Obstructive and Central Sleep Apnea Treatment

Policy Number: 2022T0525II
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➲ Instructions for Use

Related Commercial Policies
• Attended Polysomnography for Evaluation of Sleep Disorders
• Durable Medical Equipment, Orthotics, Medical Supplies and Repairs/Replacements
• Orthognathic (Jaw) Surgery
• Outpatient Surgical Procedures – Site of Service

Community Plan Policy
• Obstructive and Central Sleep Apnea Treatment

Medicare Advantage Coverage Summary
• Sleep Apnea Diagnosis and Treatment

Coverage Rationale

Nonsurgical Treatment

Removable Oral Appliances are proven and medically necessary for treating Obstructive Sleep Apnea (OSA) as documented by a sleep study (e.g., Polysomnography or Home Sleep Apnea Testing).
Refer to the Medical Policy titled Attended Polysomnography for Evaluation of Sleep Disorders for further information.

For many individuals, oral appliance therapy (OAT) may be an effective alternative to failed continuous positive airway pressure (CPAP) therapy. Documentation of the following is required:
- A patient presenting with symptoms of OSA be seen in a face-to-face evaluation with a qualified physician (MD or DO) trained in sleep medicine or with an Advanced Practice Provider working under the direct supervision of a sleep medicine physician prior to beginning treatment for OAT (AASM and AADSM, December 2012, AAO-HNS, November 2019)
- A treating physician (MD or DO) or an Advanced Practice Provider must diagnose OSA and recommend course of treatment (AAO-HNS, November 2019)
- If the patient refuses CPAP therapy, documentation of the refusal from the patient's treating physician (MD or DO) or an Advanced Practice Provider must be supplied

For information on snoring and Oral Appliances, refer to the Coverage Determination Guideline titled Durable Medical Equipment, Orthotics, Medical Supplies and Repairs/Replacements.

For medical necessity clinical coverage criteria for removable oral appliances, refer to the InterQual® CP: Durable Medical Equipment, Noninvasive Airway Assistive Devices.

Click here to view the InterQual® criteria.

The following are unproven and not medically necessary due to insufficient evidence of efficacy:
- Devices for treating Positional OSA

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- Nasal dilator devices for treating OSA
- Removable Oral Appliances for treating Central Sleep Apnea
- Prefabricated Oral Appliance/Device
- Non-surgical electrical muscular training
- Morning repositioning devices

Surgical Treatment

The following surgical procedures are proven and medically necessary for treating OSA as documented by polysomnography. For medical necessity clinical coverage criteria, refer to the InterQual® Client Defined, CP: Procedures:
- Mandibular Osteotomy (Custom) - UHG
- Maxillomandibular Osteotomy and Advancement (Custom) - UHG
- Uvulopalatopharyngoplasty (UPPP) (Custom) - UHG

Click here to view the InterQual® criteria.

Implantable hypoglossal nerve stimulation is proven and medically necessary in an adult patient with moderate to severe OSA when all of the following criteria are met:
- Body Mass Index of (BMI) less than or equal to 32kg/m2; and
- Apnea hypopnea Index (AHI) of ≥20 and ≤65 as determined with Polysomnography (Attended); and
- Total AHI < 25% for central + mixed apneas; and
- Absence of complete concentric collapse at the soft palate level; and
- Failure or intolerance of Positive Airway Pressure (PAP) treatments (such as continuous positive airway pressure [CPAP] or bi-level positive airway pressure [BPAP] machines)
  - PAP failure is defined as an inability to eliminate OSA (AHI of greater than 20 despite PAP usage) and PAP intolerance is defined as:
    - Inability to use PAP (greater than 5 nights per week of usage; usage defined as greater than 4 hours of use per night); or
    - Unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it)

Implantable neurostimulation devices for the treatment of Central Sleep Apnea (CSA) are unproven and not medically necessary due to insufficient evidence of safety and/or efficacy.

The following surgical procedures are unproven and not medically necessary for treating OSA due to insufficient evidence of efficacy:
- Laser-assisted uvulopalatoplasty (LAUP)
- Lingual suspension - Also referred to as tongue stabilization, tongue stitch or tongue fixation
- Palatal implants
- Radiofrequency ablation of the soft palate and/or tongue base
- Transoral robotic surgery (TORS)
- Distraction osteogenesis for maxillary expansion (DOME)

Documentation Requirements

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The documentation requirements outlined below are used to assess whether the member meets the clinical criteria for coverage but do not guarantee coverage of the service requested.

CPT/HCPCS Codes*	Required Clinical Information
Surgical Treatment for Obstructive Sleep Apnea (OSA)	
21199 21206 21685	Medical notes documenting the following, when applicable: • Member diagnosis • Specific procedure being requested

CPT/HCPCS Codes*	Required Clinical Information
Surgical Treatment for Obstructive Sleep Apnea (OSA)	

41599
42145
64553
64568
64570
L8679
L8680
L8686
	• History of the medical condition(s) requiring treatment or surgical intervention
	• Documentation of signs and symptoms; including onset, duration, and frequency
	• Reports of all recent imaging studies and applicable diagnostic tests, including results of sleep study confirming diagnosis of sleep apnea, including quantification of relevant indexes
	• Excessive daytime sleepiness documented by:
	  o Epworth Sleepiness Scale or other validated scale
	  o Interference with daily activity or work (e.g., causes safety issues)
	• Treatments tried, failed, or contraindicated; include the dates and reason for discontinuation, including:
	  o Failed response or intolerance to CPAP usage or other non-invasive treatment with involvement of qualified sleep specialist
	  o Failed response, intolerance, or inappropriate patient anatomy for Oral appliance therapy unsuccessful due to failure to improve symptoms, intolerance or inappropriate for patient anatomy
	  o Weight not a concern or weight loss was tried and failed
	• Other relevant medical history
	• Counseling about the benefits and risks of surgery by physician trained in sleep disorders
	
	In addition to the requirements above, medical notes documenting the following, when applicable, for:
	• Uvulopalatopharyngoplasty (UPPP)
	  o Isolated oropharyngeal narrowing demonstrated as source of airway obstruction as the cause of OSA or failure of previous uvulopalatopharyngoplasty to correct the OSA
	• Mandibular Osteotomy
	  o Functional obstruction mostly retrolingual or lower pharyngeal
	• Maxillomandibular Osteotomy and Advancement
	  o Craniofacial disproportion or deformities, with evidence of maxillomandibular deficiency
	• Implantable Hypoglossal Nerve Stimulation
	  o Body Mass Index (BMI)
	  o Presence or absence of complete concentric collapse at the soft palate level

Oral Appliance Therapy (OAT) for OSA	

E0486	Medical notes documenting the following, when applicable:
	• Documentation of most recent face-to-face encounter with prescribing physician, when applicable including face-to-face clinical evaluation by a qualified physician (MD or DO) trained in sleep medicine or with an Advanced Practice Provider working under the direct supervision of a sleep medicine physician
	• Current prescription (written order) from physician, including:
	  o Initial or replacement
	  o If replacement, current device used and reason for replacement
	• Diagnosis, including confirmation the treating physician diagnosed the member with OSA
	• Results of sleep study including severity of the OSA (AHI or RDI values, etc.)
	• Prior treatments tried, failed, or contraindicated, including documentation of the member's intolerance or refusal of CPAP, include the dates and reason for discontinuation
	• If the oral appliance is being prescribed for reasons other than OSA, an explanation of why appliance is needed

*For code descriptions, refer to the Applicable Codes section.

Definitions

Advanced Practice Providers (APPs): Non-physician, direct care providers such as Physician Assistants (PAs) and Advanced Practice Registered Nurses (APRNs) (Sarzynski and Barry, 2019).

Apnea: The cessation of airflow (≥ 90% decrease in airflow compared to baseline) lasting at least 10 seconds. Apneas are classified as obstructive, mixed, or central based on the pattern of respiratory effort. An obstructive Apnea is associated with continued or increased inspiratory effort throughout the entire period of absent airflow. A central Apnea is associated with absent inspiratory effort throughout the entire period of absent airflow. Mixed Apneas are associated with absent inspiratory effort in the initial portion of the event, followed by resumption of inspiratory effort in the second portion of the event (American Academy of Sleep Medicine (AASM) Scoring Manual, 2020).

Apnea Hypopnea Index (AHI): The number of Apneas plus the number of Hypopneas during the entire sleeping period, times 60, divided by total sleep time in minutes; unit: event per hour (AASM Scoring Manual, 2020).

Central Sleep Apnea (CSA): characterized by sleep disordered breathing associated with decreased or no respiratory effort accompanied by excessive daytime sleepiness, frequent nocturnal wakening, or both. CSA due to hypoventilation occurs when the stimulus to breathe is removed in patients with compromised neuromuscular ventilator control. Chronic ventilatory failure due to neuromuscular or chest wall disease can produce central apneas or hypopneas and may occur in patients with central nervous system disease (Centers for Medicare and Medicaid Services).

Home Sleep Apnea Testing (HSAT): The use of unattended diagnostic studies to assess for OSA without the determination of sleep stage. The term specifies the condition being assessed (i.e., sleep Apnea) by current technology without implying that "sleep" quality, staging or time are determined. Not all such studies are performed at home; however, that is where the vast majority of patients undergo these tests (AASM Style Guide, 2015). Adequate HSAT occurs over a minimum of four hours and includes a minimum of the following sensors: nasal pressure, chest and abdominal respiratory inductance plethysmography, and oximetry (Kapur et al., 2017). HSAT is also referred to as out-of-center sleep testing or portable monitoring.

Hypopnea: An abnormal respiratory event lasting at least 10 seconds associated with at least a 30% reduction in airflow and with at least a 3% decrease in oxygen saturation from pre-event baseline or the event is associated with an arousal (AASM Scoring Manual, 2020).

Obstructive Sleep Apnea (OSA): The AASM defines Obstructive Sleep Apnea as a sleep related breathing disorder that involves a decrease or complete halt in airflow despite an ongoing effort to breathe.

OSA severity is defined as:
- Mild for AHI or RDI ≥ 5 and < 15
- Moderate for AHI or RDI ≥ 15 and ≤ 30
- Severe for AHI or RDI > 30/hr.

Oral Appliance: A device inserted into the mouth for treatment of snoring or Obstructive Sleep Apnea (OSA) (Berry, 2012). These devices can be identified as prefabricated (ready-made), or custom made.

Physician or Practitioner: An individual who is qualified by education, training, licensure/regulation (when applicable) and facility privileging (when applicable) who performs a professional service within his/her scope of practice and independently reports that professional service (AMA CPT book, 2021).

Polysomnogram (Attended): A laboratory-based sleep study that uses multiple channels to record a wide range of physiological information, including brain activity, eye movements, body movements, breathing and heart rate (American Thoracic Society, 2015; updated 2019).

Positional Obstructive Sleep Apnea: The American Academy of Sleep Medicine (AASM) defines Positional Obstructive Sleep Apnea as a lower AHI in the non-supine position than in the supine position (deVries, 2015).

Respiratory Disturbance Index (RDI): The number of Apneas plus the number of Hypopneas plus the number of Respiratory Effort-Related Arousals during the entire sleeping period, times 60, divided by total sleep time in minutes; unit: events per hour (AASM Scoring Manual, 2020).

Respiratory Effort-Related Arousal (RERA): A sequence of breaths characterized by increasing respiratory effort, inspiratory flattening in the nasal pressure or PAP device flow channel or an increase in end-tidal PCO_2 (children) leading to an arousal

from sleep. Respiratory effort-related arousals do not meet criteria for Hypopnea and have a minimum duration of at least 10 seconds in adults or the duration of at least two breaths in children (AASM Scoring Manual, 2020).

Respiratory Event Index (REI): Total number of respiratory events scored during the entire sleeping period, times 60, divided by monitoring time in minutes; unit: events per hour. The REI is used for Home Sleep Apnea Testing (AASM Scoring Manual, 2020).

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

Coding Clarification: HCPCS code E0486 applies to the custom fabricated oral device/appliance used to reduce upper airway collapsibility, adjustable or nonadjustable and includes fitting and adjustment. Dental services (e.g., D9947, D9948 and D9949) are excluded from coverage under the medical plan; the member specific benefit plan document must be referenced prior to determining any coverage decision.

CPT Code	Description
0424T	Insertion or replacement of neurostimulator system for treatment of central sleep apnea; complete system (transvenous placement of right or left stimulation lead, sensing lead, implantable pulse generator)
0425T	Insertion or replacement of neurostimulator system for treatment of central sleep apnea; sensing lead only
0426T	Insertion or replacement of neurostimulator system for treatment of central sleep apnea; stimulation lead only
0427T	Insertion or replacement of neurostimulator system for treatment of central sleep apnea; pulse generator only
0428T	Removal of neurostimulator system for treatment of central sleep apnea; pulse generator only
0429T	Removal of neurostimulator system for treatment of central sleep apnea; sensing lead only
0430T	Removal of neurostimulator system for treatment of central sleep apnea; stimulation lead only
0431T	Removal and replacement of neurostimulator system for treatment of central sleep apnea, pulse generator only
0432T	Repositioning of neurostimulator system for treatment of central sleep apnea; stimulation lead only
0433T	Repositioning of neurostimulator system for treatment of central sleep apnea; sensing lead only
0434T	Interrogation device evaluation implanted neurostimulator pulse generator system for central sleep apnea
0435T	Programming device evaluation of implanted neurostimulator pulse generator system for central sleep apnea; single session
0436T	Programming device evaluation of implanted neurostimulator pulse generator system for central sleep apnea; during sleep study
21142	Application of a multiplane (pins or wires in more than 1 plane), unilateral, external fixation system (e.g., Ilizarov, Monticelli type)
21199	Osteotomy, mandible, segmental; with genioglossus advancement
21206	Osteotomy, maxilla, segmental (e.g., Wassmund or Schuchard)
21685	Hyoid myotomy and suspension
41512	Tongue base suspension, permanent suture technique

CPT Code	Description
41530	Submucosal ablation of the tongue base, radiofrequency, 1 or more sites, per session
41599	Unlisted procedure, tongue, floor of mouth
42145	Palatopharyngoplasty (e.g., uvulopalatopharyngoplasty, uvulopharyngoplasty)
42299	Unlisted procedure, palate, uvula
64553	Percutaneous implantation of neurostimulator electrode array; cranial nerve
64568	Open implantation of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator
64569	Revision or replacement of cranial nerve (e.g., vagus nerve) neurostimulator electrode array, including connection to existing pulse generator
64570	Removal of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator
64582	Open implantation of hypoglossal nerve neurostimulator array, pulse generator, and distal respiratory sensor electrode or electrode array
64583	Revision or replacement of hypoglossal nerve neurostimulator array and distal respiratory sensor electrode or electrode array, including connection to existing pulse generator
64584	Removal of hypoglossal nerve neurostimulator array, pulse generator, and distal respiratory sensor electrode or electrode array

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HCPCS Code	Description
E0485	Oral device/appliance used to reduce upper airway collapsibility, adjustable or nonadjustable, prefabricated, includes fitting and adjustment
E0486	Oral device/appliance used to reduce upper airway collapsibility, adjustable or nonadjustable, custom fabricated, includes fitting and adjustment
E1399	Durable medical equipment, miscellaneous
K1001	Electronic positional obstructive sleep apnea treatment, with sensor, includes all components and accessories, any type
K1027	Oral device/appliance used to reduce upper airway collapsibility, without fixed mechanical hinge, custom fabricated, includes fitting and adjustment
K1028	Power source and control electronics unit for oral device/appliance for neuromuscular electrical stimulation of the tongue muscle for the reduction of snoring and obstructive sleep apnea, controlled by phone application
K1029	Oral device/appliance for neuromuscular electrical stimulation of the tongue muscle, used in conjunction with the power source and control electronics unit, controlled by phone application, 90-day supply
L8679	Implantable neurostimulator, pulse generator, any type
L8680	Implantable neurostimulator electrode, each
L8686	Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension
S2080	Laser-assisted uvulopalatoplasty (LAUP)
S2900	Surgical techniques requiring use of robotic surgical system (list separately in addition to code for primary procedure)

Description of Services

Obstructive Sleep Apnea (OSA) is a breathing disorder that is defined by episodes of decrease or complete cessation of airflow during sleep. In OSA, airflow is obstructed when the muscles in the back of the throat fail to keep the airway open. Nocturnal respiration in individuals with OSA is characterized by episodes of Apnea (breathing cessation) and hypopnea (marked reduction in breathing volume). The signs and symptoms of untreated OSA include excessive daytime sleepiness, loud snoring,

nocturnal choking, apneas or choking witnessed by bed partner, unrefreshing sleep, morning headaches, reduced libido and enuresis. Physiological effects of untreated OSA include fluctuating blood oxygen levels, increased heart rate, chronic daytime hypertension and impaired glucose tolerance/insulin resistance.

Central Sleep Apnea (CSA) is distinguished by a temporary interruption of neural output from the respiratory control center, resulting in loss of respiratory stimulation and airflow cessation. The International Classification of Sleep Disorders (ICSD) identifies 6 different forms of CSA. However, the underlying pathophysiology of central sleep apnea is due to either post-hyperventilation central apnea, which may be triggered by a variety of clinical conditions or central apnea secondary to hypoventilation, which has been described with opioid use hypoventilation. This condition occurs frequently in patients with heart failure and increases the risk for morbidity and mortality. It's estimated that CSA may present in 30% to 50% of patients with heart failure. Currently available treatments for central sleep apnea are not widely accepted because of sparse effectiveness data, poor patient adherence, and potential safety risks. Implantable neurostimulation devices have however been studied for the treatment of CSA.

Diagnosis and evaluation of sleep apnea syndrome is determined through polysomnography (PSG) or limited channel testing. Treatment for OSA includes lifestyle modifications (weight loss, avoidance of alcohol or other agents that decrease upper airway patency), positional therapy, positive airway pressure, oral appliance therapy, electrostimulation devices, and surgery. Positive airway pressure therapy may use any one of the following techniques: continuous positive airway pressure (CPAP), automatic positive airway pressure (APAP), bilevel positive airway pressure (BiPAP), variable positive airway pressure (VPAP).

Non-surgical oral appliances, worn during sleep, can be an effective treatment option for snoring and OSA. These devices work by keeping the airway open in one of three ways: by pushing the lower jaw forward (a mandibular advancement device or MAD), by preventing the tongue from falling back over the airway (a tongue-retaining device) or by combining both mechanisms.

A known side effect with the use of a nighttime non-surgical oral appliance (i.e., sleep apnea appliance) for OSA is occlusal discrepancy. Morning repositioning devices, which are used after removal of the nighttime oral appliance, guide the maxillary and mandibular teeth back into their normal alignment. However, it must be noted that despite the widespread use of this technique, no evidence to date has demonstrated its effectiveness (AADSM 2017).

It is the position of the American Academy of Sleep Medicine (AASM) that dentists and physicians work collaboratively managing sleep-related breathing disorders with oral appliance therapy by conducting follow-up sleep testing to improve or confirm treatment efficacy along with periodic follow up visits (Ramar, 2015).

A nasal dilator operates by mechanically opening the nasal passages either externally or internally. External nasal dilators, also known as nasal strips, are positioned just below the bone of the nose which pull the nasal passages open. Internal nasal dilators come in a variety of shapes and sizes are positioned just inside the nose to prop the nostrils open.

Positional therapy for OSA may be an effective method to treat patients in the short-term for whom OSA is improved by sleeping on the side. Devices include but are not limited to vibrating devices, pillows, tennis balls, and chest vests that prevent the patient to sleep in the supine position.

There are a variety of surgical options used to treat OSA. The intention of surgery is to create a more open airway, so obstructions are less likely to occur.

Implantable hypoglossal nerve stimulation systems are ways to relieve upper airway obstruction. There are two hypoglossal nerve stimulation devices: The Inspire® Upper Airway Stimulation device (Inspire Medical) and the aura6000™ Sleep Therapy System (ImThera Medical). The Inspire device treats moderate to severe OSA and is designed for use in individuals who are unable or unwilling to use a CPAP device. Inspire's construction and implantation are comparable to those of a pacemaker: a surgeon implants the device containing a neurostimulator subcutaneously in the individual's chest with one lead attached to the individual's hypoglossal nerve (cranial nerve XII) at the base of the tongue and one lead implanted in the individual's chest. The lead in the chest consists of a pressure sensor that detects breathing. Information about respiration rate is relayed to the device, which stimulates the hypoglossal nerve in the tongue. When stimulated, the tongue moves forward, thus opening the airway. The individual can operate the device by remote control, which the individual activates before going to sleep. The

device turns on after 20 minutes to minimize disrupting the individual's sleep onset; the device turns off via remote when the individual wakes.

Clinical Evidence

Nonsurgical Treatment

Devices for Treating Positional OSA

There are a variety of devices used for treating positional OSA. The available literature addressing these devices is conflicting or inconclusive and thus future studies are warranted to demonstrate their safety and efficacy.

In a product brief on NightBalance Lunoa by Philips Respironics, Inc., ECRI (2020) concludes that the evidence for this technology is inconclusive due to the lack of evidence available for review.

In a Cochrane review of randomized controlled trials, Srijithesh et al. (2019) compared the efficacy of positional therapy versus CPAP and positional therapy versus inactive control (sham intervention or no positional therapy intervention) in people with OSA. Eight studies with 323 randomized participants met the inclusion criteria. The comparison between positional therapy and CPAP included 72 participants, while the comparison between positional therapy and inactive control included 251 participants. Three studies used supine vibration alarm devices, while five studies used physical positioning. The authors found that while positional therapy may have better adherence by participants, CPAP has a greater effect on improvement of AHI. The evidence was low to moderate and all studies were of short-term duration therefore future long-term studies are needed for long-term outcomes and efficacy.

In a pilot observational study, Hidalgo et al. (2019) evaluated efficacy of sleep position therapy in fourteen patients with positional OSA for four weeks. Criteria for participants to be included in study were >18 years, had a diagnosis of positional OSA by polysomnography (PSG), an AHI >10/h, total sleep time (TST) ≥180 minutes, supine time position >30% and no previous CPAP treatment. A complete overnight PSG was performed at baseline and at 1 and 4 weeks after starting the study. After the initial PSG, each participant was given a vibrating positional device that was placed on the patient's forehead via a sticker; this device was to be used for the next four weeks. The device starts vibrating with increasing intensity and has four different vibration intensities when the patient lies in the supine position for more than 30 seconds. The vibration stops when the patient changes from the supine to the non-supine position. The authors found the use of this vibrating device decreased the median AHI in patients up to 31.6%; in addition, improvement in oxygen saturation was observed. It was concluded this type of device could be useful for patients with positional OSA, but further studies are warranted. Limitations included small participation size, limited follow-up for long-term compliance and lack of a placebo group. Further RCTs are required to confirm the efficacy of this device placed on the patient's forehead.

A multicenter trial randomized ninety-nine patients with mild to moderate positional OSA (POSA) to either a sleep position trainer (SPT) group or one with oral appliance therapy (de Ruiter et al. (2018) included in the Hayes Report). SPT is a newer option for treating patients with positional OSA and the goal of the authors was to investigate the long-term efficacy, adherence and quality of life for this device. Eligible participants had a diagnosis of mild to moderate POSA (AHI of 5-30) and spent 10-90% of their sleep time in the supine position. The SPT group utilized the NightBalance device which was worn across the chest using a neoprene strap. The active comparator was a SomnoDent Flex device custom made by SomnoMed which included a blue chip for adherence. Analysis of the data indicated the AHI and oxygen desaturation index (ODI) were significantly reduced for both treatment groups at the 3- and 12-month follow up visits along with similar results for adherence of the device usage in both groups. The main limitation of this study was the higher dropout rate over the course of the study that did not allow analysis of the complete randomized sample.

Barnes et al. (2017) conducted a systematic review and meta-analysis on positional modification techniques in patients with supine OSA. Seven studies with 108 participants met the inclusion criteria in comparing any type of positional therapy (e.g., vibratory vests, foam backpacks, tennis balls) with any other intervention. In positional techniques compared to non-standard therapy, four studies included in the meta-analysis showed significant reduction in AHI favoring the positional techniques. In positional techniques compared to CPAP therapy, 2 studies showed significant reduction in AHI favoring CPAP. One study showed a significant reduction in AHI favoring the sleep position trainer when compared to a tennis ball vest. Additionally, the evidence suggested that there was no significant effect on sleepiness or sleep efficiency when position modification therapy (PMT) was compared to no treatment or the CPAP treatment. Although it was identified that participants have greater

compliance with positional techniques than CPAP in the short-term, the authors found long-term results remain unclear specifically for electronic vibratory devices. In addition, CPAP is more effective at reducing AHI. Future studies should include multiple positional devices using an adequate number of participants, comparison group and long-term follow-up.

Nasal Dilators

The available evidence for nasal dilators is conflicting but tends to support the ineffectiveness of these devices. In order to prove a benefit of nasal dilators, future research should demonstrate the clinical utility and long-term safety and efficacy of these devices.

Gelardi et al. (2019) studied 19 adult patients with a diagnosis of OSA and whether the use of internal nasal dilator was able to significantly reduce AHI and the oxygen desaturation index. Subjective parameters were evaluated by the patients, and included perception of nasal obstruction, sleep quality, and olfaction – these were all measured by a visual analogue scale (VAS). The VAS scores ranged from zero for completely blocked nose to 10, which indicated a completely patent nose, additional evaluation for smell, quality of sleep and satisfaction. Daytime sleepiness was evaluated with the Epworth Sleepiness Scale (ESS) – an ESS score of ≥10 was considered excessive daytime sleepiness. Cardiorespiratory nocturnal monitoring was performed on all participants. Oxyhemoglobin saturation, heart rate, body posture, oral-nasal air flow, snoring sounds, and thoracic and abdominal movements were recorded in detail. Each participant was given the Nas-air® device with appropriate instruction for the use. The results indicated the use of Nas-air® significantly reduced the AHI values (38.7±30 vs 31.1±27.4; p=0.000) and ODI scores (36.4±30.6 vs 29.0±26.4; p=0.001) In addition, the use of Nas-air® significantly increased the restoring sleep score (54.8±26.2 vs 73.3±21.7; p=0.000). The authors concluded the results showed that Nas-air® is a new internal nasal dilator potentially capable to significantly improve respiratory outcomes and sleep quality for patients with OSA. However, the study had some limitations including lack of comparison with established treatments, the open-label study design, the lack of follow-up, and the low number of enrolled participants. Thus, further studies should be conducted to demonstrate the clinical utility of this device.

In a systematic review and meta-analysis, Camacho et al. (2016) evaluated internal (NoZovent) and external (Breathe Right Strips) nasal dilators as treatment for obstructive sleep apnea (OSA). Five studies were found for internal dilators and nine studies for external dilators. Twelve of the fourteen studies showed no significant change in the apnea-hypopnea index (AHI) with the use of the nasal dilators. Furthermore, the meta-analysis of the combined studies did not show any benefit of the device. The essential limitation of this study is the lower quality of published studies evaluating nasal dilators. Most studies were individual case-control or prospective case series studies with often smaller sample sizes lacking randomization and other significant drawbacks. Although nasal dilators have demonstrated improved nasal breathing, they have not shown improvement in OSA outcomes, except with mild improvement in apnea when internal nasal dilators were used.

In a randomized, partially blinded, placebo-controlled trial Rossi et al. (2013) evaluated the efficacy of the Provent nasal device for preventing the recurrence of obstructive sleep apnea (OSA) following continuous positive airway pressure (CPAP) withdrawal in patients with moderate-to-severe OSA. The goal of the study was to determine if OSA patients could occasionally substitute the Provent device for their CPAP. Sixty-seven patients with OSA receiving CPAP were randomized to one of three groups for 2 weeks: continuing CPAP (n=23), active Provent (n=22) or placebo Provent (n=22). The three groups were similar at baseline and their mean apnea-hypopnea index (AHI) before CPAP treatment was 38 events per hour. Primary outcomes included for the active Provent versus the placebo Provent were OSA severity (oxygen desaturation index (ODI)), AHI and Epworth Sleepiness Scale (ESS) score. Secondary outcomes for the active Provent versus the placebo Provent included ODI from ambulatory pulse oximetry and blood pressure (BP). For CPAP versus the active Provent or CPAP versus the placebo Provent, secondary outcomes included ODI/AHI, ESS and BP. OSA recurred in the active Provent and placebo Provent groups, and there was no significant difference in ODI, AHI and ESS between active Provent and placebo Provent at 2 weeks. ODI from ambulatory pulse-oximetry and BP at 2 weeks were not different in the active Provent versus the placebo Provent groups. ODI, AHI and BP, but not ESS, were significantly higher in the active Provent and placebo Provent groups compared with CPAP. The authors concluded that Provent cannot be recommended as an alternative short-term therapy for patients with moderate to severe OSA already on CPAP. The study provides evidence for inferiority of the Provent nasal device compared to CPAP and for the ineffectiveness of nasal dilator when compared to a placebo device.

Berry et al. (2011) conducted a multicenter randomized controlled trial investigating the efficacy of the Provent nasal device, a nasal expiratory positive airway pressure (EPAP) device for treating OSA. Two hundred and fifty patients with mild to severe OSA were randomized to treatment with EPAP (n=127) or a similar sham device (n=123) for 3 months. A total of 229 completed

week 1 sleep studies (119 EPAP, 110 sham). This group was the intention to treat (ITT) group. Of these, 173 had an AHI > 5/hour on the device-off night and comprised the modified intention to treat (mITT) group (92 EPAP, 81 sham). One hundred ninety-five patients in the ITT group (100 EPAP, 95 sham) and 144 patients in the mITT group (77 EPAP, 67 sham) completed the 3-month study. All patients underwent a baseline clinic evaluation that included the Epworth Sleepiness Scale (ESS). Polysomnography (PSG) was performed on 2 non-consecutive nights (random order: device-on, device-off) at week 1 and after 3 months of treatment. At week 1, the EPAP device significantly decreased the AHI compared to device-off nights and the difference was significantly greater than with the sham device (52.7% versus 7.3%, ITT analysis). At 3 months, 51% of the EPAP device users had a 50% or greater reduction in the AHI on device-on compared to device-off nights. The authors concluded that nasal EPAP significantly reduced the AHI and improved subjective daytime sleepiness compared to the sham treatment in patients with mild to severe OSA with excellent adherence. This study is limited by short follow-up, loss to follow up, lack of comparison with established treatment approaches, patient-reported adherence, a large number of exclusion criteria and a modified intention to treat group. A potential for bias exists due to manufacturer sponsorship of the study.

Kryger et al. (2011) conducted a 13-center extension study of the 3-month Berry trial. This study was designed to evaluate the long-term effectiveness of the Provent nasal device among participants who had responded in the initial study. Forty-one patients from the EPAP arm who met adherence and efficacy criteria were continued on therapy and returned for polysomnography (PSG) after 12 months of treatment. From the analyzable subject cohort (n=34), results from the 12-month PSGs were compared against their baseline results. Median AHI was reduced from 15.7 to 4.7 events/h (week 1 device-off versus month 12 device-on). The decrease in the AHI (median) was 71.3%. The Epworth Sleepiness Scale decreased from 11.1 ± 4.2 to 6.0 ± 3.2. The median percentage of reported nights used (entire night) was 89.3%. The authors reported that long-term adherence to EPAP was excellent in those who had a positive clinical response at month 3 of the Berry trial. As with the original trial, this study is limited by patient-reported adherence and a large number of exclusion criteria. Additionally, analyses limited to responders is inherently biased to assess objectively the impact of an intervention. Furthermore, a potential for bias exists due to manufacturer sponsorship of the study.

Walsh et al. (2011) evaluated tolerability, short-term efficacy and adherence of the Provent nasal device, an EPAP nasal device, in 59 patients with OSA who refused CPAP or used CPAP less than 3 hours per night. After demonstrating tolerability to the EPAP device during approximately 1 week of home use, 47 patients (80%) underwent a baseline polysomnogram (PSG1). Forty-three patients met AHI entry criteria and underwent PSG2 within 10 days of PSG1. Twenty-four patients (56%) met prespecified efficacy criteria and underwent PSG3 after 5 weeks of EPAP treatment. Compared to PSG1, mean AHI was significantly lower at both PSG2 and PSG3. For most patients AHI at PSG3 was similar to AHI at PSG2. Device use was reported an average of 92% of all sleep hours. The authors concluded that improvements in AHI and Epworth Sleepiness Scale (ESS) scores, combined with the high degree of treatment adherence observed, suggest that the EPAP device tested may become a useful therapeutic option for OSA. Limitations of the study include lack of randomization and control, small sample size and short-term follow-up. A potential for bias exists due to manufacturer sponsorship of the study.

In a multicenter, prospective study, Rosenthal et al. (2009) evaluated the efficacy of the Provent nasal device, for the treatment of OSA and evaluated adherence to the device over a 30-day in-home trial period. Participants (n=34) with a baseline apnea-hypopnea index (AHI) ≥ 5 were evaluated. Treatment was well tolerated and accepted by the participants. The authors documented an overall reduction in AHI; however, therapeutic response was variable (and at times inconsistent) among the participants. Further research is required to identify the ideal candidates for this new therapeutic option in the management of OSA. Lack of comparison group limits the validity of the study. A potential for bias exists due to manufacturer sponsorship of the study.

Colrain et al. (2008) conducted a pilot study to test the hypothesis that the application of expiratory resistance via a nasal valve device would improve breathing during sleep in subjects with OSA and in primary snorers. Thirty men and women were recruited for the study. Twenty-four had at least mild OSA (AHI >5), and 6 were primary snorers. Subjects underwent 2 nights of polysomnographic evaluation, one with and one without a new nasal resistance device with the order of nights counterbalanced across participants. The device consisted of a small valve inserted into each nostril calibrated to provide negligible inspiratory resistance but increased expiratory resistance. Standard polysomnography was conducted to compare participants' sleep both with and without the device, with the scoring conducted blind to treatment condition. The apnea-hypopnea (AHI) and oxygen desaturation (O2DI) indices both significantly decreased, and the percentage of the night spent above 90% saturation significantly increased with device use. The results of this pilot study are suggestive of a therapeutic effect of expiratory nasal resistance for some OSA patients and indicate that this technique is worthy of further clinical study. The findings are limited by

lack of comparison group and lack of comparison to standard treatment for OSA. A potential for bias exists due to manufacturer sponsorship of the study.

Removable Oral Appliances for Treating CSA

CSA is the result of an impaired neurological function, and removable oral appliance devices are designed to manage physical obstructions. No relevant evidence has been identified to support the use of oral appliances for CSA.

Prefabricated Oral Appliances/Device

The evidence for prefabricated oral appliance or device is limited; there is little evidence to demonstrate the safety or efficacy of these devices in their use for OSA.

In an RCT, Johal and associates (2017) compare the effectiveness of ready-made versus custom made mandibular repositioning devices (MRD) in the management of mild to moderate obstructive sleep apnea (OSA). Thirty-five participants were randomized into receiving either the ready-made or custom made MRD. The primary outcome was measurement of AHI which was measured by an overnight home sleep study. The authors demonstrated custom made devices for MRD had a significant impact in the treatment of OSA in contrast to the ready-made devices. The participants overwhelmingly found the ready-made appliance difficult to tolerate due to the limitation in the device design and inability to address individual needs. Limitations included small number of participants and a withdrawal of almost 30% of the patients after the 3-month treatment interval.

Non-Surgical Electrical Muscular Training

The evidence for nonsurgical electrical muscular stimulation is limited; there is little quality evidence to demonstrate the safety or efficacy in the use for OSA. Future studies are warranted which should include comparison groups and test for safety, efficacy, and long-term outcomes.

The eXciteOSA Device is a noninvasive, intraoral electrical muscle stimulation device for the treatment of mild obstructive sleep apnea and snoring. The device works by delivering electrical muscle stimulation through a mouthpiece that sits around the tongue. The system consists of a mouthpiece, a rechargeable control unit, and a mobile app that allows the patient to control and track therapy. The suggested use for the device is 20 minutes each day during a wakeful state for 6 weeks and then once per week thereafter (Hayes, 2021).

Kotecha et al. (2021) assessed objective snoring and respiratory parameters on a case series of 70 patients with the novel eXciteOSA device. Inclusion criteria consisted of adults 18 years and older suffering from habitual snoring for greater than 6 months along with a live-in partner. Each participant received the eXciteOSA® with an explanation of how to use the device. The daily therapy of 20 minutes over 6 weeks consisted of a series of pulse bursts with intensity controlled to a tolerable level by patient. The primary outcome measure was to have a reduction in snoring. Epworth Sleepiness Score (ESS) was completed on all patients before and after the use of the device along with respiratory parameters (AHI, ODI and oxygen saturations). VAS was also obtained from the patient's partner. The mean AHI value was 5.94/h which dropped to 5.37/h following completion of eXciteOSA® device therapy. In addition, the ODI reduced from 4.92 to 4.73 post treatment. The authors concluded the device appears to be safe for patients with snoring and mild sleep apnea and could be a preferred option for patients. However, the study lacked a control group, lacked standard snoring parameters, addressed a small sample size, and lacked long-term outcomes.

Baptista et al. (2021) evaluated daytime neuromuscular electrical training (NMES) of tongue muscles in patients suffering from mild sleep apnea and snoring. 115 participants over the age of 18 years, AHI <15 and had a live-in partner were included in the study; 73 were male and 42 were female with an average mean age of 46 years. For two weeks prior to the study, the live-in partner was to rate their partner's snoring using the VAS; in addition, both the partner and participant completed sleep quality questionnaires, including the Pittsburgh Sleep Quality Index (PSQI) and ESS at the end of the two-week period. At the start of the study each participant was given the eXciteOSA device and instructed on its use. Participants were asked to use the device 20 minutes once/day for a total of 6 weeks; they were to record daily assessments of any side effects and adverse events. Patient compliance with the therapy was validated remotely via the smartphone application. The mean AHI reduced from 6.85 to 5.03, and the ODI from 5.68 to 4.33. 90% of patients demonstrated some reduction in their objective snoring time and the VAS scores for bed partners showed a significant reduction in their perception of their partner's snoring. No severe adverse events were noted, and the main side effect reported for 15% of the patients was oral pooling of their saliva. The authors

concluded the eXciteOSA device was well tolerated with a significant reduction in AHI. Limitations were acknowledged by the authors which included the need for randomization and comparison, restriction in duration and follow-up of the study, and lack of long-term outcomes.

Several clinical trials which address the eXciteOSA device along with its safety and efficacy are ongoing; please see: https://www.clinicaltrials.gov/ct2/home.

Morning repositioning devices

No published studies addressing the use of morning repositioning devices were identified; therefore, their effect on health outcomes is unproven.

Clinical Practice Guidelines

American Academy of Sleep Medicine (AASM)

The AASM Clinical Practice Guideline recommends continuous positive airway pressure (CPAP) or automatic positive airway pressure (APAP) for ongoing treatment of Obstructive Sleep Apnea (OSA) in adults (Patil, 2019).

AASM makes the following recommendations regarding oral appliance therapy (Ramar et al., 2015):
- When oral appliance therapy is prescribed by a sleep physician for an adult patient with OSA, the guidelines suggest that a qualified dentist use a custom, titratable appliance over non-custom oral devices. Strength of recommendation: Guideline. Quality of evidence: Low. Benefits clearly outweigh harms.
- Sleep physicians should consider prescription of oral appliances, rather than no treatment, for adult patients with OSA who are intolerant of CPAP therapy or prefer alternate therapy. Strength of recommendation: Standard. Quality of evidence: Moderate. Benefits clearly outweigh harms.
- Qualified dentists should provide oversight, rather than no follow-up, of oral appliance therapy in adult patients with OSA to survey for dental-related side effects or occlusal changes and reduce their incidence. Strength of recommendation: Guideline. Quality of evidence: Low. Benefits clearly outweigh harms.
- Sleep physicians should conduct follow-up sleep testing to improve or confirm treatment efficacy, rather than conduct follow-up without sleep testing, for patients fitted with oral appliances. Strength of recommendation: Guideline. Quality of evidence: Low. Benefits clearly outweigh harms.
- Sleep physicians and qualified dentists should instruct adult patients treated with oral appliances for OSA to return for periodic office visits, as opposed to no follow-up, with a qualified dentist and a sleep physician. Strength of recommendation: Guideline. Quality of evidence: Low. Benefits clearly outweigh harms.

AASM practice parameters on the treatment of central sleep apnea do not list oral appliances as a treatment option (Aurora et al., 2012).

American Academy of Dental Sleep Medicine (AADSM)

In a 2014 consensus paper, the AADSM describes the purpose, function and physical features of an effective oral appliance. It identifies an effective oral appliance as a custom-fabricated, FDA approved device which is designed to maintain airway patency during sleep for the management of OSA (AADSM, 2018.) It further states a sleep-related breathing disorder such as OSA should be diagnosed by a physician and then referred to a dentist for oral appliance therapy.

The AADSM and American Academy of Sleep Medicine recently updated their clinical practice guideline for the treatment of obstructive sleep apnea (OSA) and snoring with oral appliance therapy (OAT). The guideline included the following recommendation: "We suggest that qualified dentists provide oversight—rather than no follow-up—of oral appliance therapy in adult patients with obstructive sleep apnea, to survey for dental-related side effects or occlusal changes and reduce their incidence." In addition, many of the side effects were thought to be best addressed prophylactically with use of a morning occlusal guide to help prevent occlusal alterations or to minimize transient muscle contraction. However, it must be noted that despite the widespread use of this technique, no evidence to date has demonstrated its effectiveness (AADSM 2017).

American Association of Oral and Maxillofacial Surgeons (AAOMS)

In a position paper on evaluation and management of OSA, the AAOMS reveals oral appliances have been shown to be effective in patients with mild to moderate OSA. Custom-made oral appliances may be indicated for use in patients with severe

OSA who have failed CPAP treatment. These custom-made appliances should be fitted by qualified dental personnel (AAOSM, 2013). The paper does not address prefabricated oral devices.

American College of Physicians (ACP)

The American College of Physicians (ACP) developed a clinical practice guideline on the management of obstructive sleep apnea (OSA) in adults (Qaseem, et al., 2013). The guideline makes the following recommendations:

- All overweight and obese patients diagnosed with OSA should be encouraged to lose weight. (Grade: strong recommendation; low-quality evidence)
- Continuous positive airway pressure treatment is recommended as the initial therapy for patients diagnosed with OSA. (Grade: strong recommendation; moderate-quality evidence)

European Respiratory Society (ERS)

An ERS report on non-CPAP therapies for OSA concluded that nasal dilators cannot be recommended as effective treatments for OSA (Randerath et al., 2011).

A European Respiratory Society Task Force reviewed the evidence for mandibular advancement device (MAD) therapy and found in patients with mild to moderate OSA, mandibular advancement devices reduce daytime sleepiness and improve the quality of life when compared with that of placebo devices (Marklund et al., 2012).

Surgical Treatment

In a case series, Sundman et al. (2021) investigated the long-term effectiveness of a modified uvulopalatopharyngoplasty (UPPP) for patients with OSA. Eight years after receiving a UPPP for OSA, sixty-five patients were offered a re-evaluation of their condition with a polysomnography and the Epworth Sleepiness Scale (ESS); results were compared to their 2-year follow-up results. The authors found the modified UPPP was effective as a long-term solution for OSA patients although the AHI did decrease over time. Limitations included small sample size, the lack of comparison groups, and lack of female participants making generalization difficult.

A systematic review and meta-analysis performed by Zhou et al. (2021) evaluated the efficacy of eight different variations of maxillomandibular advancement (MMA) surgical treatment for patients with OSA. Eight articles including 227 patients were included. All studies included AHI results, but only five studies reported SpO2, and six studies reported post-op ESS scores. The authors found MMA combined with Han-uvulopalatopharyngoplasty (HUPPP) had the highest efficacy rate than any of the other MMA combinations. Limitations included the small number of articles, in addition to the small number of patients within each of the studies (due to the newer MMA methods that have been developed in recent years), and a lack of indicators used in each of the studies for OSA analysis (three factors is not considered adequate to sufficiently evaluate OSA), thus not providing a satisfactory analysis.

Gao et al. (2019) conducted a systematic review and network meta-analysis on 89 randomized controlled trails which compared and ranked the effectiveness of minimally invasive treatments for adult OSA. Since only simple surgeries performed under local anesthesia (palatal implants, laser-assisted uvulopalatoplasty, uvulopalatopharyngoplasty, septoplasty, and radiofrequency tissue ablation) were the focus, major surgeries such as maxillomandibular advancement and bariatric surgery were excluded. The findings of the authors support the guidelines that the first line treatment options for adult OSA to include PAP and MAD. Behavioral treatment which included exercise, physical therapy (PT), and Lifestyle Modification (LM) – via dietary control and weight loss, Myofunctional Therapy (MT) and Cervico-mandibular Support Collar (CMSC) were also included in the analysis. Results demonstrated that although exercise and CMSC yield insignificant effectiveness in AHI reduction when compared to no treatment, they rank first and second, respectively, in reducing ESS. In contrast, PT demonstrates significant effectiveness in AHI reduction but insignificant improvement in ESS. Among all interventions, PT ranks third in reducing both AHI and ESS. Results indicated that LM alone cannot be considered as an effective alternative to OSA treatment therefore LM lacks efficacy and ranks last in the management of adult OSA. The authors concluded that simple surgical procedures may not be curative for adult OSA; even though they improve scores for AHI or ESS, the findings are considered insignificant when compared with no treatment. According to the authors, at present, maxillomandibular advancement performed under general anesthesia has been recognized as an effective treatment for OSA because it improves polysomnographic parameters comparable to CPAP. The study is limited by the indirect nature of comparisons in network meta-analyses.

John et al. (2018) conducted a systematic review with meta-analysis on the effectiveness of maxillomandibular advancement (MMA) as a successful treatment modality in improving airway patency in patients with OSA. 462 patients from twenty studies were included for analysis. The authors found substantial improvements were seen following surgical intervention in outcome measures for AHI, RDI, ESS and LSAT and concluded MMA is a successful treatment option for OSA. Limitations included selection bias for article identification, only one article was an RCT, lack of parallel comparison group undergoing a different treatment, and few studies reported MMA as an isolated primary procedure.

Zaghi et al. (2016) conducted a meta-analysis on the value/success/effectiveness of MMA for OSA. Forty-five articles were included for review which included 518 patients. Study inclusion criteria included adults 18 years of age and older who underwent an MMA along with preop and postop outcomes for AHI and/or RDI. The authors extracted Individual patient data from each article including but not limited to BMI, AHI, RDI and Epworth Sleepiness Scale score. The main outcome measure was the change in the AHI or RDI score. The authors found 90% of patients experienced improvements in their AHI and RDI scores following surgical intervention. The authors concluded MMA is a highly effective treatment for OSA that was proved by substantial improvements in both AHI and RDI. Limitations included studies that included only reported patient data thus introducing selection bias and absence of long-term follow up (i.e., 10-15 years post-surgical treatment) and, in general, lack of comparison group of participants undergoing a different treatment approach.

Yaremchuk et al. (2011) evaluated 40 patients who had a UPPP or some form of UPPP surgical intervention. The Epworth Sleepiness Scale (ESS) results were used to identify excessive sleepiness in OSA patients. The authors found after surgical intervention, patients had a reduction in their ESS scores; and only three patients did not have improvement. The authors concluded most patients had a substantially higher ESS score following UPPP than previous CPAP usage. The study is limited by lack of comparison group.

Caples et al. (2010) conducted a systematic review and meta-analysis of literature reporting outcomes following various upper airway surgeries for the treatment of OSA in adults, including maxillomandibular advancement (MMA), pharyngeal surgeries such as uvulopalatopharyngoplasty (UPPP), laser assisted uvulopalatoplasty (LAUP) and radiofrequency ablation (RFA), as well as multi-level and multi-phased procedures. The authors found that the published literature is comprised primarily of case series, with few controlled trials and varying approaches to pre-operative evaluation and postoperative follow-up. Surgical morbidity and adverse events were reported but not systematically analyzed. The change in the apnea-hypopnea index (AHI) was the primary measure of efficacy. Substantial and consistent reductions in the AHI were observed following MMA; adverse events were uncommonly reported. Outcomes following pharyngeal surgeries were less consistent; adverse events were reported more commonly. Papers describing positive outcomes associated with newer pharyngeal techniques and multi-level procedures performed in small samples of patients appear promising. The authors concluded that further research is needed to better clarify patient selection, as well as efficacy and safety of upper airway surgery in those with OSA. The findings are limited to the lack of comparison group in several of the included studies.

In a case series, Lundkvist et al. (2009) evaluated 139 men and 19 women with a median age of 45 years and a median BMI of 29 kg/m^2 who underwent a UPPP. Preoperative results presented an oxygen desaturation index (ODI) of 23 and ESS was 12. All patients had a follow up visit 2 months following surgery and a questionnaire at 1 year. Out of the 158 patients, 120 had a second sleep apnea recording at one year following surgery; the results showed a significant decrease in the ODI from a median of 23 to 8. The BMI remained unchanged for 117 patients. Upon analysis of the data, the authors found that a UPPP surgical intervention was safe and effective for patients who had failed or refused non-surgical treatment. A limitation of the study included lack of comparison group.

Khan et al. (2009) conducted a retrospective case series of 63 patients that underwent a UPPP for the treatment of OSA. A polysomnography was performed before and after the surgical procedure along with analysis of BMI data. The UPPP surgery caused a 54.4% reduction in the mean AHI postoperatively along with a 38.4% decrease in the mean arousal index. The authors concluded UPPP was successful for OSA and a potential cure for those patients with a milder case of OSA and normal BMI. Limitations included lack of comparison group, small number of participants and lack of long-term follow up results.

In a Cochrane review, Sundaram and Lasserson (2005; reviewed 2008) evaluated surgical treatment for obstructive sleep apnea. Ten studies (602 participants) of mixed quality met the inclusion criteria. Data from eight studies were eligible for assessment in the review. No data could be pooled. The authors concluded that there are now a small number of trials assessing different surgical techniques with inactive and active control treatments. The studies assembled in the review do not provide evidence to support the use of surgery in sleep apnea/hypopnea syndrome, as overall significant benefit has not been

demonstrated. The participants recruited to the studies had mixed levels of AHI but tended to suffer from moderate daytime sleepiness where this was measured. Short-term outcomes are unlikely to consistently identify suitable candidates for surgery. Long-term follow-up of patients who undergo surgical correction of upper airway obstruction is required. This would help to determine whether surgery is a curative intervention, or whether there is a tendency for the signs and symptoms of sleep apnea to re-assert themselves, prompting patients to seek further treatment for sleep apnea.

Hypoglossal Nerve Stimulation

In a product brief by ECRI (2020), evidence from four retrospective observational studies suggest that the Inspire® Upper Airway Stimulation (UAS) system works better than surgery for improving sleep and reducing OSA symptoms. The authors note that the evidence is somewhat favorable and also the following limitation in the body of evidence: short follow-up, risk of bias, and patient attrition. Future controlled studies that provide long-term data are needed to validate Inspire benefits and compare it against CPAP therapy.

A Hayes report concluded that the overall quality of the evidence evaluating hypoglossal nerve stimulation (HNS) for treating OSA is very low. However, evidence does suggest that the intervention is relatively safe and may reduce the severity of OSA and improve PROMs (excessive daytime sleepiness, function, quality of life) for patients with OSA that have failed or are intolerant to CPAP therapy. 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. Additional good-quality comparative studies with larger sample sizes are needed to define the patient population that is most likely to respond to this therapy option (Hayes, 2016. Updated 2020).

Costantino et al. (2020) conducted a meta-analysis of nine case series which evaluated HNS for treatment of moderate to severe OSA comparing before and after treatment. Inspire was implanted in 68% of the patients with success rate of 75% at five years. In contrast, 18% of the patients were treated with the Aura 6000 system with a success rate of 35%. All primary clinical outcomes such as AHI, ODI and ESS showed improvement at the 12- and 60-month assessment. Several minor adverse effects were experienced by several patients, but all were non-serious and found resolution. While the authors found HNS was an effective and safe surgical procedure for patients with OSA, a subgroup analysis demonstrated there is not enough data to compare clinical outcomes to different stimulation systems. The STAR trial (see Strollo and Woodson below) was the only study to include long-term data, a limitation of this analysis along with lack of comparison groups or RCTs.

A National Institute for Health and Care Excellence (NICE) guideline states the current evidence on the safety and efficacy of hypoglossal nerve stimulation for moderate to severe OSA is limited in quantity and quality therefore the use of this procedure should only be used with special arrangements for clinical management, consent and research (NICE, 2017).

Kompelli et al. (2018) performed a meta-analysis of available hypoglossal nerve stimulator (HNS) studies to analyze objective and subjective outcomes and side effects of treated obstructive sleep apnea (OSA). A comprehensive literature search of PubMed and Scopus was performed, and 16 case series were found that included the analysis of 381 patients. At 6 months, the mean Sleep Apnea Quality of Life Index (SAQLI) improved by 3.1 (95%CI, 2.6-3.7). At 12 months, the mean Apnea Hypopnea Index (AHI) was reduced by 21.1 (95%CI, 16.9-25.3), the mean oxygen Desaturation Index (ODI) was reduced by 15.0 (95%CI, 12.7-17.4), the mean Epworth Sleepiness Scale (ESS) was reduced by 5.0 (95%CI, 4.2-5.8), the mean Functional Outcomes of Sleep Questionnaire (FOSQ) improved by 3.1 (95%CI, 2.6-3.4). Unexpected events of the study included pain, tongue abrasion, and internal/external device malfunctions. The authors concluded that HNS is a safe and effective treatment for CPAP refractory OSA, however further studies comparing HNS to other therapies are required.

The Stimulation Therapy for Apnea Reduction (STAR) trial (Strollo et al. 2014, included in the Hayes and ECRI reports and Costantino (2020) above) evaluated the clinical safety and effectiveness of upper airway stimulation at 12 months for the treatment of moderate to severe obstructive sleep apnea. Using a multicenter, prospective case series design, an upper airway stimulation device was surgically implanted in patients with obstructive sleep apnea who had difficulty either accepting or adhering to CPAP therapy. The primary outcome measures were the apnea-hypopnea index (AHI; the number of apnea or hypopnea events per hour, with a score of ≥15 indicating moderate-to-severe apnea) and the 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 outcome measures were the Epworth Sleepiness Scale, the Functional Outcomes of Sleep Questionnaire (FOSQ), and the percentage of sleep time with the oxygen saturation less than 90%. The study included 126 participants; 83% were men. The mean age was 54.5 years, and the mean body-mass index (the weight in kilograms divided by the square of the height in meters) was 28.4. The median AHI score at 12 months decreased 68%, from 29.3 events per hour to 9.0 events per hour; the

ODI score decreased 70%, from 25.4 events per hour to 7.4 events per hour. Secondary outcome measures showed a reduction in the effects of sleep apnea and improved quality of life. In the randomized phase, the mean AHI score did not differ significantly from the 12-month score in the nonrandomized phase among the 23 participants in the therapy-maintenance group (8.9 and 7.2 events per hour, respectively); the AHI score was significantly higher (indicating more severe apnea) among the 23 participants in the therapy-withdrawal group (25.8 vs. 7.6 events per hour). The ODI results followed a similar pattern. The rate of procedure-related serious adverse events was less than 2%. The authors concluded that upper airway stimulation led to significant improvements in objective and subjective measurements of the severity of obstructive sleep apnea. The lack of a control group limits the validity of the results of this study. This study was funded by Inspire Medical Systems.

Follow-up studies of the same patient population at 18 and 36 months, indicate that the treatment effects are maintained over time. Limitations are the same as the original study (Strollo et al., 2015; Woodson et al., 2016).

In a subgroup analysis of the STAR trial, Woodson et al. (2014, included in the Hayes and ECRI reports and Costantino (2020) above) assessed the efficacy and durability of upper airway stimulation via the hypoglossal nerve on obstructive sleep apnea (OSA) severity including objective and subjective clinical outcome measures. The study included a consecutive cohort of 46 responders at 12 months from a prospective phase III trial of 126 implanted participants. Participants were randomized to either therapy maintenance ("ON") group or therapy withdrawal ("OFF") group for a minimum of 1 week. Short-term withdrawal effect as well as durability at 18 months of primary (apnea hypopnea index and oxygen desaturation index) and secondary outcomes (arousal index, oxygen desaturation metrics, Epworth Sleepiness Scale, Functional Outcomes of Sleep Questionnaire, snoring, and blood pressure) were assessed. Both the therapy withdrawal group and the maintenance group demonstrated significant improvements in outcomes at 12 months compared to study baseline. In the randomized assessment, therapy withdrawal group returned to baseline, and therapy maintenance group demonstrated no change. At 18 months with therapy on in both groups, all objective respiratory and subjective outcome measures showed sustained improvement similar to those observed at 12 months. The authors concluded that withdrawal of therapeutic upper airway stimulation results in worsening of both objective and subjective measures of sleep and breathing, which when resumed results in sustained effect at 18 months. The authors state that reduction of obstructive sleep apnea severity and improvement of quality of life were attributed directly to the effects of the electrical stimulation of the hypoglossal nerve. The author-reported limitations of this study include the selection bias of only including responders to upper airway stimulation device therapy and the lack of subject or investigator blinding. This study was funded by Inspire Medical Systems.

Implantable Neurostimulation Devices for the Treatment of Central Sleep Apnea (CSA)

The remedé system (Respicardia Inc, Minnetonka, MN) is an implantable device intended to monitor and stabilize nighttime breathing patterns in adults with moderate to severe CSA (Hayes 2020) continuously and automatically. The current evidence for implantable neurostimulation devices for the treatment of central sleep apnea is insufficient thus requiring additional research for its safety and efficacy.

Potratz et al. (2021) conducted a prospective case series of 24 patients with heart failure (HF) and CSA diagnosed by polysomnography. They evaluated polysomnography (to determine hypoxemic burden), echocardiography and a standardized 6-min walk test prior to device implantation (baseline) and after 6 months of follow-up. The results showed the 6-min walk distance was 369.5 ± 163.5 m at baseline and significantly improved during follow-up (to 410 ± 169.7 m). Hypoxemic burden, determined based on time with oxygen saturation < 90% improved from 81 ± 55.8 min at baseline to 27.9 ± 42.8 min during PNS therapy. The authors concluded that in addition to safely and effectively treating CSA, PNS is also associated with improved physical performance capacity and reduced hypoxemic burden in patients with HF. The study is however limited by lack of comparison group. Although the findings are promising, the clinical benefits of PNS therapy in this patient population needs to be determined in a large, randomized controlled study with robust and objective clinical endpoints, including mortality.

In a Post Approval Study (PAS) to the remedē System Pivotal Trial (Costanzo et al., 2016), Costanzo et al. (2021) collected clinical evidence addressing long-term safety and efficacy through five years following the placement of the remedē implant which supplied transvenous phrenic nerve stimulation (TPNS). Fifty-two out of the original 151 participants took part to the five-year visit. Clinical data was collected for AHI, central-apnea index (CAI), arousal index, oxygen desaturation index, and sleep architecture. The median ESS for participants at baseline was 9 and dropped to 6 by the five-year visit demonstrating a clinically meaningful reduction; AHI and CAI showed similar results for improvement. Severe adverse effects (SAEs) were minimal and included one lead dislocation, two stimulation lead component failures and one implant infection. The authors results suggest TPNS delivered with remedē is safe and effective resulting in improved sleep for patients. Limitations included lack of control group, lack of data availability for a large proportion of initial participants, which could have led to an underestimation of SAEs.

In a 2020 systematic review and meta-analysis, Voigt et al. compared the outcomes of therapies for patients with CSA and heart failure (HF) with reduced ejection fraction (REF). Nineteen randomized studies were identified that met the inclusion criteria of apnea hypopnea index (AHI) ≥10, predominant CSA, and heart failure with reduced ejection fraction (HFrEF) ≤ 50%. Most trials examined adaptive servo ventilation (ASV) (8 studies) and continuous positive airway pressure (CPAP) (9 studies). The author identified only one randomized controlled trial for transvenous phrenic nerve stimulation (TPNS) described in detail below (Costanzo, et al. 2016).

A 2020 Hayes technology assessment concluded there is very-low-quality body of evidence evaluating the use of phrenic nerve stimulation (PNS) with the remedē System in adults with CSA. The evidence is insufficient to draw conclusions about the efficacy and safety of PNS due to an evidence base consisting of only 2 studies with small sample sizes and limited follow-up. The clinical impact for patients with CSA, especially those with HF, remains uncertain. While results suggest a statistically significant reduction in apnea-hypopnea index (AHI) events, average AHI scores did not achieve normal-to-mild disease severity. According to the authors of the report, studies that compare the efficacy, safety, patient acceptance, and cost-effectiveness of PNS with other noninvasive, available therapies for CSA are needed. In addition, studies with longitudinal data are needed to assess the effect of PNS on CSA-related morbidity and mortality.

An updated 2021 ECRI clinical evidence assessment on the remedē System focused on the safety and efficacy for treating patients with moderate to severe CSA. The available evidence suggests transvenous phrenic nerve stimulation (TPNS) with remedē improves sleep quality and quality of life (QOL) in patients with moderate to severe CSA for up to five years. The literature consisted of 1 systematic review (SR), 3 publications of 1 RCT, and 1 pre-/post-treatment study. The systematic review consisted of five studies that compared the severity of apnea patients with active remedē implants against controls. The RCT compared a change in apnea severity by collecting AHI scores over a 5-year period along with conducting patient global assessments and daytime sleepiness in patients with active remedē implants against controls that received inactive remedē implants; however, after six months the study was no longer considered an RCT due to the permission of patients in the control arm to cross over to active stimulation. The pre-/post-treatment study reported apnea severity, daytime sleepiness, QOL, deaths, and AEs in 57 patients with moderate to severe CSA that were treated with remedē system. Limitations included high risk of bias in the SR due to small sample size, single center focus and subjective outcomes in the unblinded patients; risk of bias in the RCT due to reporting of subjective measures; and small sample size along with lack of controls for the pre-/post-treatment study. Additional studies that compare remedē with alternative treatment options and long-term outcomes to assess and compare the system's safety and efficacy are needed.

As a follow up to the study discussed below (Costanzo, et al. 2016), Costanzo et al (2018) conducted an analysis of all 96 patients randomized in the manufacturer sponsored remedē System Pivotal Trial. Effectiveness data from treatment and former control groups were pooled based on months since therapy activation. Changes from baseline to 6 and 12 months in sleep metrics, Epworth Sleepiness Scale, patient global assessment health-related quality of life, Minnesota Living with Heart Failure Questionnaire (MLHFQ), and echocardiographic parameters are reported. Heart Failure (HF) hospitalization, cardiovascular death, and the composite of HF hospitalization or cardiovascular death within 6 months were reported by the original randomized group assignment for safety assessment. Sleep metrics and quality of life improved from baseline to 6 and 12 months. At 12 months, MLHFQ scores changed by -6.8 ± 20.0. The 6-month rate of HF hospitalization was 4.7% in treatment patients and 17.0% in control patients. Reported adverse events were as expected for a transvenous implantable system. The authors concluded that phrenic nerve stimulation reduces CSA severity in patients with HF. In parallel, this CSA treatment was associated with benefits on HF quality of life. These findings are limited by the lack of comparison group undergoing a different treatment.

In a manufacturer sponsored, prospective, multicenter randomized clinical trial, Costanzo, et al. (2016) sought to evaluate the safety and effectiveness of unilateral neurostimulation in patients with central sleep apnea. Patients were recruited from 31 hospital-based centers in Germany, Poland, and the USA. Participants had to have been medically stable for at least 30 days, have received appropriate guideline recommended therapy, be aged at least 18 years, be expected to tolerate study procedures, and willing and able to comply with study requirements. Eligible patients with an apnea-hypopnea index (AHI) of at least 20 events per hour, tested by a polysomnography, underwent device implantation and were randomly assigned by a computer-generated method to either stimulation (treatment) or no stimulation (control) for 6 months. The primary effectiveness endpoint in the intention-to-treat population was the comparison of the proportions of patients in the treatment versus control groups achieving a 50% or greater AHI reduction from baseline to 6 months, measured by a full-night polysomnography assessed by masked investigators in a core laboratory. The primary safety endpoint of 12-month freedom from serious adverse

events related to the procedure, system, or therapy was evaluated in all patients. 151 eligible patients were randomly assigned to the treatment or control groups. In the analysis of results, significantly more patients in the treatment group had an AHI reduction from baseline of 50% or greater at 6 months (51%), as compared to the control group (11%; difference between groups 41%, 95% CI 25–54, p<0.0001). 138 of 151 patients had no serious-related adverse events at 12 months. Seven cases of related-serious adverse events occurred in the control group and six cases were reported in the treatment group. 27 of 73 patients in the treatment group reported non-serious therapy-related discomfort that was resolved with simple system reprogramming in 26 patients but was unresolved in one patient. According to the authors, this study shows that transvenous neurostimulation can significantly reduce the severity of central sleep apnea and concluded it may be a promising therapeutic approach. Further research is needed to determine the clinical relevance of these findings. One of the study limitations was that patients and physicians were aware of treatment assignment, which could have introduced biases. Lack of long-term follow up and a relatively small sample size are other limitations of this study.

Abraham et al. (2015) conducted a small (57 patients) prospective, multicenter, case series pilot study to evaluate chronic, transvenous, unilateral phrenic nerve stimulation to treat CSA using the implantable Respicardia remedē System. Results showed improvement in apnea-hypopnea index (AHI), central apnea index, arousals, sleep efficiency, and rapid eye movement sleep after 3 months of treatment. These improvements were sustained at 6 months and were accompanied by alleviation of both sleepiness and heart failure symptoms. The author's conclusion was that transvenous, unilateral phrenic nerve stimulation appears safe and effective for treating CSA, but as the study was limited by its size, the lack of a parallel control arm, and the diversity of the patient population, they recommended that findings should be confirmed in a prospective, randomized, controlled trial.

The TREAT-CSA Study is a study registered in clinicaltrials.gov in 2015 that was terminated in 2017 (NCT02577445). It was designed as a cohort study comparing approximately 300 participants with or without implantation of the remedé® system to treat sleep-disordered breathing. The study appears to have been terminated after recruitment of 31 participants. Results reported on clinicaltrials.gov show that among the 17 participants implanted with the remedé® system, there were 6 (35%) severe adverse events, including cardiac decompensation, cardiac arrest, other cardiac disorders, lead dislocation, and acute renal failure. None of the 14 participants without implantation of the remedé® system developed severe adverse events. The clinicaltrials.gov entry also reports 4 (23%) other (not including serious) adverse events among the 17 participants with implantation of the remedé® system, while none of the participants without implantation of the remedé® system developed such adverse events.

Laser-Assisted Uvulopalatoplasty (LAUP)

There is insufficient quality evidence to conclude LAUP is effective for obstructive sleep apnea treatment therefore, additional research involving larger, well-designed studies is needed to establish its safety and efficacy.

Camacho et al. (2017) performed a systematic review and meta-analysis to evaluate the use of laser-assisted uvulopalatoplasty (LAUP) alone as a treatment for obstructive sleep apnea (OSA) in adults. Twenty-three adult studies including 717 patients were selected for review. Individual patient data analyses demonstrate a 23% success rate (≥50% reduction in apnea-hypopnea index (AHI) and <20 events/hr.) and an 8% cure rate. Additionally, 44% of patients had worsening of their AHI after LAUP. In this meta-analysis, LAUP reduced AHI by 32% among all patients, while the LSAT only changed minimally. There are three important points to note in this review: First, LAUP can potentially worsen obstructive sleep apnea. Second, primary snoring patients who no longer snore after LAUP should be tested for OSA post-operatively if they develop signs and symptoms of OSA. Third, given that reflexogenic dilation of the pharyngeal airway is at least partially mediated by pharyngeal mucosa afferent nerve fibers, it is possible that by destroying the surface of the soft palate with a laser, that there may be blunting of the reflexogenic dilation of the pharyngeal airway. The authors conclude that LAUP be performed with caution or not performed at all given the unfavorable results of currently published studies. Limitations in this review are that most studies were case series studies, and only two were randomized controlled trials.

Lin et al. (2006) conducted a prospective, controlled trial in which they evaluated LAUP as treatment for moderately severe or severe OSA in 25 subjects. After LAUP, impedance in non-responders remained elevated, but impedance in responders returned to levels comparable to those in the 15 healthy controls.

An RCT conducted by Larrosa et al. (2004, included in the Camacho systematic review) focused primarily on LAUP for treatment of snoring; however, it included some patients with mild OSA and evaluated outcomes other than snoring intensity.

Patients were randomized to LAUP or a placebo surgery control group. This study was small (n=25) and did not involve any follow-up after the post treatment assessment at 3 months; however, it found that there were no statistically significant differences between the control group and LAUP treatment group in snoring, daytime sleepiness, apnea-hypopnea index, or QOL measures. A shortcoming of the trial is that patients underwent only one LAUP treatment rather than the multiple treatments provided by Terris and Ferguson.

Two of the reviewed studies were randomized trials that evaluated LAUP. Ferguson et al. (2003, included in the Camacho systematic review) conducted a small RCT (n=45) with 8 months of follow-up to evaluate LAUP versus no treatment for mild OSA. Although patients who underwent an average of 2.4 LAUP procedures had statistically significant improvements in snoring and apnea-hypopnea index relative to the control group, improvements in daytime sleepiness and sleep apnea QOL scores were not statistically significant. Moreover, the benefits were limited, corresponding to a 44% decrease in mean snoring intensity and 35% decrease in apnea-hypopnea index.

Terris et al. (2002) also conducted a randomized trial of LAUP but used a randomized crossover design in which patients were randomly assigned to LAUP or RFA of the palate and then allowed to undergo the non-assigned treatment if their assigned treatment did not provide adequate improvement. Although this study was small (n=17) and involved only 16 weeks of follow-up, the results suggest that multiple LAUP and RFA treatments of the palate reduce snoring but do not significantly reduce the other symptoms of sleep-disordered breathing such as daytime sleepiness or upper airway collapse.

Lysdahl et al. (2002) compared the outcomes of 121 patients treated for bronchopathy, the majority of whom also reported apneas. Sixty-one were treated with uvulopalatopharyngoplasty and 60 with laser-assisted uvulopalatoplasty. The patients were requested to assess the frequency of symptoms associated with OSA prior to surgery, at 3-month follow up and 5 to 8 years postoperatively. Both groups reported significant improvements; however, UPPP was superior to LAUP in terms of all clinical effect parameters. However, the surgeries are not directly comparable as more tissue is removed in UPPP, and the OSA was self-reported.

Lingual Suspension/Tongue Fixation

No studies on the long-term success of this procedure are available, and there is little quality clinical data to demonstrate its efficacy.

Lingual suspension is intended to keep the tongue from falling back over the airway during sleep. This procedure involves inserting a bone screw into the lower jaw. A cable is then threaded through the base of the tongue and anchored to the bone screw. It is usually performed in conjunction with other procedures.

Bostanci and Turhan (2016) evaluated, in a systematic review, existing research for 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 met the eligibility criteria, mostly case series or observational studies comparing two different TBS techniques. Four of seven studies (62 patients) used the Repose® system and three studies (51 patients) used the modified TBS technique. The success rates were higher in the studies that used the modified technique (74.5 %) versus those that used the Repose® (25.8 %) system. Ten studies which included 300 patients met the eligibility criteria for TBS combined with UPPP. Seven of ten studies included 176 patients which used the Repose® system, and three studies included 124 patients which used the modified TBS technique. The success rates in this group were similar between the modified TBS technique (73.4 %) and Repose® system (67.6 %). When the aggregate data of 413 patients were compared, the modified TBS technique was found to be associated with significantly higher success rates. The authors found the evidence supported primarily grade C recommendation for the benefits of both techniques with or without UPPP, but none of the results were convincing enough to provide an answer to the question of which TBS technique is most effective and safe for patients with hypopharyngeal obstruction especially in the tongue base. Limitation of the included studies was lack of comparison with other established approaches to OSA treatment.

Handler et al. (2014) performed a systematic review of suture-based tongue suspension procedures as a stand-alone therapy for hypopharyngeal obstruction in OSA. The review also compared outcomes of tongue suspension as part of various multilevel approaches to OSA surgery. Studies published after 1997 were included and involved four cohorts: tongue suspension alone, tongue suspension with uvulopalatopharyngoplasty (UPPP), tongue suspension with genioglossus advancement (GA) plus UPPP and tongue suspension with genioglossus advancement with hyoid suspension (GAHM) plus UPPP. Twenty-seven studies were included. Six studies qualified for the tongue suspension-alone group with a surgical success rate of 36.6%. Eight

studies qualified for the cohort of tongue suspension with UPPP with a surgical success rate of 62.3%. Eighteen studies qualified for the remaining two cohorts: GA plus UPPP and GAHM plus UPPP. The surgical success rates for both were 61.1%. Surgical outcomes were similar among the various combined procedures. Author noted limitations include the inability to measure statistical significance due to lack of patient demographic data for the individual studies. Secondly, of the studies used to create the surgical cohorts, three were level 2 evidence, while the remaining 24 were considered level 4 evidence. Lastly, some studies used pre- and postoperative respiratory distress index (RDI), while others used the apnea-hypopnea index (AHI), making comparisons difficult. The findings are limited by the lack of comparison with established approaches to OSA treatment. (Authors Kuhnel 2005, Miller 2002, DeRowe 2000 and Woodson 2000 which were previously cited in this policy, are included in the Handler (2014) systematic review).

In a multicenter, prospective case series, Woodson et al. (2010) assessed the safety and effectiveness of an adjustable lingual suspension device (Advance System) for treating OSA. Forty-two surgically naive patients with moderate to severe OSA and tongue base obstruction underwent surgical insertion of a midline tissue anchor into the posterior tongue and connected to an adjustable mandibular bone anchor with a flexible tether. Outcomes included changes in AHI, sleepiness, sleep-related quality-of-life, snoring, swallowing, speech and pain. After six months, all patients noted improvement for AHI, sleepiness and sleep-related quality of life. Post implant pain scores were mild to moderate at day one and resolved by day five. Device related adverse events included wound infection (7%) and edema or seroma (5%), which resolved. However, in 31 percent of patients, asymptomatic tissue anchor barb fractures were observed radiographically. The tissue anchor failure rate of the tested device precludes its clinical use. Further investigation is warranted. The findings of this case series are limited by the lack of comparison group.

Palatal Implants

There is insufficient evidence to conclude palatal implants are effective for obstructive sleep apnea treatment. Additional research involving larger, randomized control trials is needed to establish their safety, efficacy and long-term outcomes.

Palatal implants consist of three small woven polyester or similar inserts that are placed in the soft palate to stiffen the palate and thereby reduce the number of episodes of partial or complete blockage of breathing during sleep. Pillar® and Elevo® are trade names using this technology. The woven consistency of the polyester inserts is designed to facilitate an inflammatory response that results in the formation of a fibrous capsule surrounding each insert which stiffens the palate and reduce snoring (Berry 2015).

Gillespie et al. (2011) conducted a small RCT on fifty-one patients with mild to moderate sleep apnea to determine if the Pillar palatal implant system could decrease CPAP pressures which in turn would lead to higher patient compliance and satisfaction with CPAP therapy. The participants received a preloaded delivery system that contained either the pillar implant (active treatment) or no implant (sham). Physicians inserting the implant were instructed to not inspect the inside of the device once the preloaded cartridge had been discharged; no major adverse determinations were noted. Primary outcome assessment was CPAP pressures and collected by a smartcard device at 30, 60 and 90 days postimplant procedure. Secondary outcomes included Functional Outcome of Sleep Questionnaire (FOSQ), the Epworth Sleepiness Scale (ESS), and a 10-cm visual analog scale (VAS) for CPAP satisfaction with 0 indicating no satisfaction and 10 indicating complete satisfaction. The study failed to identify between-group differences in the changes in CPAP pressure or in adherence to treatment over time. The authors found while the active treatment group did have a slight improvement in CPAP satisfaction compared to the sham group, it was unclear as to why. The findings did not support the use of pillar implants to aid in the treatment for improved CPAP compliance.

Choi et al. (2013) performed a meta-analysis of studies evaluating the efficacy of the Pillar implant for treating mild to moderate obstructive sleep apnea (OSA). Seven studies were included: 5 case series (n=287) and 2 controlled trials (n=76). Mean follow-up duration ranged from 3 to 29 months. The Pillar implant significantly reduced the Epworth Sleepiness Scale and the apnea-hypopnea index (AHI) compared to pre-procedure values. The authors concluded that the Pillar implant has a moderate effect on mild to moderate OSA but acknowledged that most of the relevant studies were case series and not placebo controlled. Most studies were also limited by short-term follow-up.

In a randomized, double-blind, placebo-controlled trial (n=22), Maurer et al. (2012) assessed the effects of palatal implants in patients with mild to moderate sleep apnea due to palatal obstruction. Respiratory parameters and sleep efficiency (evaluated by polysomnography), snoring (evaluated by the bed partner) and daytime sleepiness (evaluated by ESS) were assessed before and 90 days after surgery. The apnea-hypopnea index (AHI), hypopnea index (HI) and lowest oxygen saturation (LSAT) showed statistically significant improvement in the treatment group. Snoring as rated by bed partners also showed statistically

significant improvement within the treatment group. There was no statistical difference when comparing the means of the treatment group with the placebo group. There was no peri- or postoperative complications and no extrusions during the follow-up period. The authors concluded that the study supports the idea that palatal implants lead to a reduction in respiratory events in patients with mild to moderate OSA, although a statistically significant superiority of palatal implants over placebo could not be demonstrated in this trial. In addition, the significance of this study is limited by the small sample size.

A National Institute for Health and Care Excellence (NICE) guideline states that current evidence on soft-palate implants for obstructive sleep apnea (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. Therefore, soft-palate implants should not be used in the treatment of OSA (NICE, 2007).

Friedman et al. (2008, reviewed in the Choi systematic review reported above) performed a double-blinded, placebo-controlled RCT that enrolled 62 patients with mild-to-moderate OSA who underwent palatal implantation (Treatment Group, n=31) or mock implantation (Control Group, n=31). In the patients who completed 3 months of follow-up, mean AHI scores had decreased from 24 to 16 points for the Treatment Group versus an increase from 20 to 21 (1 4) points for the Control Group. Although improvements were statistically significant, they were relatively small. Furthermore, the study was limited by short follow-up.

In a multi-institution, double-blind, placebo-controlled study, Steward et al. (2008, reviewed in the Choi systematic review reported above) randomly assigned one hundred patients with mild to moderate OSA and suspected retropalatal obstruction to treatment with three palatal implants or sham placebo. Palate implants demonstrated efficacy over placebo for several important outcome measures with minimal morbidity, but overall effectiveness remains limited. The investigators concluded that further study is needed.

In a retrospective, case series, Friedman et al. (2006a) evaluated the Pillar implant system alone and in combination with other procedures for treatment of mild-to-moderate OSA/hypopnea syndrome (OSAHS). A total of 125 patients (mean age 42 11 years) who had mild-to-moderate OSAHS were assigned to palatal implantation alone (Palatal Group, n=29), or in combination with other procedures. The authors report an "objective cure rate" of 34%. The study is limited by lack of comparison group receiving treatments other than the Pillar implant system.

Walker et al. (2006, reviewed in the Choi systematic review reported above) studied the Pillar implant system in 53 patients in a 90-day multicenter noncomparative study. Inclusion criteria were OSA caused by palatal obstruction, an AHI score of 10 to 30, a BMI less than or equal to 32 kg/m2, age greater than or equal to 18 years, and a soft palate of sufficient length for the implants. Mean AHI score decreased from 25.0 at baseline to 22 at 90 days follow-up. Although this decrease was small, it was statistically significant (P=0.05). These findings were limited by lack of comparison group receiving established OSA treatments.

Three other small, uncontrolled studies have been performed to evaluate the Pillar Palatal Implant System for mild-to moderate OSA. These studies enrolled 16 to 26 patients who had an AHI score of 5 to 30. These studies reported that, compared with baseline, patients obtained small-to-moderate but statistically significant improvements in outcomes such as AHI and Epworth Sleepiness Scale (ESS) scores at up to 1 year of follow-up; however, these studies do not provide reliable evidence of efficacy since they did not involve any control or comparison groups (Friedman, 2006b; Goessler, 2007, reviewed in the Choi systematic review reported above; Nordgard, 2007).

Radiofrequency Ablation of the Soft Palate and/or Tongue

While the evidence for radiofrequency ablation may provide support for short-term results for patients with OSA, additional larger studies and randomized trials are needed to support the long-term safety, efficacy of this procedure.

Radiofrequency tissue volume reduction (RFTVR) involves the use of low-intensity radiofrequency energy to shrink the size of the uvula, soft palate and/or tongue. Somnoplasty™ and Coblation® are two trade names using this technology. The procedure may be performed in conjunction with other therapies.

An ECRI (2020) clinical evidence assessment on radiofrequency ablation for treating OSA determined the evidence was of low quality and inconclusive. All 29 studies were determined to have high bias, very small sample sizes and lack of control groups. In addition, the studies assessed patients with varying severities of OSA, lacked long term outcome results and were inconsistent in radiofrequency ablation sites.

Amali et al. (2017) conducted a randomized clinical trial which compared the efficacy of modified radiofrequency tissue ablation (MRFTA) with that of uvulopalatopharyngoplasty (UPPP) in patients with mild to moderate obstructive sleep apnea (OSA). Forty patients with mild to moderate OSA were randomly divided into two groups; one for UPPP and the other for MRFTA. Evaluation was made immediately before surgery based on the apnea hypopnea index (AHI), Sleep Apnea Quality of Life Index (SAQLI) and Epworth Sleepiness Scale (ESS), and again 6 months postoperatively. The results demonstrated the postoperative AHI scores were improved significantly in both groups, although the postoperative AHI in the UPPP group was significantly lower than in the MRFTA group (P = .02). Comparing postoperative ESS scores in the 2 groups showed no significant difference (P = .24) and the SAQLI total score were significantly higher in the MRFTA group. The authors concluded MRFTA as well as UPPP can greatly improve daytime sleepiness and AHI, especially in patients with mild OSA. MRFTA proved to be more effective than UPPP to enhance quality of life of patients with OSA. Further studies with longer follow-up are required to evaluate long-term safety and efficacy of these procedures. The findings are limited by lack of comparison to other non-surgical approaches to OSA.

Baba et al. (2015) conducted a systematic review and meta-analysis to determine the efficacy of temperature-controlled radiofrequency tissue ablation (TCRFTA) to alleviate symptoms of OSA. A total of 20 studies were included in the meta-analysis. Effectiveness of TCRFTA was measured separately at the base of tongue and soft palate, and for multilevel intervention using the respiratory disturbance index (RDI), lowest oxygen saturation (LSAT), Epworth sleepiness scale (ESS) and bed partner's rating of snoring using a visual analogue scale (VAS snoring). The authors concluded that, in the short term, TCRFTA is clinically effective in reducing respiratory disturbance index (RDI) levels and symptoms of sleepiness in patients with OSA syndrome when directed at the base of tongue or as a multilevel procedure but had limited efficacy on the soft palate. Author noted limitations include heterogeneity between studies, short term follow-up and inclusion of lower quality studies. (publications by Atef 2005, Steward 2004a and 2004b, Terris 2002, Woodson 2001 and 2003 which were previously cited in this policy, are included in the Baba (2015) systematic review).

Franklin et al. (2009) conducted a systematic review evaluating the efficacy (randomized controlled trials only) and adverse effects (including observational studies) of surgery for OSA. The authors reported that only a small number of randomized controlled trials with a limited number of patients assessing some surgical modalities for sleep apnea are available. For RFA, the studies reviewed did not support any benefit on daytime sleepiness, apnea reduction or quality of life. Furthermore, several persistent adverse effects were detected.

In a pilot randomized study, RFTVR of palate and uvula was compared to radiofrequency channeling (Bassiouny, 2007). The authors concluded that their preliminary findings "confirms the favorable effects of radiofrequency in the treatment of patients with snoring and mild to moderate obstructive sleep apnea (OSA) particularly on snoring".

Hofmann et al. (2006) compared temperature controlled RFTVR to conventional surgery using a non-randomized comparative (cohort study) design. Both UPPP and RFTVR reduced snoring, but UPPP led to improvement in AHI and HI, while RFTVR did not. While postoperative pain was shorter in duration for RFTVR, the number of treatments was higher, leading to a comparable length of postoperative pain.

Transoral Robotic Surgery (TORS)

TORS has been introduced as a novel tool for accessing and resecting tissue from the tongue base and hypopharynx. Based on studies using TORS to treat head and neck cancers, researchers are investigating the use of this technology for patients with OSA along with the procedure's safety and efficacy. The published literature is limited by lack of comparison group and therefore high risk of bias. Studies that include concurrent comparison groups, long-term follow-up, and sufficient power to demonstrate safety and efficacy are lacking.

Tsou and Chang (2020) conducted a systematic review of eight articles which compared the clinical outcomes and success rates of TORS with that of other alternative procedures such as coblation tongue base resection (CTBR), upper airway stimulation (UAS), radiofrequency, CO_2 laser, and endoscopic partial midline glossectomy (EPMG). Clinical outcomes assessed were AHI, O_2 saturation and ESS score. While the authors found all the procedures significantly reduced AHI and ESS scores along with increase in O_2 saturation, no significant differences between the surgical procedures were found in operation time, in success rates or complication rates; the success rate of TORS was no more effective than that of the other compared alternative procedures. Limitations of analysis included lack of RCTs, lack of long-term outcomes, comparison to non-established approaches, and the retrospective design of most of the included studies.

Lan et al. (2019, included in Tsou and Chang (2020) above) retrospectively compared the efficacy of trans-oral robotic surgery (TORS) with that of coblation assisted tongue base reduction surgery in patients with obstructive sleep apnea syndrome (OSAS). Thirty-three cases were analyzed; sixteen received TORS and seventeen received coblation surgery. Both groups received concomitant uvulopalatoplasty and surgical outcomes were evaluated by comparing the initial polysomnography results with a follow-up PSG within at least 3 months after the surgery. Epworth sleepiness scale (ESS) and complications were also utilized in the comparison between the two groups. The authors found no difference in the success rate between the two procedures. Limitations were this the retrospective nature of the study and lack of comparison with established approaches to OSA; another limitation was the difficulty in comparisons due to the different surgical techniques utilized for TORS. The authors concluded surgical performance in combination with uvulopalatoplasty is an effective approach for OSAS, however future randomized controlled trials are needed to evaluate the efficacy of TORS.

Miller et al. (2017) conducted systematic review and meta-analysis on the effect of transoral robotic surgery (TORS) base of tongue (BOT) reduction sleep-related outcomes in patients with obstructive sleep apnea (OSA). Studies on TORS BOT reduction as part of OSA treatment in adult patients with pre- and postoperative apnea-hypopnea index (AHI) scores were included. Studies on TORS as treatment for diseases other than OSA were excluded. A total of six case series were reviewed and 353 patients met inclusion criteria. Pooled analyses (baseline vs. post-surgery) showed significant improvement in the following: AHI (44.3 ± 22.4 to 17.8 ± 16.5, $P < .01$), Epworth Sleepiness Scale (12.9 ± 5.4 to 5.8 ± 3.7, $P < .01$), lowest oxygen saturation (79.0 ± 9.5 to 84.1 ± 6.5, $P < .01$), and snoring visual analog scale (9.3 ± 0.8 to 2.4 ± 2.43, $P < .01$). Surgical success rate was 68.4%. Cure rate was 23.8%. The authors concluded TORS BOT is considered successful in the majority of adult patients with OSA, however further studies must be performed to optimize patient selection criteria to achieve higher rates of success. The findings are however limited by lack of comparison group in the included studies and the retrospective nature of most of these studies.

Justin et al. (2016) conducted a systematic review of the literature evaluating the effectiveness, complications and safety of TORS for the treatment of OSA. Sixteen studies were included. Three of these studies were case series with comparison to historical controls and the other were case series without comparison group. TORS was almost always combined with other sleep surgery procedures. The summary estimate of the decrease in AHI using TORS as part of a multilevel surgical approach was 24.0. The summary estimate of a decrease in ESS score was 7.2 and of the overall surgical "success" (defined as AHI <20 and 50% reduction) was 48.2%. Three large studies reported complication rates with an average of 22.3%. The authors concluded that initial results for the use of TORS as part of a multilevel surgical approach for OSA are promising for select patients. However, the morbidity may be greater than with other techniques, offsetting its advantages in visualization and precision. More prospective studies are needed to determine the optimal role of this tool. The findings are limited by lack of concurrent comparison group in the included studies.

In a prospective, nonrandomized trial using historical controls, Lee et al. (2012, reviewed in the Miller 2017 and the Justin 2016 systematic reviews cited above) assessed the use of transoral robot-assisted lingual tonsillectomy and uvulopalatopharyngoplasty for the surgical management of tongue base obstruction in patients with obstructive sleep apnea. Twenty patients had completed the study to date. The rate of surgical success was 45%, and the rate of surgical response was 65%. The mean preoperative apnea-hypopnea index of 55.6 decreased by 56.7%, to a mean postoperative value of 24.1, and the minimum arterial oxygen saturation increased from the mean preoperative value of 75.8% to the mean postoperative value of 81.7%. The mean Epworth Sleepiness Scale score improved from 13.4 to 5.9. One patient had postoperative bleeding that required cauterization, resulting in a major complication rate of 4.2%. This study is limited by lack of randomization, comparison group, and small sample size.

Friedman et al. (2012, reviewed in the Miller 2017 and the Justin 2016 systematic reviews cited above) assessed the feasibility and efficacy of robotically assisted partial glossectomy without tracheotomy by comparing obstructive sleep apnea-hypopnea syndrome (OSAHS) outcomes with those of established techniques. Using a historical cohort study, 40 consecutive patients underwent transoral robotic surgery (TORS) for OSAHS and were followed up with regard to complications, morbidity and subjective and objective outcomes. Data from 27 of these patients who underwent concomitant z-palatoplasty with 6-month follow-up were compared with those of 2 matched cohorts of patients who underwent either radiofrequency or Coblation reduction of the tongue base and z-palatoplasty. No major bleeding or airway complications were observed. Postoperative pain and length of admission were similar between groups. All groups saw Epworth score and snore score improvement. Patients undergoing robot-assisted surgery took longer than their radiofrequency counterparts to tolerate normal diet and resume normal activity. Apnea hypopnea index (AHI) reduction averaged $60.5\% \pm 24.9\%$ for TORS versus $37.0\% \pm 51.6\%$ and $32.0\% \pm 43.3\%$ for Coblation and radiofrequency, respectively. Only the robotic group achieved statistically significant improvement in

minimum oxygen saturation. Surgical cure rate for TORS (66.7%) was significant compared with radiofrequency (20.8%) but not compared with Coblation (45.5%). The authors concluded that it is feasible to perform robotically assisted partial glossectomy without the need for tracheotomy. This technique resulted in greater AHI reduction, but increased morbidity compared with the other techniques studied. This study is limited by a retrospective observational design and small sample size.

Vicini et al. (2010, reviewed in the Miller 2017 and the Justin 2016 systematic reviews cited above) evaluated the feasibility, tolerability and efficacy of tongue base management using transoral robotic surgery (TORS) in patients with obstructive sleep apnea-hypopnea syndrome (OSAHS). Seventeen patients with OSAHS, principally related to tongue base hypertrophy, underwent TORS (Intuitive da Vinci®). Patients with a minimum follow-up of 3 months were evaluated. Ten patients [mean preoperative apnea-hypopnea index (AHI): 38.3 +/-23.5 SD] were included in the study. The postoperative polysomnographic results were fairly good (mean postoperative AHI: 20.6 +/- 17.3 SD), and the functional results (pain, swallowing and quality of life) were encouraging. Complications were rare and of minor importance. The authors concluded that transoral robotic tongue base management in patients with OSAHS primarily related to tongue base hypertrophy is feasible and well tolerable and that these preliminary results encouraging and worthy of further evaluation. The study is however limited by lack of comparison group and large loss to follow-up.

Distraction Osteogenesis for Maxillary Expansion (DOME)
There is insufficient quality evidence to conclude DOME is effective for the treatment of adult OSA. The published literature lacks randomized control trials needed to establish the safety, efficacy and long-term outcomes. Future studies including comparison groups are warranted.

In a retrospective case series, 75 patients with a diagnosis of OSA intolerant of CPAP along with no palatine or lingual tonsillar hypertrophy underwent a DOME procedure (Yoon et al., 2020). The custom designed hybrid (bone-borne and tooth-borne) distractors were individually fabricated for each patient using 3-D cone-beam computed tomography (CBCT) and placed with mini-screws. The expander device was activated 5 to 7 days postop by using an axial screw for expansion daily. This continued for 3 months but the device was kept in place for an additional 6 to 8 months. Each patient completed the Epworth Sleepiness Scale (ESS) and Nasal Obstruction Symptom Evaluation (NOSE) questionnaires before to and during the 3-to-6-month postop period. The participants followed the attended PSG process which was conducted and scored 3 to 8 months following the DOME procedure. Apnea and hypopnea were both measured as well. The authors determined the results showed significant improvements in alleviating nasal obstruction, decreasing AHI, and improving the amount of REM sleep. Limitations of the study included small sample size, lack of parallel comparison group, and lack of long-term outcomes.

Abdelwahab et al. (2019) retrospectively evaluated a case series of 32 patients with OSA that underwent DOME by assessing subjective and objective outcomes. The patients included in the study were intolerant to CPAP, had no hypertrophy of either the lingual or palatine tonsils, had class 3 or 4 Mallampati and a suffered a narrow palatal arch. The procedure was performed with application of the maxillary expander with fixation of 4 to 6 screws to the midpalate and maxillary bone and then performance of LeFort I maxillary osteotomy. Postoperatively the patients were taught to turn the expander daily for the next five weeks. NOSE and ESS scores were obtained for evaluation. The authors found that DOME procedure widened the maxilla and therefore was deemed successful by improvement of the NOSE and ESS scores. Limitations included lack of comparison group, small sample size, retrospective design, single institution experience, and lack of long-term outcomes.

Liu et al. (2017) described the safety and efficacy of DOME for a case series of 20 patients. Each patient underwent pre- and post-DOME polysomnographies along with outcome measurements from ESS, NOSE rhinomanometry and CT measurements of the nasal floor. Following the surgical procedure, significant decline was noted in all the measurements along with airflow resistance and it was concluded that the DOME procedure was successful at widening the maxilla in all the adult patients with OSA. However, limitations included lack of comparison group, small sample size and no long-term data for safety and efficacy.

Clinical Practice Guidelines
American Academy of Otolaryngology–Head and Neck Surgery (AAO-HNS)
The AAO-HNS considers Uvulopalatopharyngoplasty (UPPP) a valid and safe treatment for OSA in appropriately selected patients. (AAO-HNS website; revised January 2019).

The AAO-HNS considers upper airway stimulation (UAS) via the hypoglossal nerve for the treatment of adult OSA syndrome to be a safe and effective second-line treatment for patients with moderate to severe OSA and intolerant or unable to achieve benefit with positive pressure therapy. (AAO-HNS website; revised November 2019).

American Academy of Sleep Medicine (AASM)

In a practice parameter document, the AASM recommends weight reduction be combined with other primary treatments for patients with moderate to severe OSA (Morgenthaler, et al. 2006).

The AASM recommends surgery as a treatment option for OSA when noninvasive treatments such as CPAP or oral appliances have been unsuccessful. The use of hypoglossal nerve stimulation is not addressed as a therapeutic option (Aurora, 2010a).

A 2010 AASM practice parameter (Aurora, 2010a; Aurora, 2010b; Caples, 2010) on surgical options for OSA makes the following recommendations:

- *Uvulopalatopharyngoplasty (UPPP)*: UPPP as a single surgical procedure, with or without tonsillectomy, does not reliably normalize the AHI when treating moderate to severe OSA. 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. The clinical evidence for UPPP is very low quality (Option recommendation – either inconclusive or conflicting evidence or conflicting expert opinion). This recommendation is a change from the previous practice parameter.
- *Maxillomandibular Advancement (MMA) Surgery*: MMA is indicated for surgical treatment of severe OSA in patients who cannot tolerate or who are unwilling to adhere to PAP 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. Although the clinical evidence is very low quality, studies tend to demonstrate consistent effectiveness in severe OSA. MMA is not well described in mild and moderate OSA making recommendations in less severe OSA unclear (Option recommendation – either inconclusive or conflicting evidence or conflicting expert opinion).
- *Multi-Level or Stepwise Surgery (MLS)*: Multi-level surgery, as a combined procedure or as stepwise multiple operations, is acceptable in patients with narrowing of multiple sites in the upper airway, particularly when UPPP as a sole treatment has failed (Option recommendation – either inconclusive or conflicting evidence or conflicting expert opinion).
- *Radiofrequency Ablation (RFA)*: RFA can be considered as a treatment in patients with mild to moderate OSA who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances have been considered and found ineffective or undesirable. The clinical evidence for RFA is very low quality (Option recommendation – either inconclusive or conflicting evidence or conflicting expert opinion).
- *Laser-Assisted Uvulopalatoplasty (LAUP)*: LAUP is not routinely recommended as a treatment for OSA syndrome. LAUP does not generally normalize the AHI and the literature does not demonstrate significant improvement in secondary outcomes. Some studies actually saw worsening of the overall AHI. The clinical evidence for LAUP is low quality. (Standard recommendation – generally accepted patient-care strategy).
- *Palatal Implants*: Palatal implants may be effective in some patients with mild obstructive sleep apnea who cannot tolerate or who are unwilling to adhere to positive airway pressure therapy, or in whom oral appliances have been considered and found ineffective or undesirable. There is limited research that adequately assesses the efficacy of palatal implants for the treatment of OSA. Available studies suggest marginal efficacy (Option recommendation – either inconclusive or conflicting evidence or conflicting expert opinion).

The AASM recommends surgery as a treatment option for OSA when noninvasive treatments such as CPAP or oral appliances have been unsuccessful; and one of the most common surgical methods is the uvulopalatopharyngoplasty procedure. (AASM website; accessed June 25, 2021).

The AASM (Aurora 2016) recommends the following for treatment of central sleep apnea syndrome (CSAS) related to CHF:

Recommendation 1: Adaptive servo-ventilation (ASV) targeted to normalize the apnea-hypopnea index (AHI) should not be used for the treatment of CSAS related to CHF in adults with an ejection fraction ≤ 45% and moderate or severe CSA predominant, sleep-disordered breathing. (STANDARD AGAINST)

Recommendation 2: Adaptive servo-ventilation (ASV) targeted to normalize the apnea-hypopnea index (AHI) can be used for the treatment of CSAS related to CHF in adults with an ejection fraction > 45% or mild CHF related CSAS. (OPTION)

Sleep Foundation

The Sleep Foundation suggests surgery is rarely a first line form of treatment for OSA. Surgery is to be considered when treatments such as CPAP or oral appliance therapy have been unsuccessful. (Sleep Foundation website; accessed June 25, 2021).

American Sleep Apnea Association (ASAA)

The ASAA position is that while positive airway pressure therapy is the first line of treatment for moderate to severe sleep apnea, patient compliance represents a problem. For the noncompliant patient, surgery may be a feasible alternative. The surgeon must first determine what part of the upper airway is causing the obstruction to airflow. The sites of obstruction could be anywhere in the upper respiratory tract including the nose, tongue and throat.

It considers that there are many surgical options for the treatment of sleep apnea for patients who cannot tolerate CPAP therapy. Because the airway pattern and the severity of obstruction vary greatly between individuals, the surgical regimen must be catered to a particular individual. Often it takes a combination of procedures to achieve success. A logical stepwise approach must be taken when a patient seeks surgery, and it is a requisite that the patient finds a surgeon who understands both the pathophysiology of sleep apnea and the anatomy of the upper respiratory tract to ensure the best chance of success (ASAA, 2015).

European Respiratory Society (ERS)

An ERS report on non-CPAP therapies for OSA concluded that maxillomandibular osteotomy seemed to be as efficient as CPAP in patients who refused conservative treatment. Radiofrequency tonsil reduction, tongue base surgery, uvulopalatal flap, laser midline glossectomy, tongue suspension and genioglossus advancement cannot be recommended as single interventions. Uvulopalatopharyngoplasty, palatal implants and hyoid suspension should only be considered in selected patients and potential benefits should be weighed against the risk of long-term side-effects. Multilevel surgery is only a salvage procedure for OSA patients (Randerath et al., 2011).

Department of Veterans Affairs (VA)/Department of Defense (DoD)

The 2019 guideline for the management of chronic insomnia disorder and OSA makes the following recommendations for patients with OSA:

- In appropriate patients with mild to moderate obstructive sleep apnea (apnea-hypopnea index <30 per hour), suggest offering mandibular advancement devices, fabricated by a qualified dental provider, as an alternative to positive airway pressure therapy. (Weak)
- For patients with obstructive sleep apnea with an apnea-hypopnea index of 15 – 65 per hour and a body mass index <32 kg/m2 who cannot adhere to positive airway pressure therapy, suggest evaluation for surgical treatment with hypoglossal nerve stimulation therapy. (Weak)
- For patients with severe obstructive sleep apnea who cannot tolerate or are not appropriate candidates for other recommended therapies, suggest evaluation for alternative treatment with maxillomandibular advancement surgery. (Weak)

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Oral appliances for OSA are regulated by the FDA, but products are too numerous to list. See the following website for more information (use product codes LRK or LQZ). Available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (Accessed June 1, 2021)

The Lunoa System (NightBalance BV) received 510(k) Premarket Notification (K180608) from the FDA on June 5, 2018. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?ID=K180608. (Accessed June 1, 2021)

Bongo, manufactured by InnoMed Healthscience, Inc., received 510(k) approval (K180619) from the FDA on August 16, 2018. The device is an intranasal appliance indicated for use in the treatment of mild to moderate obstructive sleep apnea (OSA) in adults >66 lbs. Refer to the following website for additional information: https://www.accessdata.fda.gov/cdrh_docs/pdf18/K180619.pdf. (Accessed June 1, 2021)

Radiofrequency ablation (RFA) systems for surgery are regulated by the FDA as Class II devices, and a large number of these RFA systems have been approved via the 510(k) process. The following devices are among the RFA devices specifically approved for coagulation of tissues in the head and neck.

- The Somnoplasty™ System, manufactured by Olympus (formerly Gyrus ENT), received 510(k) approval (K982717) from the FDA on November 2, 1998. Intended for the reduction of the incidence of airway obstructions in patients suffering from upper airway resistance syndrome (URAS) or obstructive sleep apnea syndrome (OSAS), the system generates heat for creating finely controlled lesions at precise locations within the upper airway. As the tissue heals, it reduces tissue volume, opening the airway. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf/K982717.pdf.
- Coblation® technology, manufactured by ArthroCare ENT, received 510(k) approval (K030108) from the FDA on February 3, 2003. The system is a bipolar, high frequency electrosurgical system indicated for ablation, resection and coagulation of soft tissue and hemostasis of blood vessels in otorhinolaryngology (ENT) surgery. Using low temperatures, the technology destroys tissue using radiofrequency energy to excite electrolytes in a conductive medium, such as saline. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf3/K030108.pdf. (Accessed June 1, 2021)

The eXciteOSA device (DEN200018) is a removable tongue muscle stimulation device that delivers neuromuscular stimulation to the tongue in order to reduce snoring and mild obstructive sleep apnea (AHI<15) for patients that are 18 years or older. The FDA concluded this device as de novo on February 5, 2021 and classified it into Class II (product code QNO). Refer to the following website for additional information: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?id=DEN200018 (Accessed January 11, 2022)

The remedē® System, manufactured by Respicardia, is an implantable phrenic nerve stimulator indicated for the treatment of moderate to severe central sleep apnea (CSA) in adult patients that received FDA approval on October 6, 2017. Available at: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P160039. (Accessed June 1, 2021)

The AIRvance™ Tongue Suspension system (formerly Repose™), manufactured by Medtronic ENT, received 510(k) approval (K981677) from the FDA on August 27, 1999. The system is intended for 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 suture. It is also suitable for the performance of a hyoid procedure. It is indicated for the treatment of OSA and/or snoring. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf/K981677.pdf. (Accessed June 1, 2021)

The Pillar® System for treating obstructive sleep apnea, manufactured by Medtronic ENT, received 510(k) approval (K040417) from the FDA on July 28, 2004. The system of palatal implants is intended to stiffen the soft palate tissue, which may reduce the incidence of upper airway obstruction in patients suffering from mild to moderate OSA. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf4/K040417.pdf. (Accessed June 1, 2021)

The FDA granted premarket approval (PMA) on April 30, 2014, to the Inspire Upper Airway Stimulation (UAS) system (Inspire Medical Systems Inc.) (P130008), which includes the Model 3024 Implantable Pulse Generator, the Model 4063 Stimulation Lead, the Model 4323 Sensing Lead, the Model 2740 Physician Programmer, and the Model 3032 Patient Programmer for treatment of patients with an AHI ≥ 20 and ≤ 65. Inspire UAS is used in adults who have been confirmed to fail or cannot tolerate PAP treatments such as CPAP or 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 20 despite PAP usage) and PAP intolerance is defined as: inability to use PAP (greater than 5 nights per week of usage; usage defined as greater than 4 hours of use per night); or unwillingness to use PAP (for example, a patient returns the PAP system after attempting to use it). Product documentation also note that "Body Mass Index (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."

The device is also referred to as the Inspire II (search *MNQ* in the Product Code field at: 510(k) Premarket Notification Database). The FDA mandated 2 post-approval studies: a prospective, single-arm cohort study to evaluate the long-term safety of the device in 124 subjects over 5 years, and a multicenter, prospective, single-arm cohort study to evaluate long-term safety and effectiveness of the device and effectiveness of the physician training program in 127 subjects over 5 years. Information available at:

- https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P130008
- https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130008C.pdf

- https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130008D.pdf

(Accessed June 1, 2021)

Additional Product Information

- Advance System (Aspire Medical) is an adjustable tongue base suspension system that is not, yet FDA approved for marketing in the U.S.
- Aura6000 (ImThera Medical) is an implantable hypoglossal nerve stimulation system that is not yet FDA approved for marketing in the U.S.

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Policy History/Revision Information

Date	Summary of Changes
06/01/2022	**Coverage Rationale** • Removed references to specific InterQual® release dates; refer to the most current InterQual® criteria **Supporting Information** • Archived previous policy version 2022T0525HH

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the member specific benefit plan document must be referenced as the terms of the member specific benefit plan may differ from the standard plan. In the event of a conflict, the member specific benefit plan document governs. Before using this policy, please check the member specific benefit plan document and any applicable federal or state mandates. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

This Medical Policy may also be applied to Medicare Advantage plans in certain instances. In the absence of a Medicare National Coverage Determination (NCD), Local Coverage Determination (LCD), or other Medicare coverage guidance, CMS allows a Medicare Advantage Organization (MAO) to create its own coverage determinations, using objective evidence-based rationale relying on authoritative evidence (Medicare IOM Pub. No. 100-16, Ch. 4, §90.5).

UnitedHealthcare may also use tools developed by third parties, such as the InterQual® criteria, to assist us in administering health benefits. UnitedHealthcare Medical Policies are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.