Medical Coverage Policy

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Surgical Treatments for Obstructive Sleep Apnea

Table of Contents

Related Coverage Resources

Bariatric Surgery and Procedures
Diaphragmatic/Phrenic Nerve Stimulation
Distraction Osteogenesis (DO) for Craniofacial Deformities
Omnibus Codes
Orthognathic Surgery
Rhinoplasty, Vestibular Stenosis Repair and Septoplasty
Sleep Disorders Diagnosis & Treatment Guidelines

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Overview

This Coverage Policy addresses surgical treatments for obstructive sleep apnea (OSA).

Coverage Policy

In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Coverage of the treatment of obstructive sleep apnea and other sleep disorders varies across plans. Refer to the customer's benefit plan document for coverage details.

Tonsillectomy and/or adenoidectomy is considered medically necessary for the treatment of obstructive sleep apnea (OSA) as diagnosed by polysomnography (PSG) or home sleep apnea test (HSAT).

Uvulopalatopharyngoplasty (UPPP) is considered medically necessary for the treatment of OSA when ALL of the following criteria are met:

- demonstrated narrowing or collapse of the retropalatal region (soft palate, uvula, tonsils, posterior pharyngeal wall) as a source of airway obstruction
- criteria for PAP met and documentation that demonstrates PAP treatment failure defined as an inability to eliminate OSA (AHI > 15); OR PAP intolerance defined as inability to use PAP > 4 hours of use per night, 5 nights per week; OR unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it)
- for mild or moderate OSA in an adult, consideration has also been given to use of mandibular repositioning appliance (MRA) or tongue-retaining appliance

Uvulectomy as a stand-alone procedure for the treatment of OSA is considered experimental, investigational or unproven. (Note: this Coverage Policy is not intended to address uvulectomy performed for other indications [e.g., acute inflammation/angioedema of the uvula]).

Multi-level or stepwise surgery (MLS) (e.g., UPPP and/or genioglossus advancement and hyoid myotomy (GAHM), maxillary and mandibular advancement osteotomy [MMO]) as a combined procedure or as stepwise multiple procedures is considered medically necessary for the treatment of OSA when ALL of the following criteria are met:

- narrowing of multiple sites in the upper airway
- criteria for PAP met and documentation that demonstrates PAP treatment failure defined as an inability to eliminate OSA (AHI > 15); OR PAP intolerance defined as inability to use PAP > 4 hours of use per night, 5 nights per week; OR unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it)
- in an adult, a mandibular repositioning appliance (MRA) or tongue-retaining appliance has been considered and found to be ineffective or undesirable

Maxillomandibular advancement is considered medically necessary for the treatment of severe OSA when ALL of the following criteria are met:

- criteria for PAP met and documentation that demonstrates PAP treatment failure defined as an inability to eliminate OSA (AHI > 15); OR PAP intolerance defined as inability to use PAP > 4 hours of use per night, 5 nights per week; OR unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it)
- in an adult, a mandibular repositioning appliance (MRA) or tongue-retaining appliance has been considered and found to be ineffective or undesirable
- individual has craniofacial disproportion or deformities

Tracheostomy is considered medically necessary for the treatment of OSA when other medical and surgical options do not exist, have failed or are refused, or when deemed necessary by clinical urgency.

A U.S. Food and Drug Administration (FDA)-approved implantable upper airway hypoglossal nerve stimulation device is considered medically necessary for the treatment of moderate to severe OSA when ALL of the following criteria are met:

- age 22 years or older
- AHI on PSG* of 15-65 events per hour with < 25% central + mixed apneas
- body mass index (BMI) ≤ 32 kg/m^2
- absence of a complete concentric collapse at the soft palate level on drug induced sleep endoscopy
- documentation that demonstrates PAP treatment failure defined as an inability to eliminate OSA (AHI > 15); OR PAP intolerance defined as inability to use PAP > 4 hours of use per night, 5 nights per week; OR unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it)
- no anatomical finding that would compromise the performance of upper airway stimulation (e.g., tonsil size 3 or 4 per tonsillar hypertrophy grading scale)

The replacement of an FDA-approved implantable upper airway hypoglossal nerve stimulation device, generator battery and/or leads is considered medically necessary when a previously implanted device, generator battery and/or leads is no longer functioning appropriately and the device is no longer under warranty.

The replacement of a remote that is used with an FDA-approved implantable upper airway hypoglossal nerve stimulation device is considered medically necessary when there is documentation confirming that the remote is malfunctioning and is no longer under warranty.

NOTE: Off-the-shelf batteries, used in the remote for the hypoglossal nerve stimulation device, are generally considered not medically necessary because they are not primarily medical in nature.

***Note: Criteria for the HSAT and PSG testing pre- and post- upper airway hypoglossal nerve stimulator implantation are covered in the Sleep Disorders Diagnosis and Treatment Guidelines.**

ADDITIONAL PROCEDURES/SERVICES

The following procedures for the treatment of OSA are considered experimental, investigational or unproven:

- atrial overdrive pacing
- cautery-assisted palatal stiffening operation (CAPSO)
- injection Snoreplasty
- laser-assisted uvulopalatoplasty (LAUP)
- Pillar™ Palatal Implant System
- radiofrequency volumetric tissue reduction (RFVTR) of the soft palate, uvula, or tongue base (e.g., Coblation®, Somnoplasty®)
- tongue-base suspension (e.g., AIRvance™ System, ENCORE™ Tongue Suspension System)
- tongue implant (e.g., ReVent System)
- transpalatal advancement pharyngoplasty

The treatment of snoring alone by any method is considered not medically necessary.

General Background

Obstructive sleep apnea (OSA) is a disorder characterized by obstructive apneas and hypopneas due to repetitive collapse of the upper airway during sleep. Untreated OSA is associated with symptoms of excessive daytime sleepiness, metabolic dysfunction, impaired daytime function and an increased risk of cardiovascular disease and mortality. For most adults, first-line therapy for OSA consists of behavioral modification, including weight loss if appropriate, and positive airway pressure (PAP) therapy. Generally, surgical treatment of OSA is reserved as a second-line therapy for OSA, either as secondary therapy in individuals with OSA who cannot adhere to continuous positive airway pressure (CPAP) or as adjunctive therapy along with CPAP or an oral appliance. The choice among various second-line options depends on the severity of the OSA and the patient's anatomy, risk factors and preferences. Although surgical treatment for OSA provides long-term benefits in selected individuals, complete elimination of OSA is often not achieved. Various surgical procedures have generally not been compared directly with one another, and surgical decisions are individualized based on patient anatomy and surgeon preferences (Weaver and Kapur, 2021).

Procedures
Surgical treatment of OSA includes multiple procedures and approaches that enlarge and/or stabilize the upper airway. These procedures can be categorized as nasal, upper pharyngeal, lower pharyngeal and global upper airway procedures. Careful patient and procedure selection, especially related to the anatomy, physiology, and function of the upper aerodigestive tract, and perioperative risk management, are key considerations in the surgical evaluation of patients with OSA (Weaver and Kapur, 2021).

Upper pharyngeal procedures: The goal of upper pharyngeal procedures in the context of OSA is to relieve upper pharyngeal obstruction. If other obstructing areas are present (e.g., lower pharyngeal obstruction), additional treatment is required (e.g., lower pharyngeal procedures, oral appliance, or CPAP). Examples of upper pharyngeal procedures include:

- Uvulopalatopharyngoplasty (UPPP): UPPP is the most common surgical procedure for OSA since upper pharyngeal obstruction is the most common anatomic airway abnormality. UPPP is a surgical reconstructive procedure that involves reducing, tightening and/or repositioning the soft palate and related oropharyngeal structures with the goal of improving the airway while asleep. It often includes reduction, removal, or reconfiguration of the uvula. There are many variations of this procedure including: uvulopalatal flap, expansion sphincter pharyngoplasty, lateral pharyngoplasty, palatal advancement pharyngoplasty and relocation pharyngoplasty. Each procedure focuses on correcting pharyngeal airway compromise. Some of the variants may be combined to address complicated palatal obstruction. Usually a palatine tonsillectomy is performed simultaneously if the tonsils are still present. Selection of the optimal UPPP variant depends on individual anatomy and functional examination of the upper pharynx and palate.
- Tonsillectomy and Adenoidectomy: Tonsillectomy is part of UPPP when the palate procedure is performed simultaneously. Isolated tonsillectomy is reserved for individuals with isolated palatine tonsillar hypertrophy without palatal abnormalities. Adenoidectomy is performed with tonsillectomy or in isolation.
- Laser-Assisted Uvulopalatoplasty (LAUP): LAUP does not treat OSA as well as the other surgical techniques, and it poses a risk of abnormal palatal scarring and oropharyngeal stenosis, so it is not advocated. Numerous palatal stiffening techniques have been studied (e.g., radiofrequency palatal stiffening, injection sclerotherapy and palatal implants), but they have minimal effect on OSA.

Lower pharyngeal and laryngeal procedures: The goal of lower pharyngeal and laryngeal procedures in the context of OSA is to relieve a variety of types of obstruction or collapse in these areas. These procedures are typically used in conjunction with surgery to relieve upper pharyngeal obstruction. There are multiple proposed procedures for improving the lower pharyngeal airway (e.g., tongue reduction, tongue advancement/stabilization and epiglottis correction). Each procedure is focused at a specific target area or problem. Some procedures occur in the lower pharyngeal airway (e.g., midline glossectomy) and others occur at adjacent sites with effects on the lower pharyngeal airway (e.g., genioglossus advancement).

Tongue reduction procedures are performed by multiple methods including lasers, electrocautery and radiofrequency. Transoral robotic surgery for tongue reduction relies on electrocautery. Radiofrequency tongue reduction is a minimally invasive procedure which creates a submucosal scar that stiffens the tissue and reduces tongue size. Lingual tonsillectomy improves the airway by removing obstructing lingual tonsil tissue identified on indirect mirror exam or flexible laryngoscopy.

Several procedures are proposed to advance or stabilize the tongue base and pharyngeal musculature. These procedures are used individually or in combination, depending on the location and severity of tongue base obstruction. Examples include:

- Genioglossus advancement involves creating an osteotomy around the genial tubercle on the anterior mandible and advancing it 10-15 mm forward without moving the teeth.
- Mandibular advancement moves forward most of the anterior mandible, including the genial tubercle, other sites of tongue attachment and the lower teeth.
- Hyoid suspension advances and stabilizes the hyoid bone to the thyroid cartilage or to the mandible. The hyoid bone is attached to the base of the tongue and other pharyngeal musculature.Ttherefore, stabilization of the hyoid bone can help stabilize the lower tongue base and pharynx.
- Tongue suspension anchors a suture or tether to the anterior mandible, creating a tongue base sling.

Global upper airway procedures: Global upper airway procedures include three procedures, each with specific indications that are proposed to improve the upper and lower pharyngeal airway globally or bypass the upper airway; they are not site-directed. Among the various types of surgical procedures, maxillomandibular advancement and tracheotomy are generally associated with the greatest degree of improvement in polysomnographic parameters of OSA. Global upper airway procedures include:

- Maxillomandibular advancement: Maxillomandibular advancement projects the entire lower facial skeleton and attached soft tissues forward. This is a major operation that is typically reserved for patients with persistent, significant OSA following other site-directed surgical treatments or with baseline maxillary or mandibular hypoplasia.
- Tracheotomy: Tracheotomy bypasses the entire upper airway. An OSA tracheotomy cannula is usually used instead of a standard tracheotomy tube. The cannula is smaller, more comfortable and easier to manage than a standard tracheotomy tube. Individuals can eat and speak normally with the cannula capped during waking hours and can breathe easily with the cannula open during sleeping hours. Most patients wish to avoid tracheotomy, so it is typically reserved for patients with severe OSA who fail CPAP therapy and who cannot tolerate upper airway reconstruction because of critical comorbidities.
- Upper airway stimulation: Upper airway stimulation via an implantable neurostimulator device activates the protrusion muscles of the tongue via the hypoglossal nerve to open the lower pharyngeal airway.

Nasal procedures: The utility of nasal procedures in the context of OSA is to relieve nasal obstruction as an adjunctive measure to improve outcomes with CPAP, an oral appliance or other surgery. It is recommended that nasal procedures not be used as a stand-alone therapy for treatment of moderate or severe OSA. Examples of nasal procedures include:

- Turbinate reduction: Turbinate reduction reduces obstruction caused by inferior turbinate hypertrophy, which is a common cause of nasal obstruction, especially related to recumbent position. The goal of turbinate surgery is to reduce size without compromising mucosal function. Turbinate mucosa is important for humidifying, warming and filtering air. Several methods are available for turbinate reduction including: radiofrequency, turbinate outfractures, submucous resection, intramural cauterization and cryotherapy.
- Septoplasty, nasal valve surgery and rhinoplasty. (See Medical Coverage Policy Rhinoplasty, Vestibular Stenosis Repair and Septoplasty for information on treatment of OSA with these procedures).
- Endoscopic procedures: Concha bullosae (enlarged middle turbinates with an indwelling sinus cell) and nasal polyposis are corrected with endoscopic nasal procedures.

Epiglottis procedures: Epiglottis procedures treat epiglottis collapse and obstruction. Partial epiglottidectomy shortens the epiglottis to prevent critical collapse. Epiglottopexy stabilizes the base of the epiglottis to the tongue base to prevent retroflexion or collapse. Hyoid suspension stabilizes the epiglottis indirectly through its attachment to the hyoid bone via the hyoepiglottic ligament. Some of these epiglottis procedures require a neck incision.

Literature Review

Uvulopalatopharyngoplasty (UPPP): Franklin et al. (2009) conducted a systematic review to evaluate the efficacy and adverse effects of surgery for snoring and OSA. The review included four randomized controlled trials of surgery vs. either sham surgery or conservative treatment in adults. The trials included outcome measures of daytime sleepiness, quality of life, AHI, and snoring. There was no significant effect on daytime sleepiness and quality of life after laser-assisted uvulopalatoplasty (LAUP). The AHI and snoring were reduced in one trial after LAUP but not in another. A total of 45 observational studies were also reviewed to evaluate adverse effects following surgical treatment. Persistent side-effects occurred after uvulopalatopharyngoplasty (UPPP) and uvulopalatoplasty (UPP), with difficulty swallowing, globus sensation, and voice changes commonly observed.

A Cochrane systematic review assessed the results of any surgery in the treatment of OSA in adults (Sundaram, et al., 2005). UPPP was one of several procedures evaluated. The authors concluded that available studies do not provide evidence to support the use of surgery in OSA because overall significant benefit has not been

demonstrated. Long-term follow-up of patients who undergo surgical treatment is required to determine whether surgery is curative or whether the signs and symptoms of OSA tend to recur, requiring further treatment.

Sher et al. (1996) conducted a systematic literature review with meta-analysis to provide an overview of the surgical treatment of OSA to provide the basis for the AASM practice parameters on this subject. Studies included in the meta-analysis provided preoperative and postoperative PSG data on at least nine patients treated with UPPP for OSA. Analysis of the UPPP studies revealed that this procedure is, at best, effective in treating less than 50% of patients with OSA. AASM practice parameters based on this review state that UPPP, with or without a tonsillectomy, may be appropriate for patients with narrowing or collapse in the retropalatal region. The recommendations also state that effectiveness of UPPP is variable, and the procedure should only be performed when nonsurgical treatment options, such as PAP, have been considered.

The recommendation for UPPP in the 2010 AASM practice parameters for surgical modification of the upper airway (Aurora, et al., 2010) states that UPPP does not reliably normalize the AHI in moderate to severe OSA; patients with severe OSA should therefore initially be offered PAP therapy, while those with moderate OSA should initially be offered either PAP therapy or an oral appliance. This recommendation differs from the previously published guideline that recommended UPPP for patients with narrowing or collapse of the retropalatal area.

Uvulectomy: Uvulectomy has been proposed as a surgical treatment for snoring and mild obstructive sleep apnea. There are no well-designed studies in the peer-reviewed medical literature that evaluate uvulectomy for the treatment of obstructive sleep apnea. Based on the available evidence, it is not possible to determine the safety and efficacy of this procedure compared to established medical and surgical treatment. Uvulectomy performed as a separate procedure is not addressed in relevant published specialty society guidelines.

(Note: This Coverage Policy is not intended to address uvulectomy when performed for other indications [e.g., acute inflammation/angioedema of the uvula]).

Multi-Level or Stepwise surgery (MLS): This category includes a wide array of combined procedures that address narrowing of multiple upper airway sites. MLS often consists of phase I, utilizing UPPP and/or genioglossus advancement and hyoid myotomy (GAHM). Phase II procedures, consisting of maxillary and mandibular advancement osteotomy (MMO), may be considered for patients who fail phase I surgeries (Aurora, et al., 2011).

AASM Practice Parameters for the Surgical Modification of the Upper Airway for OSA (Aurora, et al, 2010) discussed above state that use of multi-level or stepwise surgery (MLS), as a combined procedure or as stepwise multiple operations, is acceptable in patients with narrowing of multiple sites in the upper airway, particularly if they have failed UPPP as a sole treatment. Although a large volume of literature addressing MLS exists, the evidence is of low quality, consisting of observational case series or comparative studies without randomization. While a multilevel approach may eventually result in significant improvement in AHI, available data are heterogeneous, clinical outcomes such as cardiovascular events are not well studies, and multiple procedures could be associated with increased morbidity and mortality.

Maxillomandibular Advancement (MMA): Maxillomandibular advancement is a surgical procedure that involves the simultaneous advancement of the maxilla and mandible through sagittal split osteotomies. The procedure provides enlargement of the retrolingual airway, and some advancement of the retropalatal airway (Aurora, et al., 2010).

Holty and Guilleminault (2010) conducted a systematic review and meta-analysis of 22 studies (n=627 patients) to evaluate the clinical efficacy and safety of maxillomandibular advancement for the treatment of OSA. The mean AHI decreased from 63.9/hour to 9.5/hour ($p<0.001$) following surgery. The pooled surgical success and cure (AHI<5) rates were 86.0% and 43.2%, respectively. Younger age, lower preoperative weight and AHI, and greater degree of maxillary advancement were predictive of increased surgical success. The major and minor complication rates were 1.0% and 31%, respectively. Long-term surgical success was maintained at a mean follow-up of 44 months. Statistically significant improvements in quality of life measures, OSA symptomatology (i.e., excessive daytime sleepiness) and blood pressure control were reported after MMA. The authors concluded

that MMA appears to be a safe and highly effective treatment for OSA, but further research is needed to assess clinical outcomes of MMA more thoroughly in long-term cohort studies, and to identify which OSA patients would benefit most from MMA.

AASM Practice Parameters for the Surgical Modification of the Upper Airway for OSA (Aurora, et al., 2010), discussed above, state that MMA is indicated for surgical treatment of severe OSA in patients who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances, which are more often appropriate in mild and moderate OSA patients, have been considered and found ineffective or undesirable. The evidence was considered to be very low quality, consisting of nine case series, but did tend to demonstrate consistent effectiveness in severe OSA. In the published series, AHI was reduced to at least 10/hour in most patients, but PAP remains more effective in normalizing AHI, and improvement in other measures such as sleepiness and quality of life are well supported for PAP but are lacking for MMA. PAP or oral appliance therapy therefore should be suggested ahead of MMA in appropriate candidates.

Traditional “stepped” care frequently utilizes MMA as a final approach for surgical treatment of OSA, but MMA may be considered as an initial or sole approach in treating OSA. The authors recommended multidisciplinary evaluation to identify which patients would benefit from MMA as initial or sole therapy. There is a need for further clarification regarding the relative risks and benefits of MMA compared with other treatment modalities

Tracheostomy: AASM practice parameters (Aurora, et al., 2010) state that tracheostomy has been shown to be an effective single intervention to treat OSA. This operation should be considered only when other options do not exist, have failed, are refused, or when this operation is deemed necessary by clinical urgency. This recommendation is considered an Option; although tracheostomy is nearly always successful in bypassing the upper airway obstruction and normalizing AHI, it is not recommended as primary therapy based on placing a high value on patient safety, autonomy, and quality of life.

Implanted Upper Airway Stimulation Devices: Diminished muscle activity or tone in the upper airway during sleep can cause the tongue to slip from its normal position and occlude the pharynx, thereby obstructing the airway, creating the conditions for OSA. Implantable upper airway stimulation devices have been proposed to treat moderate to severe OSA. The devices provide mild electrical stimulation to the medial branch of the hypoglossal nerve which produces selective motor stimulation of the muscle fibers that draw the tongue forward via activation of the major muscle responsible for protruding the tongue. It has been proposed that this results in improvement of upper airway obstruction, ideally without arousal or patient discomfort (Hayes, 2018).

Hypoglossal nerve stimulation (HGNS) devices are implanted by a pulmonologist, thoracic surgeon, or other qualified physician. Hospitalization is generally not required for device implantation. The standard of care for patients with moderate to severe OSA is CPAP. Oral appliances may also be considered for patients with less severe conditions or for those who are intolerant of CPAP. Proposed surgical procedures can include tracheostomy, nasal reconstruction, uvulopalatopharyngoplasty, and tongue advancement or reduction (Hayes, 2018; Vanderveken, et al., 2017).

A novel device delivering bilateral HGNS via a small implanted electrode activated by a unit worn externally, to treat OSA is being investigated. The Genio™ system (Nyxoah S.A, Belgium) received CE Mark approval in Europe. Presently it is the world’s first and only battery-free, leadless and minimally invasive device. The Genio system differs from previous HGNS devices as it does not require any leads (connective wires between the sensor/cuff electrodes and the pulse generator). An incision under the chin is required without tunneling. Stimulation is delivered bilaterally and controlled from an externally worn unit that activates a small implanted battery-free submental stimulator at a predetermined, adjustable rate and duty cycle (Eastwood, et al., 2020). According to the manufacturer website the Genio system is not available in the United States (Nyxoah, 2020).

Inspire® Upper Airway Stimulation (UAS) (Inspire Medical Systems Inc., Maple Grove, MN) received FDA approval through the PMA process on April 30, 2014 (P130008). The implanted components of the Inspire therapy system consist of the Inspire II implantable pulse generator, the stimulation lead, and the respiratory sensing lead model. When therapy is on, the Inspire system detects the patient’s respiratory effort and maintains airway patency with mild stimulation of the hypoglossal nerve. Therapy settings are stored in the pulse generator

and configured by the physician using an external programmer. The patient uses the Inspire Sleep Remote™ to turn therapy on before sleep and to turn therapy off on awakening.

The April 14, 2020 FDA PMA supplemental document for Inspire UAS (P130008 S039) has an approval order statement stating that approval for the Inspire Upper Airway Stimulation (UAS) the device is used to treat a subset of patients with moderate to severe obstructive sleep apnea (OSA) (apnea-hypopnea index [AHI] of greater than or equal to 15 and less than or equal to 65). Inspire UAS is used in adult patients 22 years of age and older who have been confirmed to fail or cannot tolerate positive airway pressure (PAP) treatments (such as continuous positive airway pressure [CPAP] or bi-level positive airway pressure [BPAP] machines) and who do not have a complete concentric collapse at the soft palate level. PAP failure is defined as an inability to eliminate OSA (AHI of greater than 15 despite PAP usage), and PAP intolerance is defined as: 1) Inability to use PAP (greater than 5 nights per week of usage; usage defined as greater than 4 hours of use per night); or 2) Unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it). Inspire UAS is also indicated for use in patients between the ages of 18 and 21 with moderate to severe OSA (15<=AHI<=65) who: 1) Do not have complete concentric collapse at the soft palate level; 2) Are contraindicated for or not effectively treated by adenotonsillectomy; 3) Have been confirmed to fail, or cannot tolerate PAP therapy despite attempts to improve compliance; and 4) Have followed standard of care in considering all other alternative/adjunct therapies.

The FDA Labeling document for Inspire UAS (P130008) states contraindications for the use of Inspire UAS therapy include the following:

- Central + mixed apneas > 25% of the total apnea–hypopnea index (AHI)
- Any anatomical finding that would compromise the performance of upper airway stimulation, such as the presence of complete concentric collapse of the soft palate
- Any condition or procedure that has compromised neurological control of the upper airway
- Patients who are unable or do not have the necessary assistance to operate the sleep remote.
- Patients who are pregnant or plan to become pregnant.
- Patients who will require magnetic resonance imaging (MRI).
- Patients with an implantable device that may be susceptible to unintended interaction with the Inspire system. Consult the device manufacturer to assess the possibility of interaction.

The FDA warnings and precautions section of the Labeling documents states that BMI greater than 32 was not studied as part of the pivotal trial. Based on data from the feasibility study, it may be associated with decreased likelihood of response to treatment. Use of Inspire UAS in higher BMI patients is not recommended due to unknown effectiveness and safety.

Hypoglossal nerve stimulator devices that have not received FDA approval include the aura6000 (Imthera Medical Inc., San Diego CA) and HGNS® System (Apnex Medical, Inc., Minneapolis, MN). Apnex did not complete the clinical trial for approval by the FDA, however, and is no longer commercially available. In November 2014, ImThera Medical, Inc., received FDA approval to conduct an investigational device exemption trial for its THN3 clinical study. The THN3 study will evaluate the safety and effectiveness of the aura6000 system for moderate to severe OSA in individuals who are unable to comply or unwilling to try PAP therapy or other OSA treatments. Data from this clinical study will be used to support a Pre-Market Approval (PMA) application for the aura6000 system. LivaNova (London, UK) purchased ImThera Medical Inc. in January 2018.

The Inspire UAS device generator, which includes the battery, may need to be replaced when the device nears the end of the battery life. Typical battery life is 10 years. Generator battery life depends on how often therapy is used and the therapy settings. Most generator batteries will last at least seven years. To replace the generator battery, requires replacing the entire generator. A surgical procedure is required The Inspire Sleep Remote has a five year minimum life and runs on over-the-counter batteries. The Inspire warranty period for implanted products is three years. All other products have a warranty period of one year (Inspire, 2021).

Presently there are no available randomized controlled trial that compares HGNS to CPAP or other surgical therapies. The majority of the available HGNS studies are prospective, retrospective or case series. The limited available evidence shows that HGNS has obtained a high surgical success rate with reasonable long-term

complication rate related to the device implanted. The procedure represents an effective and safe surgical treatment for moderate-severe OSA in selected adult patients > 22 years of age who had difficulty accepting or adhering to CPAP (Costantino, et al., 2019).

HGNS has been studied in a pilot study and few small case series studies (n=1-20) for patients < 22 years of age with Down syndrome (Caloway, et al., 2020; Van de Perck, et al., 2019; Diercks, et al., 2018, 2016).

Strollo et al. (2014) conducted a multicenter single-group cohort study, the STAR trial (Stimulation Therapy for Apnea Reduction), to evaluate the safety and effectiveness of a surgically implanted upper airway stimulation device (Inspire UAS) for the treatment of patients with moderate to severe OSA who had difficulty either accepting or adhering to CPAP therapy (n=126). The mean age was 54.5 years (83% men) and mean body mass index (BMI) was 28.4. A total of 17% of the participants had undergone an uvulopalatopharyngoplasty for the treatment of OSA. The mean AHI score on preimplantation screening polysomnography was 32.0 events per hour, and the mean ODI score was 28.9 events per hour. At the baseline visit before implantation, the mean FOSQ score was 14.3, and the mean Epworth Sleepiness Scale score was 11.6. The mean AHI score on the second baseline polysomnography was 31.9 events per hour. There was no significant difference between the two baseline AHI assessments (p=0.83). Exclusion criteria were a BMI of more than 32.0, neuromuscular disease, hypoglossal-nerve palsy, severe restrictive or obstructive pulmonary disease, moderate-to-severe pulmonary arterial hypertension, severe valvular heart disease, New York Heart Association class III or IV heart failure, recent myocardial infarction or severe cardiac arrhythmias (within the past 6 months), persistent uncontrolled hypertension despite medication use, active psychiatric disease, and coexisting nonrespiratory sleep disorders that would confound functional sleep assessment. Approximately one month after implantation, all the participants underwent a second baseline diagnostic polysomnographic examination before activation of the device. The primary outcome measures were apnea-hypopnea index (AHI) and oxygen desaturation index (ODI) (the number of times per hour of sleep that the blood oxygen level drops by ≥ 4 percentage points from baseline). Secondary outcomes were Epworth Sleepiness Scale (ESS), Functional Outcomes of Sleep Questionnaire (FOSQ), and percentage of sleep time with the oxygen saturation less than 90%. The median AHI score at 12 months decreased 68% from 29.3 events/hour to 7.4 events/hour (p<0.001). Scores on the FOSQ and ESS indicated significant improvement at 12 months; the increase in the FOSQ score exceeded the 2.0 point increase typically considered to be a clinically meaningful improvement, and the ESS score at 12 months was consistent with normalization of the measure (i.e., score <10.0). At 12 months, the criteria for the co-primary outcomes of AHI reduction and reduction in ODI were met by 66% and 75% of participants, respectively. Consecutive patients with a response were included in a randomized, controlled therapy withdrawal trial. In this randomized phase the mean AHI did not differ significantly from the 12-month score in the initial phase among the 23 patients in the therapy-maintenance group (8.9 and 7.2 events/hour, respectively). The AHI was significantly higher in the 12 participants in the therapy withdrawal group (25.8 vs. 7.6 events/hour, p<0.001). (The device was turned off in the therapy withdrawal group).The rate of serious adverse events was less than 2%. The lack of a control group limits the validity of the results of this study. Follow-up studies of the same patient population at 18, 24 and 36 months, indicate that the treatment effects are maintained over time. Limitations are the same as the original study (Soose, et al., 2016; Woodson, et al., 2016; Strollo, et al., 2015).

Gillespie et al. (2017) reported the four year outcomes of the STAR trial as described above (Strollo, et al., 2014). A total of 91 of the 126 participants completed the four year follow-up. This study focused on the self-reported patient secondary outcomes collected every six months through a total of 48 months. Secondary outcome measures include subjective sleepiness and sleep-related quality of life with the validated Epworth Sleepiness Scale (ESS) and the Functional Outcomes of Sleep Questionnaire (FOSQ) and snoring level. Daytime sleepiness as measured by ESS was significantly reduced (p=0.01), and sleep-related quality of life as measured by FOSQ significantly improved (p= 0.01) when compared with baseline. Soft to no snoring was reported by 85% of bed partners. At 48 months three participants had undergone elective explantation of the Inspire UAS system, three died and 25 participants were lost to follow-up. Two patients required reoperation between 36 and 48 months for lead-related failure. The reported main study limitation was the increased number of patients lost to follow-up at 48 months compared with 36 months (25 versus 4).

Woodson et al. (2018) reported the five year outcomes of the STAR trial as described above (Stroll et al., 2014). This study evaluated the safety and effects of upper airway stimulation (UAS) therapy on the propensity for daytime sleepiness, as measured by the Epworth Sleepiness Scale (ESS); daytime functioning, as measured by

the Functional Outcomes of Sleep Questionnaire (FOSQ); intrusive snoring, as reported by participant and bed partner; and (4) sleep-disordered breathing, as found in an overnight polysomnography (PSG). Of the 126 participants who underwent implantation, 97 (78%) completed the 5-year follow-up visit. Of the 97 patients meeting the 5-year follow-up protocol, 71 volunteered for an overnight in-laboratory polysomnographic evaluation. A total of 21 were lost to follow-up within the pre-specified time frame; five died of unrelated causes; and three had the device explanted. Patients who did and did not complete the protocol differed in baseline AHI, oxygen desaturation index, and Functional Outcomes of Sleep Questionnaire scores but not in any other demographics or treatment response measures. Improvement in sleepiness (Epworth Sleepiness Scale) and quality of life was observed, with normalization of scores increasing from 33% to 78% and 15% to 67%, respectively. The AHI response rate improved by 50% or to less than 20 in 75% of patients (n=71). Forty-four percent and 78% of participants had AHIs <5 and <15 at 5-year PSG, respectively. When a last observation carried forward analysis was applied, the responder rate was 63% at five years. Based on partner report, intrusive snoring was reduced from 54% at baseline to 2% at 60 months; no snoring or soft snoring increased from 17% to 90%. Participant self-reports of nightly device use were 86%, 81%, and 80% at years 1, 3, and 5, respectively. Serious device-related events all related to lead/device adjustments were reported in 6% of patients. The authors report that the biggest limitations of this study are related to the lack of a control group and the assessment of treatment effects other than withdrawal of stimulation at 12 months. The study group was predominantly male, obese, CPAP intolerant, and of European descent, conclusions about generalizability to women and other ethnic groups may require additional study.

Thaler et al. (2020) reported the outcomes of the ADHERE Registry. This international multicenter prospective observational study followed outcomes of UAS therapy in patients who have failed continuous positive airway pressure therapy for OSA. The registry enrolled adult participants who meet the approved indications of UAS including AHI between 15 to 65 events per hour inclusive, who are intolerant to CPAP, and who are free of complete concentric collapse during sedated endoscopy. Average age was 60 years, BMI of 29.3 kg/m2 and 74% male. A total of 97% of participants reported history of positive airway pressure use for treatment of OSA: 20% with oral appliances, 22% with nasal procedures, 29% with palatal procedures, and 5% with tongue-base procedures. Demographic and sleep study data collection occurred at baseline, implantation visit, post-titration (six months), and final visit (12 months). Patient and physician reported outcomes were collected. Predictors of therapy response were defined as ≥50% decrease in AHI and AHI ≤20 at the 12-month visit. The registry has enrolled 1,017 patients from October 2016 through February 2019. To date, 640 patients have completed their six-month follow-up and 382 have completed the 12-month follow-up. After 12 months, median AHI was reduced from 32.8 to 9.5. Epworth Sleepiness Scale was similarly improved from 11.0 to 7.0. Therapy usage was 5.6 ± 2.1 hours per night after 12 months. Only female sex and lower baseline body mass index remained as significant predictors of therapy response. Stimulation related discomfort was reported by 12% of participants at six months and 8% of participants at 12 months postimplantation. Surgical intervention was required for device revision in three cases: in one participant due to stimulation electrode dislodgement within six months and in another two individuals with stimulation electrode repositioning within 12 months. A reported limitation of this study is that both home and in-laboratory studies were used in the analysis, with attendant lack of uniformity of AHI recording. Home sleep studies may underestimate AHI. The authors concluded that across a multi-institutional study, UAS therapy continues to show significant improvement in subjective and objective OSA outcomes. This registry analysis shows that the therapy effect is durable and adherence is high.

Boon et al. (2018) conducted a retrospective and prospective registry study (n=301) to collect retrospective and prospective objective and subjective outcome measures across multiple institutions (n=10) in the United States and Germany. Patients were included who had moderate to severe OSA, were intolerant to CPAP, and were undergoing upper airway stimulation (UAS) implantation. Baseline demographic and sleep study data were collected. Objective and subjective treatment outcomes, adverse events, and patient and physician satisfaction were reviewed. The study cohort consisted of a middle-aged and primarily male (82%), Caucasian (97%), and overweight population. The authors reported that mean AHI decreased from 35.6 to 10.2 events per hour ($p<0.0001$), and Epworth Sleepiness Scale scores decreased from 11.9 to 7.5 ($p<0.0001$) from baseline to the post-titration visit. The post-titration visit occurs after the therapy has been optimally titrated, approximately two to six months after implant. In general, it is the first office visit after titration. The mean and median follow-up duration was 134 and 123 days after implant, respectively. Patients utilized therapy for 6.5 hours per night. There were low rates of procedure- and device-related complications. At the post-titration visit, 63 adverse events were reported for 54 (18% of 301) patients. Clinical global impression scores demonstrated that the majority of

physicians (94%) saw improvement in their patients. symptoms with therapy. The majority of patients (90%) were more satisfied with UAS than CPAP. This study is limited by the homogenous patient population.

Heiser et al. (2017a) conducted a multicenter single-arm prospective study (n=60) to obtain additional safety and efficacy data on the use of selective upper airway stimulation (i.e. Inspire UAS) during daily clinical routine. Key study selection criteria were based on those established from the STAR trial. Every patient who received an implant of selective upper airway stimulation was included in this trial (apnea-hypopnea index ≥15/h and ≤65/h and body mass index \35 kg/m^2). Before and six months after surgery, a two-night home sleep test was performed. Data regarding the safety and efficacy were collected. Every patient reported improvement in sleep and daytime symptoms. The average usage time of the system was 42.9 ± 11.9 h/wk. The median apnea-hypopnea index was significantly reduced at six months from 28.6/h to 8.3/h. No patient required surgical revision of the implanted system. The lack of a control group and limited follow-up limits the validity of the results of this study.

Heiser et al. (2017b) conducted a single-center prospective study (n=30) to analyze the application and outcome of UAS with the Inspire device in patients with moderate to severe OSA. The mean age was 59.6 years with thirty patients being male. Data at twelve months was reported. The mean pre-implantation AHI of 32.9/h could be reduced to 7.1/h after 12 months (p<0.001). The mean pre-implantation oxygen saturation and desaturation index (ODI) of 30.7/h could be reduced to 9.9/h (p=0.004). The mean pre-implantation ESS of 12.6 could be reduced to 5.9 (p=0.006). Serious adverse events did not occur. Therapy adherence was a usage of 6.6 h/night after 12 months. The lack of a control group, small sample size and limited follow-up limits the validity of the results of this study.

Steffen et al. (2018) conducted a multicenter prospective single-arm study (n=60) reporting on objective and patient-reported outcome after 12 months of implantation of an upper airway stimulation (UAS) device. The study included patients with moderate-to-severe obstructive sleep apnea (OSA) who could not adhere to continuous positive airway pressure. Key study exclusion criteria included body mass index>35 kg/m^2, apnea–hypopnea index (AHI) <15 or>65, or complete concentric collapse at the soft palate during sedated endoscopy. Data collection at six- and 12-month visit include home sleep test and patient-reported outcome measures. The median AHI reduced from 28.6 to 9.5 from baseline to 12 months. Patient-reported outcome measured in Epworth Sleepiness Scale and Functional Outcomes of Sleep Questionnaire both improved significantly from baseline to 12 months. The average usage time was 39.1±14.9 hours per week among all participants based on recordings by the implanted device. One patient requested a removal of the device for cosmetic and other personal reasons and was completed without sequelae. The lack of a control group, small sample size and limited follow-up limits the validity of the results of this study.

In a retrospective study, Mahmoud et al. (2017) reported if prior airway surgery for obstructive sleep apnea (OSA) had increased benefit following implantation with a hypoglossal nerve stimulator. Following implantation with hypoglossal nerve stimulator device, the outcomes of patients who underwent prior airway surgery for OSA were compared with those who did not. Primary outcome measures included apnea-hypopnea index (AHI) and nadir oxyhemoglobin saturation (NOS) as measured by polysomnography. Secondary outcome measures included Epworth Sleepiness Scale. Forty-seven patients underwent implantation with hypoglossal nerve stimulator. Of these, 30 patients had undergone prior airway surgery for OSA, whereas 16 did not. Mean preoperative AHI and NOS were 39.3 and 78% for all patients, 39.4 and 79% for patients with prior airway surgery, and 39.1 and 77% for patients without prior surgery. Mean postoperative AHI and NOS were 3.9 and 91% for all patients, 4.2 and 91% for patients with prior surgery, and 3.4 and 93% for patients without prior surgery (p=0.756 and 0.053, respectively). There were no major adverse events noted in this study.

In a retrospective case series study, Shah et al. (2018) compared outcomes in patients with moderate to severe OSA who underwent hypoglossal nerve stimulation (HNS) surgery (Inspire Medical Systems) and those who underwent traditional airway reconstructive surgery, specifically uvulopalatopharyngoplasty (UPPP). Patients who underwent HNS implantation (n=20), all with moderate to severe OSA, inability to adhere to positive pressure therapy, and compliant with previously published inclusion criteria, were compared to a historical cohort that were intolerant of CPAP with similar inclusion criteria who all underwent UPPP (n=20) with some also undergoing additional procedures such as septoplasty/turbinate reduction. For the HNS group device activation and initiation of therapy was completed at one month after surgery with follow up polysomnography testing done

2–3 months after implantation. For the UPP group, the timing of follow-up polysomnography ranged from 2 to13 months after surgery with most patients (17/20) completing the postoperative sleep study between 3 and 6 months. Data including body mass index (BMI), pre- and post-implant apnea-hypopnea index (AHI) were assessed. For patients who underwent HNS, mean preoperative BMI was 28.0. Mean AHI decreased significantly from 38.9-4.5. All patients achieved an AHI < 20 post implant with 65% (13/20) with an AHI ≤ 5. For patients who underwent traditional airway surgery, mean preoperative BMI was 27.5; mean AHI decreased from 40.3-28.8. The lack of a control group, small sample size and limited follow-up limits the validity of the results of this study.

Huntley et al. (2018) conducted a retrospective study comparing demographic and polysomnographic data and proportion of patients achieving surgical success using upper airway stimulation (UAS) or expansion sphincter pharyngoplasty (ESP). The ESP cohort consisted of 33 patients. The mean preoperative AHI, O2 nadir, Epworth Sleepiness Scale (ESS), and BMI were 36.47, 82.63, 10.69, and 29.6, which improved to 13.47, 84.84, 7.00, and 29.92 postoperatively. There was a 63.64% success rate. The UAS cohort consisted of 75 patients. The mean preoperative AHI, O2 nadir, ESS, and BMI were 36.76, 80.24, 11.18, and 29.50, which improved to 7.25, 88.71, 5.36, and 29.36 postoperatively. The success rate was 86.67%. There was a significant difference in gender, age, preoperative AHI, postoperative AHI, postoperative O2 nadir, surgical success, and patients reaching an AHI less than 10 and 5. The authors reported that future studies with prospectively randomized patients would be needed to explore these preliminary conclusions.

Huntley et al. (2017) conducted a two-center case series study of patients undergoing UAS at Thomas Jefferson University Hospital (TJUH) and University of Pittsburgh Medical Center (UPMC). The investigators recorded demographic data, Epworth Sleepiness Scale (ESS), and preoperative and postoperative polysomnographic information. They compared outcome data between institutions and subsequently combined the cohorts and compared baseline to posttreatment results. A total of 63 UAS device implantations were performed at TJUH and 57 at UPMC. Those patients who completed a postoperative titration PSG and outpatient follow-up were included in this study. This consisted of 48 patients at TJUH and 49 at UPMC The mean time from UAS implantation to postoperative PSG was 90.39 days at TJUH and 85.23 days at UPMC. The TJUH cohort consisted of 30 males and 18 females with a mean age of 60.88 years and body mass index of 29.29. The mean preoperative apnea-hypopnea index (AHI), O_2 nadir, and ESS were 35.88, 80.96, and 11.09, respectively. The mean postoperative AHI, O_2 nadir, and ESS were 6.34, 88.04, and 5.77, respectively. The UPMC cohort consisted of 30 males and 19 females with a mean age of 62.84 years and body mass index of 27.74. The mean preoperative AHI, O2 nadir, and ESS were 35.29, 79.58, and 10.94, respectively. The mean postoperative AHI, O2 nadir, and ESS were 6.28, 84.35, and 6.60, respectively. We found no difference in patients reaching a postoperative AHI less than 15, 10, and 5 when comparing the cohorts. After combining cohorts, we found a significant improvement in postoperative AHI, O2 nadir, and ESS compared to preoperative values. The lack of a control group, small sample size and limited follow-up limits the validity of the results of this study.

In a retrospective case series study (n=20), Kent et al. (2016), reported outcome measures and objective adherence data for patients treated with hypoglossal nerve stimulation (HNS) therapy for moderate to severe obstructive sleep apnea (OSA). All patients had moderate to severe OSA, were unable to adhere to positive pressure therapy, and met previously published inclusion criteria for the commercially available implantable HNS system. Data included demographics, body mass index (BMI), apnea-hypopnea index (AHI), Epworth Sleepiness Score (ESS), nightly hours of device usage, and procedure- and therapy-related complications. Clinical follow-up after device implantation included a postoperative examination within 1-2 weeks, device activation and initiation of therapy one month after implantation, and follow-up polysomnography testing and clinical assessment 2-6 months after implantation. Mean BMI was unchanged postoperatively (26.5 -26.8 kg/m^2). Mean AHI (33.3 6 -5.1) and mean ESS (10.3- 6.0) decreased significantly. Seventy percent (14/20) of patients achieved a treatment AHI <5, 85% (17/20) an AHI <10, and 95% (19/20) an AHI <15. Average stimulation amplitude was 1.89 V after titration. Adherence monitoring via device interrogation showed high rates of voluntary device use (mean 7.0 h/night). The lack of a control group, small sample size and limited follow-up limits the validity of the results of this study.

Costantino et al. (2019) conducted a systematic review and meta-analysis evaluating hypoglossal nerve stimulation (HNS) clinical outcomes in the treatment of moderate to severe obstructive sleep apnea (OSA). This review excluded redundant cohort of same studies with different follow-up lengths (STAR Trial) and the German

Post-MarketStudy. A total of 350 patients from 12 studies (median age 54.3 years and median BMI 29.8) were included. The authors reported that all primary outcomes showed a significant improvement. HNS has resulted in an AHI reduction of 56.2% (Inspire), 53.5% (ImThera), and 44.3% (Apnex) at 12 months and 59.2% (Inspire) at 60 months, respectively, with a surgical success rate of 72.4% (Inspire), 76.9% (ImThera), and 55%(Apnex) at 12 months and 75% (Inspire) at 60 months. The ODI has shown a reduction of 53.4% (Inspire), 47.6% (ImThera), and 24.9% (Apnex) at 12 months and 63.6% (Inspire) at 60 months, respectively. Self-reported outcome measures followed the same trend with an ESS mean reduction of − 5.27 (Inspire), − 2.90 (ImThera), and − 4.20 (Apnex) at 12 months and − 4.40 (Inspire) at 60 months, respectively. The data showed that the optimal clinical improvement obtained at 12-month follow-up is maintained after five years. HNS has shown to be a safe surgical procedure with a low rate of serious adverse events such as permanent impairment, life-threatening illness, or new or prolonged hospitalization with serious health impairment. A total of 6% of patients required surgical repositioning or replacement of the neurostimulator or implanted leads after 5 years. The authors reported limitations of this study include that the STAR trial is actually the only prospective patient cohort with a follow-up longer than 12 months with only 57% (n=71) of the STAR trial cohort completing the 5-year polysomnographic study. All studies included were prospective single-arm cohort studies. There is no currently available randomized controlled trial that compares HNS to CPAP or other surgical therapies. In addition, the majority of patients (n = 237; 72%) were not recruited consecutively.

Kompelli et al. (2018) conducted a systematic review and meta-analysis of available HGNS studies investigating treatment of OSA to analyze objective and subjective outcomes and side effects. Across 16 studies, 381 patients were analyzed. The methodological quality of the studies was assessed as level of evidence 4, since they were case series. At six months mean Sleep Apnea Quality of Life Index improved by 3.1 (2.6-3.7). At 12 months mean AHI was reduced by 21.1 (16.9-25.3), mean ODI was reduced by 15.0 (12.7-17.4), mean ESS was reduced by 5.0 (4.2-5.8), mean Functional Outcomes of Sleep Questionnaire improved by 3.1 (2.6-3.4). Pain (6.2%:0.7-16.6), tongue abrasion (11.0%:1.2-28.7), and internal (3.0%:0.3-8.4)/external device (5.8%:0.3-17.4) malfunction were common adverse events. The authors reported that a key limitation to this review is the lack of long-term follow-up data for implanted patients. Further investigation is needed to compare traditional airway surgery to HGNS.

Certal et al. (2015) conducted a systematic review of the evidence regarding the efficacy and safety of hypoglossal nerve stimulation as an alternative therapy in the treatment of OSA. A total of six prospective studies with 200 patients were included in this review. Studies were included that evaluated the efficacy of hypoglossal nerve stimulation to treat OSA in adults with outcomes for apnea-hypopnea index (AHI), oxygen desaturation index (ODI), and effect on daytime sleepiness (Epworth Sleepiness Scale [ESS]). Tests for heterogeneity and subgroup analysis were performed. At 12 months, the pooled fixed effects analysis demonstrated statistically significant reductions in AHI, ODI, and ESS mean difference of -17.51 (95% CI: -20.69 to -14.34); -13.73 (95% CI: -16.87 to -10.58), and -4.42 (95% CI: -5.39 to -3.44), respectively. Similar significant reductions were observed at 3 and 6 months. Overall, the AHI was reduced between 50% and 57%, and the ODI was reduced between 48% and 52%. Despite using different hypoglossal nerve stimulators in each subgroup analysis, no significant heterogeneity was found in any of the comparisons, suggesting equivalent efficacy regardless of the system in use. The authors reported that further studies comparing hypoglossal nerve stimulation with conventional therapies are needed to definitively evaluate outcomes.

In an updated 2018 Hayes Directory Report on Hypoglossal Nerve Stimulation (HGNS) for Treatment of Obstructive Sleep Apnea, the authors concluded that the overall quality of the evidence evaluating hypoglossal nerve stimulation is very low. A moderate evidence base was identified pertaining to the efficacy and safety of HGNS for the treatment of moderate-to-severe OSA in adult patients who have failed or are intolerant of continuous positive airway (CPAP) therapy. Ten studies were included for review (n=8-126), with 16 associated follow-up or subgroup reports, for a total of 26 publications. Follow-up ranged from 1– 60 months. Stimulation of the hypoglossal nerve may provide a treatment option for patients with moderate-to-severe OSA for whom CPAP has failed to provide relief, but the procedure may carry risks for complications and post implantation surgical procedures. The evidence remains unclear as to whether improvements translate to improved quality of life and better sleep. Additional high-quality comparative studies with larger sample sizes are needed to define the patient population that is most likely to respond to this intervention (Hayes, 2018).

The American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS) Position Statement: Hypoglossal Nerve Stimulation for Treatment of Obstructive Sleep Apnea (OSA) considers upper airway stimulation via the hypoglossal nerve for the treatment of adult OSA syndrome to be a safe and effective second-line treatment of moderate to severe OSA in patients who are intolerant or unable to achieve benefit with PAP. This is not an evidence-based practice guideline rather the position statement is based on an informal process of expert or committee consensus (AAO-HNS, 2021).

The 2009 AASM Clinical Guideline for the Evaluation, Management and Long-Term Care of Obstructive Sleep Apnea in Adults does not mention the use of a hypoglossal nerve stimulator device as treatment option for the treatment of OSA (Epstein, et al., 2009). Per the AASM website, a clinical practice guideline is in development that will provide recommendations regarding if and under what circumstances adult patients with OSA should be referred for surgical consultation. This guideline will update and replace the existing practice parameters.

The 2013 American College of Chest Physicians Clinical Guideline on Management of Obstructive Sleep Apnea in Adults does not mention the use of a hypoglossal nerve stimulator device as treatment option for the treatment of OSA (Qaseem, et al., 2013).

In 2013 the American Thoracic Society (ATS) updated their 1994 clinical practice guideline on the management of sleep apnea. This guideline does not mention the use of a hypoglossal nerve stimulator as a treatment option for OSA.

The American Society of Anesthesiologists (ASA) does not mention the use of hypoglossal nerve stimulation as a treatment option for OSA in their 2014 clinical practice guideline.

Atrial Overdrive Pacing: Atrial overdrive pacing by means of an implantable cardiac pacemaker has been proposed as a treatment for central sleep apnea patients and in certain OSA patients with some degree of heart failure. Atrial overdrive pacing consists of pacing at a rate higher than the mean nocturnal sinus rate. Investigators theorized that atrial overdrive pacing would improve vagal tone and increase upper airway muscle activity in patients with OSA.

Anastasopoulos et al. (2016) conducted a systematic review of 22 studies to evaluate the effect of different types of cardiac pacing on sleep-related breathing disorders in patients with or without heart failure. The included studies were classified according to the type of sleep disorder and the intervention undertaken. The authors reported that the evidence shows that cardiac resynchronization therapy, not atrial overdrive pacing, can reduce apneic events in central sleep apnea patients. Their effect on obstructive sleep apnea is controversial and pacing cannot be used alone as treatment of sleep-related breathing disorders. Further research is needed in order to elucidate the effect of these interventions in individual with sleep apnea.

Weng et al. (2009) conducted a meta-analysis of eight randomized controlled trials to determine the effects of atrial overdrive pacing on sleep apnea syndrome (n=129). Atrial overdrive pacing, as compared to non-pacing, reduced the apnea-hypopnea index (AHI) and increased the minimum arterial oxygen saturation (SaO2) significantly in the central sleep apnea-predominant trials. No statistically significant increase in minimum SaO2 was observed in the obstructive sleep apnea syndrome-predominant trials, however, and it was unclear whether AHI was reduced in these patients. The authors concluded that the role of atrial overdrive pacing in obstructive sleep apnea syndrome remains unclear.

Guidelines for device-based therapy published by the American College of Cardiology (ACC) and the American Heart Association (AHA) state that, a variety of heart rhythm disturbances my occur in OSA. Sinus bradycardia or pauses may occur during hypopneic episodes, and atrial tachyarrhythmias may also be observed, especially following an apnea episode. The guideline states that although a small retrospective trial demonstrated a decrease in central or OSA without reducing the total sleep time, subsequent randomized trials have not validated a role for atrial overdrive pacing in OSA (Epstein et al., 2013, 2008).

There is insufficient evidence to demonstrate the safety and efficacy of atrial overdrive pacing in the treatment of OSA.

Cautery-Assisted Palatal Stiffening Operation (CAPSO): CAPSO is an office-based procedure in which a midline strip of soft palate mucosa is removed, and the wound is left to heal by secondary intention. The procedure has been proposed as a treatment for OSA based on the premise that the resulting midline palatal scar stiffens the palate and eliminates palatal snoring. CAPSO has been performed with and without tonsillectomy and in conjunction with expansion pharyngoplasty.

In a systematic review and meta-analysis, Llewellyn et al. (2018) evaluated CAPSO with and without tonsillectomy and/or in conjunction with expansion pharyngoplasty. A total of eight studies (n=307) were evaluated including case series and prospective studies. The authors concluded that AHI improved by 41% for CAPSO alone, 61.7% for CAPSO with tonsillectomy and 52.1% for CAPSO with expansion pharyngoplasty. Lowest oxygen saturation, sleepiness and snoring improved after CAPSO.

Wassmuth et al. (2000) conducted a case series (n=25) to evaluate the ability of CAPSO to treat OSA. PSG was performed preoperatively and at three months following the procedure on all patients. Patients with a reduction in the AHI of 50% or more and an AHI of 10 or less were classified as responders. Based on these criteria, 40% of patients were considered to have responded to CAPSO. Mean AHI improved from 25.1 ± 12.9 to 16.6 ± 15.0. The ESS improved from 12.7 ± 5.6 to 8.8 ± 4.6. The authors concluded that CAPSO is as effective as other palatal surgeries in the management of OSA.

There is insufficient evidence in the published medical literature to demonstrate the safety, efficacy, and long-term outcomes of CAPSO in the treatment of OSA. Data from well-designed trials with adequate numbers of patients that compare this procedure with other treatments of OSA are lacking.

Injection Snoreplasty: Injection Snoreplasty is a treatment for snoring that involves the injection of a hardening agent into the upper palate. Sodium tetradecyl sulfate is the most common hardening agent used. Following the injection, scar tissue is reported to pull the uvula forward to eliminate palatal flutter associated with snoring. There is no evidence in the published medical literature to demonstrate the safety and efficacy of injection Snoreplasty in the treatment of OSA.

Laser-Assisted Uvulopalatoplasty (LAUP)/Uvulectomy: LAUP differs from UPPP in that much less palatal tissue is removed, the tonsils and pharyngeal pillars are not altered, and a carbon dioxide laser is used rather than a scalpel. Vertical transpalatal laser incisions measuring approximately one cm are made bilaterally through the soft palate lateral to the base of the tongue, followed by partial vaporization of the uvula. Up to seven separate treatment sessions may be required. Well-designed trials evaluating the safety and efficacy of LAUP are lacking.

Camacho et al. (2017) conducted a meta-analysis and systematic review of 23 studies (n=717) to evaluate LAUP alone as a treatment for OSA in adults. Most of the published studies were case series with two randomized controlled trials. The authors concluded that LAUP reduced AHI by 32% among all patients; while the lowest oxygen saturation only changed minimally. The individual data demonstrated a 23% success rate and a cure rate of 8%. AHI worsened among 44% of the patients. The authors recommended that LAUP be performed with caution or not at all due to unfavorable results of the published studies.

AASM 2010 Practice Parameters for the Surgical Modification of the Upper Airway for OSA, as noted above, state that LAUP is not routinely recommended. The evidence was judged to be low quality LAUP does not generally normalize the AHI, and the literature does not demonstrate significant improvement in secondary outcomes. Two studies performed since the last review in 2001 actually reported worsening of the overall AHI.

Pillar™ Palatal Implant System: The Pillar Palatal Implant System (Restore Medical, St. Paul, MN) received FDA 510(k) approval on December 18, 2002, for the treatment of snoring. On June 7, 2004, FDA approval of the Pillar System was expanded to include treatment of OSA. According to the FDA summary, the Pillar System consists of an implant and delivery tool, and is designed to stiffen the tissue of the soft palate to reduce the incidence of snoring in some patients and to reduce the incidence of airway obstruction in patients with mild to moderate OSA. The implant is a cylindrical-shaped segment of braided polyester filaments. The delivery tool consists of a handle and needle assembly that allows for positioning and placement of the implant in the submucosa of the soft palate.

A meta-analysis of the efficacy of the Pillar implant in the treatment of snoring and OSA was conducted by Choi et al. (2013). Efficacy for snoring (seven studies) and for mild to moderate OSA (seven studies) was analyzed separately. For patients with mild to moderate OSA, the Pillar implant significantly reduced the Epworth Sleepiness Scale ($p<.001$) and AHI ($p=.002$) compared to pre-procedure values. The authors noted that these results indicate that the Pillar implant has a moderate effect on snoring and mild to moderate OSA, but more studies with a high level of evidence are needed to arrive at a definite conclusion.

Friedman et al. (2007) conducted a retrospective review to assess subjective and objective improvement in 145 patients with mild to moderate OSA treated with a single-stage multilevel minimally invasive technique. All patients were treated with nasal surgery, palatal stiffening by Pillar implants, and radiofrequency volume reduction of the tongue base. Of 145 patients, 122 had a minimum follow-up of six months and complete data available for review. The primary outcome measure was change from baseline in AHI. The mean AHI decreased from 28.2 ± 7.6 preoperatively to 14.5 ± 10.2 postoperatively ($p<.0001$). Mean Epworth Sleepiness Scale (ESS) decreased from 9.7 ± 3.9 to 7.0 ± 3.3 ($p<.0001$). It is difficult to draw conclusions from this study due to its retrospective design, lack of long-term outcomes, and the inability to determine the individual impact of each procedure on short-term outcomes.

Nordgard et al. (2006) conducted a prospective nonrandomized study of 25 patients with untreated OSA with an AHI of 10–30, as determined by preoperative PSG, and BMI ≤ 30. Three permanent implants were placed in the soft palate of each patient in an office setting under local anesthesia. A repeat PSG showed a mean decrease in AHI from 16.2 to 12.1 for the study group. Twenty of 25 patients demonstrated a reduced AHI, and 12 of 25 patients demonstrated an AHI of 10 or less 90 days post-implant. The mean ESS score decreased from 9.7 to 5.5. The authors concluded that palatal implants can significantly improve AHI and other sleep-related parameters in patients with mild to moderate OSA and BMI ≤ 30, with short-term results comparable to those reported for UPPP. The authors acknowledged the lack of long-term outcomes in this study and the limited number of patients. As with other palatal procedures, reduction in effectiveness over time may be expected. The authors further concluded that while short-term durability and effectiveness have been established, longer-term research needs to be conducted.

A multicenter non-comparative study was conducted by Walker et al. (2006) to evaluate the safety and effectiveness of the Pillar Palatal Implant System (n=53). Primary inclusion criteria were primary palatal contribution to OSA as determined by the investigator, an AHI of 10–30 events per hour, BMI ≤ 32 kg/m^2, age 18 or greater, and soft palate length adequate to accommodate a 28-mm implant. Each patient had three implants placed in the soft palate in an office procedure under local anesthesia. The primary outcome measure was AHI. PSG was performed prior to and 90 days following Pillar implantation. The AHI decreased from 25.0 ± 13.9 to 22.0 ± 14.8 events/hour ($p=0.05$). ESS scores, a secondary outcome measure, decreased from 11.0 ± 5.1 to 6.9 ± 4.5 ($p=<0.001$). The AHI was reduced to below 10 in 12 patients (23%), and the AHI increased in 18 patients (34%). There were no serious complications. The most common adverse event was partial extrusion. Of 202 implants, 20 became partially exposed through the mucosa of the soft palate. All were removed and, in most cases, the implant was replaced.

AASM Practice Parameters for the Surgical Modification of the Upper Airway for OSA (Aurora, et al., 2010) discussed above, state that palatal implants may be effective in some patients with mild obstructive sleep apnea who cannot tolerate or are unwilling to adhere to PAP therapy, or in whom oral appliances have been considered and found ineffective or undesirable. Evidence is of very low quality, and while this procedure may be an alternate mode of therapy for mild OSA, it is difficult to predict if it will ultimately be found to be a reliably effective intervention.

There is insufficient evidence in the published medical literature to demonstrate the safety, efficacy, and long-term outcomes of the Pillar System in the treatment of OSA.

Radiofrequency Volumetric Tissue Reduction (RFVTR): RFVTR (e.g., Coblation®, Somnoplasty®) is a procedure used to remove redundant tissue in the upper airway. Although the procedure has been used to remove tissue from the turbinates and tonsils, recent studies of RFA in the treatment of OSA have limited the procedure to the soft palate, uvula and tongue base.

The ENTec™ ReFlex™ Wand (ArthroCare Corp., Sunnyvale, CA) received FDA approval through the 510(k) process on February 4, 2000, for ablation and coagulation of soft tissue in otolarygological (ENT) surgery, including tissue in the uvula/soft palate for the treatment of snoring and submucosal palatal shrinkage. The ReFlex Wand is used to perform Coblation® treatment using radiofrequency energy. In 2002, the ENTec Plasma Wand received 510(k) approval for ablation, resection, and coagulation of soft tissue and hemostasis of blood vessels in ENT surgery, including tissue of the uvula/soft palate for the treatment of snoring.

The Somnoplasty system (Somnus Medical Technologies, Sunnyvale, CA) received FDA 510(k) approval on July 17, 1997, for coagulation of soft tissue, including the uvula/soft palate. The 510(k) summary states that the Somnoplasty system may reduce the severity of snoring in some individuals. An expanded approval on November 2, 1998, states that the system is intended for the reduction of the incidence of airway obstruction in patients with upper airway resistance syndrome and OSA. The Somnoplasty system is comprised of an RF generator and tissue coagulating electrodes. The procedure is usually performed on an outpatient basis with local anesthesia.

AASM practice parameters discussed above (Aurora, et al., 2010) state that RFA can be considered in patients with mild to moderate OSA who cannot tolerate or are unwilling to adhere to PAP therapy, or in whom oral appliances have been considered and found ineffective or undesirable. This is noted to be a new recommendation based on very low quality evidence. The average post-procedure AHI was found in 7 case series and one randomized controlled trial to be 14.9, consistent with residual mild OSA. The authors noted that RFA studies have shown improvement in subjective sleepiness and, in one study, quality of life. Because cardiovascular complications of OSA are associated with even lower values of AHI, patients treated with RFA should receive follow-up assessments for residual AHI, even if symptoms have improved. The authors also note that long-term sequelae of RFA are not published.

The systematic review by Franklin et al. (2009) to evaluate the efficacy and adverse effects of surgery for snoring and OSA, discussed above, concluded that there was no significant effect on daytime sleepiness and quality of life after radiofrequency ablation.

There is insufficient evidence in the published medical literature to demonstrate the safety, efficacy, and long-term outcomes of RFVTR (e.g., Somnoplasty, Coblation) in the treatment of OSA.

Tongue-Base Suspension (e.g., The AIRvance™ System, ENCORE™ Tongue Suspension System): The Repose Bone Screw System (Influence, Inc., San Francisco, CA) received FDA 510(k) approval on August 27, 1999. The device name was changed to AIRvance in 2011, and is marketed by Medtronic. The system is used to perform anterior tongue base suspension by fixation of the soft tissue of the tongue base to the mandible bone using a bone screw with pre-threaded sutures. It is indicated for the treatment of OSA and/or snoring. The AIRvance System has been proposed as a sole treatment of OSA and has also been use in conjunction with UPPP and radiofrequency ablation.

A similar device to the AIRvance System is the ENCORE™ Tongue Suspension System (Siesta Medical, Inc., Los Gatos, CA). The ENCORE Tongue Suspension System received FDA 510(k) approval on July 1, 2011. The Encore System is intended for anterior advancement of the tongue base and hyoid suspension. It is indicated for the treatment of mild or moderate OSA and /or snoring. The AIRLIFT procedure utilizes the Encore™ System and the Revolution™ Suture Passer, an integrated set of instruments and implants specifically designed for hyoid and tongue suspension.

Bostanciand Turhan (2016) conducted a systematic review to evaluate existing research into the effectiveness and safety of two tongue base suspension (TBS) techniques (Repose® system and modified TBS) with or without uvulopalatopharyngoplasty (UPPP) in obstructive sleep apnea. Seven studies including 113 patients met the eligibility criteria for TBS as a stand-alone procedure. Four of seven studies including 62 patients used the Repose, and three studies including 51 patients used the modified TBS. The success rates were higher in the studies that used modified technique (74.5 %) than those that used the Repose (25.8%), ($p<0.001$). Ten studies including 300 patients met the eligibility criteria for TBS combined with UPPP. Seven of ten studies including 176 patients used the Repose and three studies including 124 patients used the modified TBS. The success rates in

this group were similar between the modified TBS (73.4%) and Repose (67.6%), (p=0.341). When aggregate data of 413 patients were compared, the modified TBS was found to be associated with significantly higher success rates (73.7 vs. 56.7%, p<0.001). The evidence supports primarily grade C recommendations for the benefits of both techniques with or without UPPP. There is a trend toward improved outcome with the modified technique.

Kuhnel et al. (2005) conducted a prospective nonrandomized study (n=28) to demonstrate the efficacy of tongue base suspension with the Repose System in the treatment of OSA. PSG was performed before as well as three and 12 months after surgery. Lateral cephalometric radiography and videoendoscopy of the pharynx were performed preoperatively and postoperatively to identify morphological changes in the posterior airway space. A suspension suture anchored intraorally at the mandible was passed submucosally in the body of the tongue, with suture tightness adjusted individually. The posterior airway space was widened by at least 2 mm in 60% of cases. Daytime sleepiness improved subjectively in 67% of patients, and the RDI improved postoperatively in 55% of patients. The correlation between posterior airway space widening and the improvements in daytime sleepiness and respiratory disturbance index was not significant. The authors concluded that surgical intervention in obstructive sleep apnea syndrome with the Repose System does not result in permanent anatomical change in the posterior airway space.

Miller et al. (2002) conducted a retrospective analysis of the Repose System for the treatment of OSA to describe preliminary experience using the system in conjunction with UPPP in the multilevel surgical approach. The authors evaluated 19 consecutive patients undergoing UPPP and the Repose System tongue base suspension for the management of OSA during a one-year period (1998 through 1999). Fifteen patients had complete preoperative and postoperative PSG data. A 46% reduction in RDI was demonstrated at a mean of 3.8 months after surgery. The apnea index demonstrated a 39% reduction. The authors concluded that the Repose System in conjunction with UPPP has been shown to produce significant reductions in the RDI and apnea index, as well as a significant increase in oxygen saturation. Despite the improvement in these objective parameters, the overall surgical cure rate was only 20% (three of 15 patients) in this retrospective series. Further research is warranted to define the role of the Repose System in the management of obstructive sleep apnea patients.

There is insufficient evidence in the published medical literature to support the safety, efficacy, and long-term outcomes of the use of tongue-base suspension in the treatment of OSA.

Tongue Implant (e.g., The ReVent System): The ReVent System (ReVent® Medical, Inc., Alamo, CA) has CE mark approval and is available on a limited basis in Europe. The device is not FDA-approved. The system is intended for use in stabilizing the tongue for the reduction of the incidence of tongue based airway obstruction in patients with OSA. The implants are inserted using a minimally invasive technique providing a light spring-like force to the tissue. After the implants heal into place with the looped ends acting as an anchoring mechanism, the bio-absorbable sections between the looped ends of the implants erode allowing the implants to contract over time. The spring-like force is designed to maintain an open airway (Pavelec, et al., 2016)

There is insufficient evidence in the published medical literature to support the safety, efficacy, and long-term outcomes of the use of the ReVent System in the treatment of OSA.

Transpalatal Advancement Pharyngoplasty: Volner et al. (2017) conducted a systematic review and meta-analysis to evaluate if apnea-hypopnea index (AHI) and lowest oxygen saturation (LSAT) improve after transpalatal advancement pharyngoplasty (TPAP) with OSA in adults. All studies that included patients who underwent TPAP alone were included in the analysis. Five studies met criteria (n=199). Although improvements were seen in both AHI and LSAT after TPAP, the authors recommend additional studies, especially prospective studies. Research comparing TPAP procedures with palatal advancement are needed to determine the optimal role for this procedure.

Evidence evaluating this technique is limited, consisting primarily of retrospective reviews. There is insufficient evidence in the published medical literature to determine the safety and efficacy of this procedure or to determine how it compares to available treatment options for OSA.

Professional Societies

American Academy of Sleep Medicine (AASM): Referral of adults with obstructive sleep apnea for surgical consultation: an American Academy of Sleep Medicine clinical practice guideline (Kent, et al., 2021), based on a systematic review of the literature and an assessment of the evidence using the GRADE process, is an update to the practice parameters published in 2010. The previous practice parameters addressed specific surgical procedures, but did not address when the appropriate time is to consider surgical treatment.

Recommendations are assigned a strength of "STRONG" if considered a recommendation clinicians should follow under most circumstances, or "CONDITIONAL" if clinicians should use clinical knowledge, experience, patient values and patient preferences to determine the best course of action. The recommendations include:

1. We recommend that clinicians discuss referral to a sleep surgeon with adults with OSA and BMI<40 who are intolerant or unaccepting of PAP as part of a patient-oriented discussion of alternative treatment options. (STRONG)
2. We recommend that clinicians discuss referral to a bariatric surgeon with adults with OSA and obesity (class II/III, BMI ≥35) who are intolerant or unaccepting of PAP as part of a patient-oriented discussion of alternative treatment options. (STRONG)
3. We suggest that clinicians discuss referral to a sleep surgeon with adults with OSA, BMI<40, and persistent inadequate PAP adherence due to pressure-related side effects as part of a patient-oriented discussion of adjunctive or alternative treatment options. (CONDITIONAL)
4. We suggest clinicians recommend PAP as initial therapy for adults with OSA and a major upper airway anatomic abnormality prior to consideration of referral for upper airway surgery. (CONDITIONAL)

Practice Parameters for the Surgical Modification of the Upper Airway for Obstructive Sleep Apnea in Adults (Aurora, et al., 2010), based on a systematic review of the literature (Caples, et al., 2010), updated earlier practice parameters published in 1996.

Recommendations are classified as Standard, Guideline, or Option, in descending order based on the benefits vs. harms and the quality of evidence. Recommendations for individual procedures are included in the relevant sections below.

Standard:

- The presence and severity of obstructive sleep apnea (OSA) must be determined before initiating surgical therapy
- The patient should be advised about potential surgical success rates and complications, the availability of alternative treatment options such as nasal positive airway pressure and oral appliances, and the levels of effectiveness and success rates of these alternative treatments.
- The desired outcomes of treatment include resolution of the clinical signs and symptoms of OSA and the normalization of sleep quality, the apnea-hypopnea index, and oxyhemoglobin saturation levels.

Option

- Maxillo-mandibular advancement (MMA) is indicated for surgical treatment of severe OSA in patients who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances, which are more often appropriate in mild and moderate OSA patients, have been considered and found ineffective or undesirable.
- Uvulopalatopharyngoplasty (UPPP) as a sole procedure, with or without tonsillectomy, does not reliably normalize the apnea hypopnea index (AHI) when treating moderate to severe OSA syndrome. Therefore, patients with severe OSA should initially be offered positive airway pressure (PAP) therapy, while those with moderate OSA should initially be offered either PAP therapy or oral appliances.
- Use of multi-level or stepwise surgery (MLS), as a combined procedure or as stepwise multiple operations, is acceptable in patients with narrowing of multiple sites in the upper airway, particularly if they have failed UPPP as a sole treatment.
- Laser-assisted uvulopalatoplasty (LAUP) is not routinely recommended as a treatment for obstructive sleep apnea syndrome.

- Radiofrequency ablation (RFA) can be considered as a treatment in patients with mild to moderate OSA who cannot tolerate or who are unwilling to adhere to PAP therapy, or in whom oral appliances have been considered and found ineffective or undesirable.
- Palatal implants may be effective in some patients with mild OSA who cannot tolerate or who are unwilling to adhere to PAP therapy, or in whom oral appliances have been considered and found ineffective or undesirable.

American Academy of Otolaryngology-Head and Neck Surgery (AAO-HNS): No evidence-based practice guidelines were found by the AAO-HNS that address the treatment of OSA. The AAO-HNS has published several position statements related to OSA treatment options; however, these documents are based on an informal process of expert or committee consensus (AAO-HNS website).

American Academy of Pediatrics (AAP): The 2012 AAP Clinical Practice Guideline, Diagnosis and Management of Childhood Obstructive sleep Apnea Syndrome key action statement for adenotonsillectomy states that if a child is determined to have OSA, has a clinical examination consistent with adenotonsillar hypertrophy, and does not have a contraindication to surgery, the clinician should recommend adenotonsillectomy as the first line of treatment. If the child has OSA but does not have adenotonsillar hypertrophy, other treatment should be considered. Clinical judgment is required to determine the benefits of adenotonsillectomy compared with other treatments in obese children with varying degrees of adenotonsillar hypertrophy. (Evidence Quality: Grade B, Recommendation Strength: Recommendation) (Marcus, et al., 2012).

Use Outside the U.S.
A European Respiratory Society (ERS) task force report evaluated non-CPAP therapies, including mandibular advancement devices (MADs), for the treatment of OSA (Randerath, et al., 2011). The report states that MADs reduce sleep apneas and subjective daytime sleepiness and improve quality of life compared to control treatments. CPAP is more effective at reducing the number of sleep apneas, but the positive effects on symptoms and health are similar, and patients generally prefer MAD over CPAP. The device should be custom-made, evaluated, and should advance the mandible at least 50% of maximal protrusion. The authors noted that a titration procedure is essential, since the improvement in symptoms is not a precise indicator of treatment success, and long-term follow-up should be performed. Tongue retaining devices (TRD), however, were not recommended for patients with OSA. They may be used, however, in selected patients with mild to moderate OSA when other treatments have failed or are not possible. Patients may have a trial with the device if treatment effect is monitored and strict follow-up is performed.

Guidance issued by the National Institute for Health and Clinical Excellence (NICE, United Kingdom) in 2007 states that the current evidence on soft palate implants for OSA raises no major safety concerns, but there is inadequate evidence that the procedure is efficacious in the treatment of this potentially serious condition for which other treatments exist. The guidance states that soft palate implants should therefore not be used to treat this condition.

National Institute for Health and Clinical Excellence (NICE, United Kingdom) issued updated interventional procedure guidance on radiofrequency ablation of the soft palate in 2014, stating that current evidence suggests that, there are no major safety concerns associated with the procedure as a treatment for snoring. The evidence on the short-term efficacy of the procedure is adequate, although uncertainties remain about its efficacy in the longer term. The NICE guidance states that this procedure should not be used without special arrangements for audit, consent and research.

Interventional Procedure Guidance issued by the National Institute for Health and Clinical Excellence (NICE, United Kingdom) in November 2017 states that current evidence on the safety and efficacy of hypoglossal nerve stimulation for moderate to severe obstructive sleep apnea is limited in quantity and quality. The NICE guidance states that this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

Medicare Coverage Determinations

	Contractor	Policy Name/Number	Revision Effective Date
NCD		No National Coverage Determination found	
LCD	Palmetto GBA	Hypoglossal Nerve Stimulation for Obstructive Sleep Apnea (L38276)	6/21/2020
LCD	First Coast Service Options, Inc.	Hypoglossal Nerve Stimulation for the Treatment of Obstructive Sleep Apnea (L38398)	3/15/2020
LCD	National Government Services, Inc.	Hypoglossal Nerve Stimulation for the Treatment of Obstructive Sleep Apnea (L38387)	4/1/2020
LCD	Novitas Solutions, Inc.	Hypoglossal Nerve Stimulation for the Treatment of Obstructive Sleep Apnea (L38385)	3/15/2020
LCD	Noridian Healthcare Solutions, LLC	Hypoglossal Nerve Stimulation for the Treatment of Obstructive Sleep Apnea (L38310 & L38312)	3/15/2020
LCD	Wisconsin Physicians Service Insurance Corporation	Hypoglossal Nerve Stimulation for the Treatment of Obstructive Sleep Apnea (L38528)	6/14/2020
LCD	CGS Administrators, LLC	Hypoglossal Nerve Stimulation for the Treatment of Obstructive Sleep Apnea (L38307)	3/25/2021
LCD	Wisconsin Physicians Service Insurance Corporation	Surgical Treatment of Obstructive Sleep Apnea (OSA) (L34526)	6/14/2020

Note: Please review the current Medicare Policy for the most up-to-date information.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered medically necessary when criteria in the applicable policy statements listed above are met for the treatment of sleep apnea. Considered not medically necessary for the treatment of snoring in the absence of sleep apnea.

CPT®* Codes	Description
21193	Reconstruction of mandibular rami, horizontal, vertical, C, or L osteotomy; without bone graft
21194	Reconstruction of mandibular rami, horizontal, vertical, C, or L osteotomy; with bone graft (includes obtaining graft)
21195	Reconstruction of mandibular rami and/or body, sagittal split; without internal rigid fixation
21196	Reconstruction of mandibular rami and/or body, sagittal split; with internal rigid fixation
21198	Osteotomy mandible segmental
21199	Osteotomy, mandible, segmental; with genioglossus advancement
21206	Osteotomy, maxilla, segmental (eg, Wassmund or Schuchard)
21685	Hyoid myotomy and suspension
31600	Tracheostomy, planned (separate procedure);
31601	Tracheostomy, planned (separate procedure); younger than 2 years
42145	Palatopharyngoplasty (eg, uvulopalatopharyngoplasty, uvulopharyngoplasty)
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

CPT®* Codes	Description
42835	Adenoidectomy, secondary; younger than age 12
42836	Adenoidectomy, secondary; age 12 or over
61886	Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to 2 or more electrode arrays
61888	Revision or removal of cranial neurostimulator pulse generator or receiver
64568	Incision for implantation cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator
64569	Revision or replacement of cranial nerve (eg, vagus nerve) neurostimulator electrode array, including connection to existing pulse generator
64570	Removal of cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator
64585	Revision or removal of peripheral neurostimulator electrode array
0466T	Insertion of chest wall respiratory sensor electrode or electrode array, including connection to pulse generator (List separately in addition to code for primary procedure)
0467T	Revision or replacement of chest wall respiratory sensor electrode or electrode array, including connection to existing pulse generator
0468T	Removal of chest wall respiratory sensor electrode or electrode array

HCPCS Codes	Description
C1767	Generator, neurostimulator (implantable), nonrechargeable
C1778	Lead, neurostimulator (implantable)
C1787	Patient programmer, neurostimulator
L8680	Implantable neurostimulator electrode, each
L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
L8688	Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension

Considered Experimental/Investigational/Unproven when used to report uvulectomy as a stand-alone procedure for the treatment of obstructive sleep apnea:

CPT®* Codes	Description
42140	Uvulectomy, excision of the uvula

Additional Procedures/Services

Considered Experimental/Investigational/Unproven for the treatment of sleep apnea:

CPT®* Codes	Description
33206	Insertion of new or replacement of permanent pacemaker with transvenous electrode(s); atrial
41512	Tongue base suspension, permanent suture technique
41530	Submucosal ablation of the tongue base, radiofrequency, 1 or more sites, per session
42160	Destruction of lesion, palate or uvula (thermal, cryo or chemical)
42950	Pharyngoplasty (plastic or reconstructive operation on pharynx)

HCPCS Codes	Description
C9727	Insertion of implants into the soft palate; minimum of three implants
S2080	Laser-assisted uvulopalatoplasty (LAUP)

Considered Experimental/Investigational/Unproven when used to report cautery-assisted palatal stiffening operation (CAPSO), injection Snoreplasty, or transpalatal advancement pharyngoplasty:

CPT®* Codes	Description
42299	Unlisted procedure, palate, uvula

Considered Experimental/Investigational/Unproven when used to report tongue implant (e.g., ReVent System):

CPT®* Codes	Description
41599	Unlisted procedure, tongue, floor of mouth

Considered Not Medically Necessary/Convenience Item when used to report PAP cleaning machines:

HCPCS Codes	Description
E1399	Durable medical equipment, miscellaneous

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