria are met: A. Individuals who are diagnosed with clinically significant OSA syndrome B. There is objective documentation of hypopharyngeal obstruction C. Individuals who have failed an adequate[a] trial of **all** of the following: 1. Continuous positive airway pressure (CPAP) 2. Oral appliance (OA)[b,c] III. Adenotonsillectomy may be considered **medically necessary** in pediatric individuals when **all** of the following criteria are met: A. An individual is diagnosed with clinically significant OSA syndrome

POLICY STATEMENT	
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B. An individual has hypertrophic tonsils	B. An individual has hypertrophic tonsils
IV. Hypoglossal nerve stimulation may be considered **medically necessary** for an adult individual when **all** of the following criteria are met: A. An individual is diagnosed with clinically significant OSA syndrome B. Age is 22 years or older C. Apnea/Hypopnea Index (AHI) is greater than or equal to 15 with less than 25% central apneas D. Failed CPAP (residual AHI greater than or equal to 15 or failure to use CPAP greater than or equal to 4 hours or more per night for at least 5 nights per week) or inability to tolerate CPAP E. Body mass index is less than or equal to 32 kg/m2 F. Non-concentric retropalatal obstruction on drug-induced sleep endoscopy	IV. Hypoglossal nerve stimulation may be considered **medically necessary** for an adult individual when **all** of the following criteria are met: A. An individual is diagnosed with clinically significant OSA syndrome B. Age is 18 years or older C. Apnea/Hypopnea Index (AHI) is greater than or equal to 15 and less than or equal to 100 with less than or equal to 25% central apneas D. Failed CPAP (residual AHI greater than or equal to 15 or failure to use CPAP greater than or equal to 4 hours or more per night for at least 5 nights per week) or inability to tolerate CPAP E. Body mass index is less than or equal to 35 kg/m^2 F. Absence of complete concentric collapse at the soft palate level
V. Hypoglossal nerve stimulation may be considered **medically necessary** in an adolescent or young individual when **all** of the following criteria are met: A. An individual is diagnosed with Down syndrome and clinically significant OSA syndrome B. Age 10 to 21 years C. AHI greater than 10 and less than 50 with less than 25% central apneas after prior adenotonsillectomy D. Documentation of **one or more** of the following: 1. Tracheotomy 2. Was ineffectively treated with CPAP due to noncompliance, discomfort, un-desirable side effects, persistent symptoms despite compliance use, or refusal to use the device E. Body mass index less than or equal to 95th percentile for age F. Non-concentric retropalatal obstruction on drug-induced sleep endoscopy	V. Hypoglossal nerve stimulation may be considered **medically necessary** in an adolescent or young individual when **all** of the following criteria are met: A. An individual is diagnosed with Down syndrome and clinically significant OSA syndrome B. Age 13 to 18 years C. AHI greater than 10 and less than 50 with less than or equal to 25% central apneas after prior adenotonsillectomy D. Documentation of **one or more** of the following: 1. Tracheotomy 2. Was ineffectively treated with CPAP due to noncompliance, discomfort, undesirable side effects, persistent symptoms despite compliance use, or refusal to use the device E. Body mass index less than or equal to 95th percentile for age F. Absence of complete concentric collapse at the soft palate level

POLICY STATEMENT	
BEFORE Red font: Verbiage removed	**AFTER** Blue font: Verbiage Changes/Additions
VI. Surgical treatment of OSA using the techniques addressed above that do not meet the required criteria is considered **not medically necessary**.	VI. Surgical treatment of OSA using the techniques addressed above that do not meet the required criteria is considered **not medically necessary**.
VII. The following are considered **investigational**: A. Laser-assisted palatoplasty or radiofrequency volumetric tissue reduction of the palatal tissues B. Radiofrequency volumetric tissue reduction of the tongue, with or without radiofrequency reduction of the palatal tissues C. Palatal stiffening procedures including, but not limited to, cautery-assisted palatal stiffening operation, injection of a sclerosing agent, and the implantation of palatal implants D. Tongue base suspension	VII. The following are considered **investigational** for the sole or adjunctive treatment of OSA or upper airway resistance syndrome: A. Laser-assisted palatoplasty or radiofrequency volumetric tissue reduction of the palatal tissues B. Radiofrequency volumetric tissue reduction of the tongue, with or without radiofrequency reduction of the palatal tissues C. Palatal stiffening procedures including, but not limited to, cautery-assisted palatal stiffening operation, injection of a sclerosing agent, and the implantation of palatal implants D. Tongue base suspension
VIII. Implantable hypoglossal nerve stimulators are considered **investigational** for all indications other than listed above.	VIII. Implantable hypoglossal nerve stimulators are considered **investigational** for all indications other than listed above.
IX. All interventions, (e.g., laser-assisted palatoplasty, radiofrequency volumetric tissue reduction of the palate, or palatal stiffening procedures,) are considered **investigational** for the treatment of snoring alone (there is no clinically significant in OSA).	IX. All interventions, (e.g., laser-assisted palatoplasty, radiofrequency volumetric tissue reduction of the palate, or palatal stiffening procedures,) are considered **investigational** for the treatment of snoring alone (there is no clinically significant in OSA).