Clinical Policy Bulletin:
Obstructive Sleep Apnea in Adults

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Policy

Aetna considers the diagnosis and treatment of obstructive sleep apnea (OSA) in adults aged 18 and older medically necessary according to the criteria outlined below.

I. Diagnosis

Aetna considers attended full-channel nocturnal polysomnography (NPSG) (Type I device) performed in a healthcare facility medically necessary for diagnosis in members with symptoms suggestive of obstructive sleep apnea, when attended NPSG is used as part of a comprehensive sleep evaluation, and member has one or more of the following indications for attended NPSG:

A. Member has at least one of the following comorbid medical conditions that degrade the accuracy of portable monitoring:

1. moderate to severe pulmonary disease (for example, COPD or ashma) (with nocturnal oxygen use or daytime hypercapnea with documented arterial blood gasses showing pO2 less than 60 or pCO2 greater than 45),
2. neuromuscular disease (e.g., Parkinson's disease, spina bifida, myotonic dystrophy, amyotrophic lateral sclerosis),
3. stroke,
4. epilepsy,
5. congestive heart failure (NYHA class III or IV or LVEF less than 45%),
6. super obesity (BMI greater than 45, or pulmonary function studies show obesity hypoventilation syndrome (BMI greater than 35 plus arterial blood gas with PCO2 greater than 45, or BMI greater than 35 plus inability to lie flat in bed)); *or*

B. Member has one or more of the following comorbid sleep disorders:

1. periodic limb movement disorder,
2. parasomnias,
3. narcolepsy,

4. central sleep apnea or complex sleep apnea; *or*

C. Member has negative or technically inadequate portable monitoring results; *or*

D. Member has low pretest probability of obstructive sleep apnea (normal BMI (less than 30), normal airway (Mallampati score 1 or 2), no snoring, and normal neck circumference (less than 17 inches in men, and less than 16 inches in women)); *or*

E. Member lacks the mobility or dexterity to use portable monitoring equipment safely at home.

Note: Where attended NPSG is indicated, a split-night study NPSG is considered medically necessary, in which the final portion of the NPSG is used to titrate continuous positive airway pressure (CPAP), if the Apnea Hypopnea Index (AHI) is greater than 15 in first 2 hours of a diagnostic sleep study. An additional full-night CPAP titration NPSG is considered medically necessary only if the AHI is less than or equal to 15 during the first 2 hours of a diagnostic sleep study, or if the split-night study did not allow for the abolishment of the vast majority of obstructive respiratory events (see section III below).

II. Aetna considers unattended (home) sleep studies using *any* of the following diagnostic techniques medically necessary for members with symptoms suggestive of OSA (see Appendix B for definition of device types), when the home sleep study is used as part of a comprehensive sleep evaluation:

A. Sleep monitoring using a Type II device; *or*

B. Sleep monitoring using a Type III device, *or*

C. Sleep monitoring using a Type IV(A) device, measuring airflow and at least 2 other channels and providing measurement of apnea-hypopnea index (AHI); *or*

D. Sleep monitoring using a device that measures 3 or more channels that include pulse oximetry, actigraphy, and peripheral arterial tone (e.g., Watch-PAT device).

Note: Sleep studies using devices that do not provide a measurement of apnea-hypopnea index (AHI) and oxygen saturation are considered not medically necessary because they do not provide sufficient information to prescribe treatment. Examples include the Biancamed SleepMinder, SNAP testing with fewer than three channels, and the SleepImage Sleep Quality Screener. Note that the ApneaLink does not meet criteria as a covered type IV device because it does not measure airflow; however, the ApneaLink Plus records 5 channels, including airflow, and meets criteria for a covered sleep study device.

III. Attended full-channel nocturnal polysomnography (NPSG) (Type I device) performed in a healthcare facility is considered medically necessary for persons diagnosed with obstructive sleep apnea who have any of the following indications for attended NPSG:

A. To titrate CPAP in persons diagnosed with clinically significant OSA for whom in-laboratory NPSG was medically necessary, but who were unable to undergo a split-night study because they had an insufficient AHI (less than 15) during the first two hours of an attended NPSG; *or*

B. To titrate CPAP in persons with clinically significant OSA for whom in-laboratory NPSG was medically necessary, and who underwent a split-night study that did not abolish the vast majority of obstructive respiratory events; *or*

C. To monitor results from CPAP in persons with OSA who have persistent significant symptoms (disturbed sleep with significant arousals) despite documented AHI less than 5 on CPAP and documented compliance with CPAP (CPAP used for 70 percent of nights for four or more hours per night, for two or more months); *or*

D. To confirm diagnosis of obstructive sleep apnea prior to surgical modifications of the upper airway.

IV. It may be necessary to perform repeat sleep studies up to twice a year for *any* of the following indications (Note: where repeat testing is indicated, attended full-channel nocturnal polysomnography (NPSG) (Type I device) performed in a healthcare facility is considered medically necessary for persons who meet criteria for attended NPSG in section I above; in all other cases, unattended (home) sleep studies are considered medically necessary):

A. To determine whether positive airway pressure treatment (i.e., CPAP, bilevel positive airway pressure (BiPAP), demand positive airway pressure (DPAP), variable positive airway pressure (VPAP), or auto-titrating positive airway pressure (AutoPAP)) continues to be effective; *or*

B. To determine whether positive airway pressure treatment settings need to be changed; *or*

C. To determine whether continued treatment with positive airway pressure treatment is necessary; *or*

D. To assess treatment response after upper airway surgical procedures and after initial treatment with oral appliances.
    Note: A home sleep study is performed over multiple nights with a single interpretation is considered a single sleep study for purposes of reimbursement.

V. Video-EEG-NPSG (NPSG with video monitoring of body positions and extended EEG channels) is considered medically necessary to assist with the diagnosis of paroxysmal arousals or other sleep disruptions that are thought to be seizure related when the initial clinical evaluation and results of a standard EEG are inconclusive.

VI. Aetna considers *any* of the following diagnostic techniques experimental and investigational in members with symptoms suggestive of OSA because their effectiveness for this indication has not been established:

A. Acoustic pharyngometry. See CPB 0336 - Acoustic Pharyngometers and SNAP Testing System; *or*

B. Actigraphy testing when used alone. Actigraphy, which consists of a small portable device that senses physical motion and stores the resulting information, has been used in research studies for the evaluation of rest-activity cycles. This technique, when used alone (single channel study), has not been validated as a method of diagnosing OSA. See CPB 0710 - Actigraphy and Accelerometry; *or*

C. Cephalographic X-rays for diagnosis of OSA. Lateral cephalographic X-rays and orthopantograms may be medically necessary for evaluating persons for oral appliances; lateral cephalographic X-rays may also be necessary to evaluate persons for OSA surgery; *or*

D. Daytime nap polysomnography; *or*

  E. Diagnostic audio recording, with or without pulse oxymetry to diagnose sleep apnea; *or*
  F. Laryngeal function studies; *or*
  G. Maintenance of wakefulness test; *or*
  H. Multiple sleep latency test (see [CPB 0330 - Multiple Sleep Latency Testing (MSLT)](#)); *or*
  I. SleepStrip; *or*
  J. Sonography; *or*
  K. The static charge sensitive bed; *or*
  L. Tomographic X-ray; *or*
  M. X-rays of the temporomandibular joint or sella turcica.

Note: SNAP testing using 3 or more channels is considered a medically necessary method of home sleep testing; SNAP testing using less than 3 channels is considered experimental and investigational. See CPB 0336 Acoustic Pharyngometers and SNAP Testing System.

VII. Treatment

Treatment of snoring alone, without significant OSA, is *not* considered medically necessary.

  A. Continuous Positive Airway Pressure (CPAP)

    It is expected that members receive lifestyle advice where applicable (i.e., helping people to lose weight, stop smoking and/or decrease alcohol consumption).

    Aetna considers CPAP or autoPAP medically necessary DME for members with a positive facility-based NPSG*, or with a positive home sleep test* including Type II, III, IV(A) or Watch-PAT devices, as defined by *either* of the following criteria:

      1. Member's apnea-hypopnea index (AHI) or respiratory disturbance index (RDI) is greater than or equal to 15 events/hour with a minimum of 30 events; *or*

      2. AHI or RDI greater than or equal to 5 and less than 15 events/hour with a minimum of 10 events and at least one of the following is met:

          a. Documented history of stroke; *or*
          b. Documented hypertension (systolic blood pressure greater than 140 mm Hg and/or diastolic blood pressure greater than 90 mm Hg); *or*
          c. Documented ischemic heart disease; *or*
          d. Documented symptoms of impaired cognition, mood disorders, or insomnia; *or*
          e. Excessive daytime sleepiness (documented by either Epworth greater than 10 (see appendix)); *or*
          f. Greater than 20 episodes of oxygen desaturation (i.e., oxygen saturation of less than 85 %) during a full night sleep study, or any one episode of oxygen desaturation (i.e., oxygen saturation of less than 70 %).

    *The sleep study is based on a minimum of 2 hours of continuous recorded sleep or shorter periods of continuous recorded sleep if the total number of recorded events during that shorter period is at least the number of events that would have been required in a 2-hour period. If the AHI or RDI is calculated based on less than 2 hours

of sleep or recording time, the total number of recorded events used to calculate the AHI or RDI (respectively) must be at least the number of events that would have been required in a 2-hour period (i.e., must reach more than 30 events without symptoms or more than 10 events with symptoms). Projections of AHI or RDI based upon shorter testing times and/or fewer events are not acceptable for use in determining whether the member meets medical necessity criteria. In addition, estimates of AHI or RDI should include all stages of sleep. Estimates of AHI or
RDI that only count events during periods of REM sleep (and exclude periods of non-REM sleep from the calculation) are not acceptable for use in determining whether the member meets medical necessity criteria.

Notes: For purposes of this policy, apnea is defined as a cessation of airflow for at least 10 seconds. Hypopnea is defined as an abnormal respiratory event lasting at least 10 seconds with at least a 30 % reduction in thoraco-abdominal movement or airflow as compared to baseline, and with at least a 4 % oxygen desaturation.

The apnea-hypopnea index (AHI) is equal to the average number of episodes of apnea and hypopnea per hour of sleep without the use of a positive airway pressure device. Sleep time can only be measured in a Type I (facility-based polysomnogram) or Type II sleep study. Thus the AHI is reported only in Tyipe I or Type II sleep studies.

The respiratory disturbance index (RDI) is equal to the episodes of apnea and hypopnea per hour of recording without the use of a positive airway pressure device. The RDI is reported in Type III, Type IV, and other home sleep studies.

Leg movement, snoring, respiratory effort related arousals (RERAs), and other sleep disturbances that may be included by some polysomnographic facilities are not considered to meet the AHI and/or RDI definition in this policy. Although AHI and RDI have been used interchangeably, some facilities use the term RDI to describe a calculation that includes these other sleep disturbances. Requests for positive airway pressure devices will be considered not medically necessary if based upon an index that does not score apneas and hypopneas separately from other sleep disturbance events. Only persons with an AHI and/or RDI, as defined in this policy that meets medical necessity criteria may qualify for a positive airway pressure device.

Aetna considers CPAP experimental and investigational for the treatment of persons with upper airway resistance syndrome (UARS) or for the improvement of seizure control in persons with epilepsy.

BiPAP without a backup rate feature, DPAP, and VPAP are considered medically necessary DME for members who are intolerant to CPAP or AutoPAP, or for whom CPAP or AutoPAP is ineffective. Ineffective is defined as documented failure to meet therapeutic goals using CPAP or AutoPAP during the titration portion of a facility-based study or during home use despite optimal therapy (i.e., proper mask selection and fitting and appropriate pressure settings). The records must document that both of the following medical necessity criteria are met:

1. An appropriate interface for the CPAP and AutoPAP has been properly fit and the member is using it without difficulty; and

2. The current pressure setting of the CPAP or AutoPAP prevents the member from tolerating the therapy and lower pressure settings of the CPAP or AutoPAP were tried but failed to:

   a. Adequately control the symptoms of OSA; *or*
   b. Improve sleep quality; *or*
   c. Reduce the AHI/RDI to acceptable levels.

   These alternatives to CPAP may also be considered medically necessary for OSA members with concomitant breathing disorders, which include restrictive thoracic disorders, COPD, and nocturnal hypoventilation. An oral pressure appliance (OPAP) is considered medically necessary DME only on an exception basis for members who are unable to tolerate a standard nasal/face mask due to facial discomfort, sinus pain, or claustrophobia from masks. A BiPAP device with a backup rate feature (e.g., adaptive servoventilation, VPAP Adapt SV) is considered experimental and investigational for obstructive sleep apnea (see CPB 0452 - Noninvasive Positive Pressure Ventilation).

   Replacement of positive airway pressure devices is considered medically necessary at the end of their 5-year reasonable useful lifetime (RUL). Replacement of these items is considered medically necessary prior to the end of the 5-year RUL due to a change in the member's condition. Replacement needed due to misuse or abuse are not covered.

B. The following accessories and supplies are considered medically necessary for members who meet criteria for positive airway pressure devices:

   ■ Chinstrap
   ■ Disposable or non-disposable filters
   ■ Full face mask with positive airway pressure device*
   ■ Headgear
   ■ Heated or non-heated humidifier
   ■ Nasal interface (mask or cannula type) for positive airway pressure device
   ■ Oral interface for positive airway pressure device
   ■ Replacement cushions and pillows for nasal application device
   ■ Replacement interface for full face mask
   ■ Tubing for heated or non-heated humidifier.

* A nasal interface (mask or cannula type) may be used with a positive airway pressure device, with or without a head strap as an alternative to a full face mask. However, upgraded face mask is considered medically necessary only if there is documentation that the member needs a different mask because he/she can not maintain CPAP pressures or that in order to get the pressure the mask needs to be so tight as to generate pressure sores.

The following positive airway pressure supplies are considered not medically necessary convenience items:

Positive airway pressure bed pillows
Batteries for positive airway pressure devices
DC adapters for positive airway pressure devices

Note: Aetna follows Medicare DME MAC rules with respect to the usual medically necessary quantity of supplies for positive airway pressure devices.

Upon individual review, positive airway pressure devices are considered a medically necessary form of non-invasive ventilation for members with lung disease without OSA. See CPB 0452 - Noninvasive Positive Pressure Ventilation. Requests for these devices for non-invasive ventilation of members with lung disease are subject to medical review.

C. Continued Medical Necessity of Positive Airway Pressure Devices Beyond Initial Authorization Period

Continued use of a positive airway pressure device beyond the initial authorization period is considered medically necessary if the treating physician documents that the member is benefiting from positive airway pressure therapy. Documentation of clinical benefit is demonstrated by:

1. Face-to-face clinical reevaluation by the treating physician with documentation that symptoms of obstructive sleep apnea are improved; *and*
2. Objective evidence of adherence to use of the positive airway pressure device, reviewed by the treating physician. Adherence to therapy is defined as use of positive airway pressure four (4) or more hours per night on at least 70% of nights during a consecutive thirty (30) day period anytime during the initial period of usage.

D. Oral Appliances

Mandibular advancement oral appliances to reduce upper airway collapsibility or tongue retaining devices are considered medically necessary for members who have sleep test results that meets one of the following criteria:

1. The AHI or RDI is greater than or equal to 15 events per hour with a minimum of 30 events; or

2. The AHI or RDI is greater than or equal to 5 and less than 15 events per hour with a minimum of 10 events and documentation of:

   a. Documented history of stroke; or
   b. Documented hypertension (systolic blood pressure greater than 140 mm Hg and/or diastolic blood pressure greater than 90 mm Hg); or
   c. Documented ischemic heart disease; or
   d. Documented symptoms of impaired cognition, mood disorders, or insomnia; or
   e. Excessive daytime sleepiness (documented by either Epworth greater than 10 or MSLT less than 6); or
   f. Greater than 20 episodes of oxygen desaturation (i.e., oxygen saturation of less than 85 %) during a full night sleep study, or any 1

episode of oxygen desaturation (i.e., oxygen saturation of less than 70 %).

3. If the AHI is greater than 30 or the RDI is greater than 30 and meets either of the following:

   a. The member is not able to tolerate a positive airway pressure (PAP) device; or
   b. The use of a PAP device is contraindicated.

E. Oral appliances to reduce upper airway collapsibility are considered experimental and investigational for indications other than OSA. For policy on oral occlusal appliances used to treat temporomandibular joint (TMJ) disorders, see CPB 0028 - Temporomandibular Disorders.

Replacement of oral appliances is considered medically necessary at the end of their 5-year RUL. Replacement of these items is considered medically necessary prior to the end of the 5-year RUL due to a change in the member's condition. Replacement needed due to misuse or abuse are not covered.

Note: All follow-up care, including fitting, adjustments, modifications, professional services (not all-inclusive) required during the first 90 days after provision of the oral appliance are considered to be included in the payment for device.

Note: Dental rehabilitation services (dentures, bridgework, etc.) as treatment for OSA, even if medically necessary, are not available benefits under standard Aetna health insurance plans. Members should review their dental benefits plan, if any.

F. Uvulopalatopharyngoplasty (UPPP)

Uvulopalatopharyngoplasty is used to treat OSA by enlarging the oropharynx; it is considered medically necessary for OSA members who meet the criteria for CPAP or AutoPAP (see above), but who are intolerant to CPAP or AutoPAP. The medical records must document that the member has attempted CPAP or AutoPAP before considering surgery.

Uvulopalatopharyngoplasty has been found to be most reliably effective in OSA members who have adequately responded to a trial of CPAP or AutoPAP. If CPAP or AutoPAP is unsuccessful in relieving a member's symptoms, this indicates that apnea is not due to obstruction. Aetna considers this procedure experimental and investigational for persons who do not respond to CPAP or AutoPAP because this surgical approach has not been shown to be effective in non-obstructive apnea.

G. Uvulectomy and Laser Assisted Uvuloplasty (LAUP)

Cold knife uvulectomy and laser assisted uvuloplasty (LAUP, laser uvulectomy) are considered experimental and investigational for OSA because they have not been shown to be as effective as UPPP for this indication. However, Aetna may consider these procedures medically necessary, upon individual case review, for members with severe OSA who have other medical conditions that make them unable to undergo

UPPP and have failed a trial of CPAP or AutoPAP or the use of an oral appliance or device. Note: Uvulectomy is considered medically necessary as an emergent treatment for acute edema of the uvula causing acute respiratory distress. Uvulectomy is considered experimental and investigational as a treatment for recurrent throat infections and for all other indications.

H. Somnoplasty and Coblation

Aetna considers radiofrequency ablation of the tongue base, uvula or soft palate (Somnoplasty) or of the nasal passages and soft palate (Coblation) experimental and investigational as a treatment for OSA because there is inadequate scientific evidence to validate the effectiveness of these procedures for this indication. Please see CPB 0592 - Radiofrequency Ablation of Hypertrophied Nasal Turbinates.

I. The Repose (AIRvance Tongue Suspension) System and the Encore Tongue Base Suspension

Aetna considers the AIRvance Tongue Suspension (formerly Repose) System, a minimally invasive technique involving tongue base suspension, and the Encore tongue base suspension, experimental and investigational. These procedures, also referred to as tongue stabilization, tongue stitch or tongue fixation, have been used for treating sleep disordered breathing (SDB) caused by tongue base collapse. No specific criteria exist regarding the diagnosis of tongue base collapse in SDB. Preliminary short-term studies of surgery targeted to alleviate tongue base collapse in SDB have shown subjective improvements in snoring and statistically significant decreases in mean RDI. However, the reported rates of success have been inconsistent among studies, and larger controlled studies with long-term follow-up are necessary to determine whether these lingual suspension procedures safe and effective.

J. Pediatric Obstructive Sleep Apnea Syndrome (OSAS): Tonsillectomy and Adenoidectomy

See CPB 0752 - Obstructive Sleep Apnea in Children.

K. Adult Lingual or Pharyngeal Tonsillectomy

Aetna considers adult lingual or pharyngeal tonsillectomy experimental and investigational for the treatment of adult OSA. Aetna considers adult tonsillectomy medically necessary for members with symptomatic tonsillar hypertrophy. Note: A tonsillectomy is considered an integral component of a uvulopalatopharyngoplasty and is not separately reimbursed.

L. Jaw Realignment Surgery (i.e., hyoid myotomy and suspension, mandibular osteotomy, genioglossal advancement)

Aetna considers jaw realignment surgery medically necessary for persons who fail other treatment approaches for OSA.

Although jaw realignment surgery may be considered medically necessary on an individual case basis, because of the extent of surgery, these cases may be subject to review by Aetna's Oral and Maxillofacial Surgery Unit to assess medical necessity.

Note: According to the medical literature, persons undergoing jaw realignment surgery must usually also undergo orthodontic therapy to correct changes in occlusion associated with the surgery. Orthodontic therapy (i.e., the placement of orthodontic brackets and wires) is excluded from coverage under standard Aetna medical plans regardless of medical necessity. Please check benefit plan descriptions for details. Benefits for orthodontic therapy may be available under the member's dental plan, if any.

M. Tracheostomy

Aetna considers tracheostomy medically necessary for those members with the most severe OSA not manageable by other interventions. Requests for tracheostomy for OSA are subject to medical review. Note: Aetna follows Medicare DME MAC rules for the medically necessary quantity of tracheostomy supplies for OSA and other indications.

N. Cardiac (Atrial) Pacing

Aetna considers cardiac (atrial) pacing for treatment of OSA experimental and investigational because the effectiveness of this procedure for OSA has not been established.

O. Injection Snoreplasty

Aetna considers injection snoreplasty, injection of a sclerosing agent into the soft palate, experimental and investigational for the treatment of OSA because its effectiveness for this indication has not been established. Treatment of snoring alone, without significant OSA, is not considered medically necessary

P. Cautery-Assisted Palatal Stiffening Operation (CAPSO)

Aetna considers cautery-assisted palatal stiffening operation (CAPSO) experimental and investigational for the treatment of OSA because its effectiveness for this indication has not been established.

Q. Pillar™ Palatal Implant System

Aetna considers the Pillar Palatal Implant System (Restore Medical, Inc.) experimental and investigational for the treatment of OSA and all other indications because its effectiveness for this and other indications has not been established.

R. Flexible Positive Airway Pressure

Aetna considers flexible positive airway pressure (C-Flex, Respironics) experimental and investigational because its effectiveness has not been established.

S. Transpalatal Advancement Pharyngoplasty

Aetna considers transpalatal advancement pharyngoplasty experimental and investigational for the treatment of OSA because its effectiveness has not been established.

T. Nasal Surgery

Aetna considers nasal surgery (including nasal valve surgery, polypectomy, septoplasty, turbinectomy) experimental and investigational for the treatment of OSA because its effectiveness has not been established.

U. The Advance System

Aetna considers the Advance System (an adjustable tongue-advancement device) experimental and investigational for the treatment of OSA because its effectiveness has not been established.

V. Tongue Base Reduction Surgery

Aetna considers tongue base reduction surgery experimental and investigational for the treatment of OSA because its effectiveness has not been established.

W. Partial Glossectomy

Aetna considers partial glossectomy experimental and investigational for the treatment of OSA because its effectiveness has not been established.

X. The Provent Sleep Apnea Therapy

Aetna considers the Provent sleep apnea therapy experimental and investigational for the treatment of OSA because its effectiveness has not been established.

Y. The Zzoma Positional Device

Aetna considers the Zzoma positional device not medically necessary because it has not been proven to be superior to other interventions to keep a person in a non-supine position.

Z. Nasal Dilators

Aetna considers nasal dilators experimental and investigational for the treatment of OSA because their effectiveness has not been established.

AA. Apnea-Triggered Muscle Stimulation

Aetna considers apnea-triggered muscle stimulation experimental and investigational for the treatment of OSA because its effectiveness has not been established.

AB. The Winx Therapy System/Oral Pressure Therapy

Aetna considers the Winx therapy system/oral pressure therapy experimental and investigational for the treatment of OSA because of insufficient evidence in the peer-reviewed published medical literature of its effectiveness and safety.

AC. Hypoglossal Nerve Neurostimulation

Aetna considers hypoglossal nerve neurostimulation (e.g., the Apnex Hypoglossal Nerve Stimulation (HGNS™) System, the aura6000™ Neurostimulation System,

ImThera's Targeted Hypoglossal Neurostimulation Therapy, Inspire® II System for Upper Airway Stimulation (UAS) Therapy, and WellStar upper airway neurostimulation implant)

AD. Expansion Sphincteroplasty

Aetna considers expansion sphincteroplasty experimental and investigational for the treatment of adult OSA because of insufficient evidence in the peer-reviewed published medical literature of its safety and effectiveness.

See also CPB 0330 - Multiple Sleep Latency Test (MSLT), CPB 0452 - Noninvasive Positive Pressure Ventilation, and CPB 0456 - Pillows and Cushions.

Background

Airway obstruction during sleep is a commonly recognized problem, which may be associated with significant morbidity. Various diagnostic studies and treatment approaches are employed in managing this condition.

Data from the history and physical examination have been shown to be sensitive but not specific for diagnosing obstructive sleep apnea (OSA). According to available guidelines (ICSI, 2006), the following signs and symptoms may suggest significant risk for OSA: reported apneas by sleep partner; awakening with choking; intense snoring; severe daytime sleepiness, especially with impairment of driving; male gender and post-menopausal females; obesity (body mass index [BMI] greater than or equal to 30); large neck circumference; and hypertension.

Diagnostic tests for OSA can be classified into 4 types. The most comprehensive type is Type I: attended, or in-facility polysomnography (PSG). There are 3 categories of portable monitors (used in both attended and unattended settings). Type II monitors have a minimum of 7 channels (e.g., electroencephalogram (EEG), electrooculogram (EOG), electromyogram (EMG), electrocardiogram (ECG), heart rate, airflow, respiratory effort, oxygen saturation). Type III monitors have a minimum of 4 monitored channels including ventilation or airflow (at least 2 channels of respiratory movement or respiratory movement and airflow), heart rate or ECG, and oxygen saturation. Type IV are all other monitors that fail to fulfill criteria for type III monitors. These are split into 2 subgroups: those assessing 3 or more bioparameters (i.e., most newer monitors fall here) and those assessing 1 or 2 bioparameters (i.e., the original ASDA level IV category) (see Appendix B).

There is no "gold standard" for the diagnosis of OSA in adults. NPSG performed in a sleep laboratory (Type I) is a definitive diagnostic tool to confirm the presence and severity of upper airway obstruction. According to current guidelines, a minimum 6-hour NPSG is preferred, which allows for the assessment of variability related to sleep stage and position with respect to the frequency of obstructive respiratory events and the occurrence of other types of nocturnal events such as periodic limb movements.

According to the available literature, NPSG performed in a sleep laboratory should include EEG, EOG, EMG, oronasal airflow, chest wall effort, body position, snore microphone, ECG, and oxyhemoglobin saturation. However, diagnostic NPSG may be performed in a healthcare facility, or for appropriate cases, in the patient's home. The use of unattended home sleep monitoring using a Type II, III, or IV device, may identify apnea-hypopnea index (AHI) suggestive of OSAHS. A technology assessment by the Agency for Healthcare Research and Quality (AHRQ) on *Home Diagnosis of Obstructive Sleep Apnea-Hypopnea Syndrome* (2007) commissioned by the Centers

for Medicare & Medicaid Services (CMS), reported the following: Type II monitors identify AHI suggestive of obstructive sleep apnea-hypopnea syndrome (OSAHA) with high positive ratios (greater than 10) and low negative likelihood ratios (less than 0.1) both when the portable monitors were studied in the sleep laboratory and at home. Type III monitors may have the ability to predict AHI suggestive of OSAHA with high positive likelihood ratios and low negative likelihood ratios for various AHI cut-offs in laboratory-based PSG, especially when manual scoring is used. The ability of type III monitors to predict AHI suggestive of OSAHS appears to be better in studies conducted in sleep laboratories compared to studies in the home setting. Some studies of type IV devices also showed high positive likelihood ratios and low negative likelihood ratios, at least for selected sensitivity and specificity pairs from ROC curve analyses. Similarly to type III devices, the ability of type IV devices to predict AHI suggestive of OSAHS appears to be better in studies conducted in sleep laboratories.

A Decision Memorandum from the Centers for Medicare & Medicaid Services (CMS, 2009) concluded that there is sufficient evidence to support the use of devices that measure 3 or more channels that include actigraphy, oximetry, and peripheral arterial tone (e.g., Watch-PAT 100, Itamar Medical, Inc.) to aid the diagnosis of OSA in persons who have signs and symptoms indicative of OSA if performed unattended in or out of a sleep lab facility or attended in a sleep lab facility. An assessment by the California Technology Assessment Forum (Tice, 2009) found sufficient evidence to support the use of the Watch-PAT device for diagnosis of OSA.

Clinical guidelines on the use of unattended home (portable) monitoring devices for the diagnosis of obstructive sleep apnea in adults, from the American Academy of Sleep Medicine (Collop, et al., 2007) for the diagnosis of OSA should be performed only in conjunction with a comprehensive sleep evaluation. The guidelines state that unattended sleep studies are not appropriate for the diagnosis of OSA in patients with significant comorbid medical conditions that may degrade the accuracy of unattended sleep studies, including moderate to severe pulmonary disease, neuromuscular disease, or congestive heart failure. The guidelines note that unattended sleep studies are not appropriate for the diagnostic evaluation of OSA in patients suspected of having other sleep disorders. The guidelines state that unattended sleep studies are not appropriate for general screening of asymptomatic populations.

According to the American Academy of Sleep Medicine (AASM) guidelines (Collop et al, 2007), unattended sleep studies may be indicated for the diagnosis of OSA in patients for whom in-laboratory NPSG is not possible by virtue of immobility, safety, or critical illness. Unattended sleep studies may be indicated to monitor the response to non-continuous positive airway pressure (CPAP) treatments for obstructive sleep apnea, including oral appliances, upper airway surgery, and weight loss. The guidelines note that in laboratory NPSG may be indicated in cases where unattended sleep studies are technically inadequate or fail to establish the diagnosis of OSA in patients with a high pretest probability.

According to the American Sleep Disorders Association (ASDA) (1997), split-night study NPSG is indicated for patients with an AHI greater than 40 events/hour during the first 2 hours of a diagnostic NPSG. Split-night studies may also be considered for patients with an AHI of 20 to 40 events/hour, based on clinical observations, such as the occurrence of obstructive respiratory events with a prolonged duration or in association with severe oxygen desaturation. Split-night studies require the recording and analysis of the same parameters as a standard diagnostic NPSG. Accepted guidelines provide that the diagnostic portion of a split-night study should be at least 2 hours duration. A minimum of 3 hours sleep is preferred to adequately titrate CPAP after this treatment is initiated.

Following a standard diagnostic NPSG, the available literature indicates that OSA patients should receive CPAP titration to specify the lowest CPAP level, which abolishes obstructive apneas, hypopneas, respiratory-effort related arousals, and snoring in all sleep positions and sleep stages. On occasion, an additional full-night CPAP titration NPSG may also be required following split-night study if the split-night NPSG did not allow for the abolishment of the vast majority of obstructive respiratory events or prescribed CPAP treatment does not control clinical symptoms. Alternatively, persons diagnosed with portable monitoring may be prescribed an auto-titrating positive airway pressure device (AutoPAP) that does not require attended titration.

According to guidelines from the American Academy of Sleep Medicine (Chesson et al, 1997), polysomnography with video recording and additional EEG channels in an extended bilateral montage may be indicated to assist with the diagnosis of paroxysmal arousals or other sleep disruptions that are thought to be seizure related when the initial clinical evaluation and results of a standard EEG are inconclusive.

Accepted guidelines indicate that nocturnal pulse oximetry alone is not appropriately used as a case finding or screening method to rule out OSA. Pulse oximetry, when used alone, has not been shown to have an adequate negative predictive value to rule out OSA (i.e., all patients with symptoms suggestive of OSA would require polysomnography regardless of whether the pulse oximetry was positive or negative).

The MESAM and the static charge sensitive bed have not been proven to be valid devices for screening or diagnosing OSA. Actigraphy has not been validated as a method of screening or diagnosing OSA although it may be a useful adjunct to other procedures in the evaluation of sleep disorders.

Although the cephalometric x-ray is not necessary for the diagnosis of OSA, it is necessary for certain non-surgical and surgical treatments. A lateral cephalometric x-ray is very helpful if an anterior mandibular osteotomy is being performed for genioglossus advancement, or if maxillomandibular surgery is being planned for surgical correction of OSA. It is also helpful in analyzing hyoid position, posterior airway space, and other cephalometric parameters used in the treatment of OSA. For sleep apnea appliances for OSA, a pre-treatment lateral cephalometric x-ray and a second cephalometric X-ray with the bite registration or appliance in place may be necessary to visualize the mandibular repositioning and the changes in the airway space.

Uvulopalatopharyngoplasty (UPPP), jaw realignment surgery, positive airway pressure devices (e.g., CPAP, BiPAP, etc.), tracheostomy, tonsillectomy and adenoidectomy, and orthodontic devices such as the tongue retaining device, may be effective treatments for properly selected patients with OSA.

Several small scale studies have examined adult tonsillectomy as treatment for tonsil hypertrophy. Martinho et al (2006) evaluated seven moderately obese obstructive sleep apnea-hypopnea syndrome (OSAHS) with obstructive palatine tonsil hypertrophy patients who were treated with tonsillectomy. The authors reported that tonsillectomy resulted in a significant reduction in AHI post-operatively and concluded that tonsillectomy could be considered an option for obese OSAHS patients with significant tonsil hypertrophy when CPAP is not possible as the first choice of treatment.

Verse et al (2000) evaluated 11 patients with substantial tonsilar hypertrophy who had undergone tonsillectomy as single-treatment. The patient population included 5 patients with severe OSA, 4 with mild OSA, and 2 patients who were simple snorers with an AHI below 10. The results of 3 to 6

months of follow-up showed surgical response rates were 80 % in severe apneics and 100 % in mild apneics. However, Verse et al also noted that substantial tonsilar hypertrophy can rarely cause OSA in adults and that their patient population was carefully selected to determine if tonsillectomy was an effective and safe surgical option in treating this disorder.

With respect to simple tonsillectomy as a treatment for adult OSA, updates to the American Academy of Sleep Medicine practice parameters for the treatment of OSA state that classic upper airway surgical techniques such as nasal-septal reconstruction, cauterization, and tonsillectomy frequently fail to correct OSA (Aurora et al, 2010).

The Food and Drug Administration (FDA) has cleared numerous types of CPAP devices under the 510(k) process. These include but are not limited to many devices that allow a patient to wear a device that collects airflow and other patient measurements into a device that records data, while treating OSA with that device. The patient then takes the device to the physician and the physician downloads information that determines whether the patient has apnea sleep-related breathing disorder including OSA or needs further sleep studies or assessment. There are currently many sleep assessment devices on the market cleared by the FDA through the 510(k) process for use in the home. Patients may have a 3-month trial period of CPAP to assess appropriate therapeutic use and response. Reports obtained via a compliance monitor may be included when making this determination.

A variety of oral appliances and prostheses, including tongue retainers and mandibular advancing devices, have been used to treat patients with OSA. These devices modify the airway by changing the posture of the mandible and tongue. A task force of the Standards of Practice Committee of the ASDA concluded that, despite the considerable variation in the design of these devices, their clinical effects in improving OSA have been consistent (Kushida et al, 2006). These devices have been shown to be effective in alleviating OSA, and present a useful alternative to CPAP or surgery (Ferguson et al, 2006; Gotsopoulos et al, 2002). Oral appliances, however, have been shown to be less reliable and effective than CPAP, and therefore the literature suggests that their use should generally be reserved for patients who are intolerant of CPAP. Oral appliances can be pre-fabricated or custom-fabricated. There is evidence of the efficacy of both pre-fabricated and custom-fabricated appliances for OSA (Vanderveken et al, 2008; Henke et al, 2000).

Patients with OSA suffer from numerous apneic events while sleeping, due to collapse of the upper airway during inspiration. Continuous positive airway pressure, and more recently, BiPAP, DPAP, VPAP, and AutoPAP, have been used in the treatment of OSA as a means of serving as a "pneumatic splint" in order to prop open the airways during inspiration.

Bilevel positive airway pressure, DPAP, and VPAP have been shown to be effective alternatives to CPAP, but are indicated only as second line measures for patients who are intolerant to CPAP. These alternatives to CPAP may also be indicated for OSA patients with concomitant breathing disorders to include restrictive thoracic disorders, COPD, and nocturnal hypoventilation. Long-term adherence to CPAP therapy was initially reported to range from 65 to 80 % (Nino-Murcia et al, 1989; Waldhorn et al, 1990; Rolfe et al, 1991; Hoffstein et al, 1992) with 8 to 15 % of patients refusing to accept treatment (Waldhorn, 1990; Krieger, 1992) after a single night's use. Other studies have evaluated compliance as regular CPAP use. More recent studies have shown up to 80 % of patients falling into the category of regular users (Pepin et al, 1999).

OPAP (Oral Pressure Appliance) is a custom fabricated intra-oral device that is used with a positive airway pressure device (e.g., CPAP, BiPAP, etc.) in place of a standard nasal mask. The oral pressure appliance positions the lower jaw forward to maximize the forward movement of the tongue and soft tissues of the back of the throat. In addition, the device has a chamber that,

according to the manufacturer, allows air flow and pressure to be delivered into the back of the throat and thereby "splint" the soft tissues of the upper airway and prevent their collapse during sleep. The oral pressure appliance is custom fitted by a dentist specializing in dental appliances for sleep disorders. The OPAP method of treatment is similar to nasal mask delivery of air pressure with CPAP or BiPAP. The oral pressure appliance is connected to the end of the hose coming from the CPAP or BiPAP, and the pressure is adjusted in the same way as through the nose. OPAP differs from nasal masks in that it does not require head gear to hold it in place. It is inserted into the mouth and held in place by the upper and lower teeth. At present, no studies of OPAP have been published in peer-reviewed medical journals. Therefore, one is unable to draw any conclusions about the effectiveness of OPAP compared to a standard nasal mask in treatment of patients with obstructive sleep apnea.

In contrast to fixed CPAP, flexible positive airway pressure (C-Flex, Respironics, Murraysville, PA) (also known as pressure-relief CPAP) is characterized by a pressure reduction at the beginning of expiration. Flexible positive airway pressure is intended to improve patient satisfaction and compliance over standard CPAP. To compare adherence and clinical outcomes between flexible positive airway pressure CPAP, Aloia et al (2005) conducted a nonrandomized, open-label controlled trial of CPAP therapy versus therapy using the C-Flex device in persons with moderate-to-severe OSA. Study participants received either therapy with CPAP (n = 41) or with the C-Flex device (n = 48), depending on the available treatment at the time of recruitment, with those recruited earlier receiving CPAP therapy and those recruited later receiving therapy with the C-Flex device. The mean (+/- SD) treatment adherence over the 3-month follow-up period was higher in the C-Flex group compared to the CPAP group (weeks 2 to 4, 4.2 +/- 2.4 versus 3.5 +/- 2.8, respectively; weeks 9 to 12, 4.8 +/- 2.4 versus 3.1 +/- 2.8, respectively). The investigators reported that change in subjective sleepiness and functional outcomes associated with sleep did not improve more in one group over the other. Self-efficacy showed a trend toward being higher at the follow-up in those patients who had been treated with the C-Flex device compared to CPAP treatment. The investigators concluded that therapy with the C-Flex device may improve overall adherence over 3 months compared to standard therapy with CPAP. The investigators stated that clinical outcomes do not improve consistently, but C-Flex users may be more confident about their ability to adhere to treatment. The investigators concluded that randomized clinical trials are needed to replicate these findings.

A study by Nilius et al (2006) found no significant differences between C-Flex and CPAP in effectiveness and compliance. During the first night of treatment, patients receiving C-Flex had less dryness of the mouth, but this difference disappeared over a period of 7 weeks. The investigators conducted a study to compare polysomnographic data and compliance in sleep apnea patients receiving continuous positive airway pressure (CPAP) and C-Flex. A total of 52 persons newly diagnosed with OSA underwent conventional CPAP titration. Thereafter, polysomnography was performed at the titrated pressure using both the fixed CPAP pressure mode and the C-Flex mode in a randomized crossover approach. The patients were then discharged home for 7 weeks of treatment with the last-applied treatment mode, and compliance data were established at the end of that time. The average AHI was 5.8/hour with CPAP, and 7.0/hour with C-Flex. The investigators reported that compliance after 7 weeks was, on average, 9.4 mins longer with C-Flex than with CPAP, a difference that was not statistically significant. Evaluation of a 13-item questionnaire (the fewer the complaints, the lower the score) showed no significant difference between scores for C-Flex (16.4) and CPAP (18.1). With regard to oral dryness, the score with C-Flex (1.4) was significantly lower than with CPAP (1.9) ($p < 0.05$). The investigators reported that this difference in oral dryness score was no longer detectable after 7 weeks. The investigators concluded that further studies are needed.

According to the Standard of Practice Committee of the American Academy of Sleep Medicine (Littner et al, 2002), central apnea may occur in some OSA patients with congestive heart failure (CHF) during CPAP titration after the airway obstruction of OSA is treated. Other patients with OSA may have central apneas after arousals as they fall back to sleep or which are the result of excessive CPAP pressure. Attempts to identify central apnea by detecting cardiac oscillations in the airflow tracing during polysomnography are not reliable because the airway can close during central apnea and the oscillations may not appear.

Adaptive servo-ventilation (ASV), a novel method of ventilatory support, is considered a bilevel positive airway pressure with a backup rate feature, and uses an automatic, minute ventilation-targeted device (VPAP Adapt, ResMed, Poway, CA) that performs breath to breath analysis and adjusts its settings accordingly. Depending on breathing effort, the device will automatically adjust the amount of airflow it delivers in order to maintain a steady minute ventilation. Most studies on the use of ASV have investigated its use for heart failure patients with central apnea or Cheyne-Stokes respiration (Teschler et al, 2001; Pepperell et al, 2003; Töpfer et al, 2004; Pepin et al, 2006; Kasai et al, 2006; Zhang et al, 2006; Banno et al, 2006; Morrell et al, 2007; Morgenthaler et al, 2007; Hastings et al, 2010). Consistent with Durable Medical Equipment Medicare Administrative Carrier (DME MAC) policy, bilevel positive airway pressure with a backup rate feature is considered experimental and investigational for OSA (NHIC, 2008).

While virtually all studies report that surgical treatment of OSA improves snoring and daytime sleepiness, improvements in objective outcomes have been inconsistent with successful results of UPPP ranging from 50 % to 75 %. Fujita is credited with developing the UPPP as a method of enlarging the oropharynx (Fujita et al, 1985). He based the UPPP on his observation that patients with OSA, without other obvious sites of obstruction, often have a large edematous uvula, wide posterior tonsillar pillar mucosa and redundant mucosal folds in the lateral posterior pharyngeal walls extending from the nasopharynx to the hypopharynx. The surgery attempts to remove the redundant tissue but preserve the underlying muscular layer. In brief, the mucosae and submucosae of the soft palate, tonsillar fossa and the lateral aspect of the uvula are resected. The posterior pillar may be resected if contributing to the narrowing. In essence the amount of tissue removed is individualized for each patient, determined by the potential space and the width of the tonsillar pillar mucosa between the 2 palatal arches (Fujita et al, 1985). For a detailed discussion of the UPPP technique and its variants see the review by Koopmann and Moran (1990).

The UPPP enlarges the oropharynx but cannot correct obstructions in the hypopharynx. Early on it was recognized that UPPP failed in about 50 % of unselected patients with OSA. Riley et al (1990) and Crumley et al (1987) proposed that these failures may have been caused by an obstruction at the base of the tongue. The surgical approach to this problem has been to either modify the tongue itself or reposition the tongue by repositioning the mandible and/or maxilla.

Riley and Guilleminault and colleagues at the Sleep Disorders Center at Stanford University (Palo Alto CA) have been the primary early advocates of maxillofacial surgery for those patients who fail other treatment approaches. A stepwise protocol has been described (Riley et al, 1986; Riley et al, 1989; Riley et al, 1990). For example a hyoid resuspension can be done at the time of a UPPP. In this procedure the hyoid is resuspended anteriorly and superiorly from the mandible with strips of fascia lata harvested from the thigh. In this way the tongue is moved anteriorly. If the patient fails this treatment, he/she then becomes eligible for the maxillary and mandibular osteotomy (MMO). While the purpose of this procedure is to enlarge the hypopharynx by advancing the mandible, the maxilla is also advanced to permit greater advancement of the mandible and to provide optimal esthetics. The maxilla is advanced by a Le Fort I osteotomy with rigid fixation and the mandible by a bilateral sagittal ramus split. The fixation must be maintained for one to three

weeks. If a dental malocclusion is created by this surgery, the MMO must be preceeded by a total mandibular subapical osteotomy with retropostioning of the dentition and bilateral repositioning of the inferior alveolar nerve. All 3 of the above procedures are frequently preformed in conjunction with removal of fatty tissue of the neck.

Jaw realignment is an aggressive, multi-step procedure requiring a 3- to 6-month interval between each step. According to the medical literature, jaw realignment surgery is generally reserved for those patients who fail other treatment approaches for OSA. An NIH Statement (1995) and American Sleep Disorders Association Guidelines (1996) state that jaw realignment surgery is a promising treatment for OSA. A systematic review of the evidence prepared for the American Sleep Disorders Association by Scher et al (1996), concluded that inferior sagittal mandibular osteotomy and genioglossal advancement with or without hyoid myotomy and suspension appears to be the most promising of procedures directed at enlarging the retrolingual region. The ASDA assessment stated that most of the experience with genioglossal advancement with or without hyoid suspension has been in conjunction with or following UPPP. Jaw fixation is necessary for 2 to 3 weeks following surgery, and a soft diet is necessary for a total of 6 weeks. Patients undergoing jaw realignment surgery must usually also undergo orthodontic therapy to correct changes in occlusion associated with the surgery. Jaw realignment surgery is generally reserved for those patients who fail other treatment approaches for OSA. According to the medical literature, patients undergoing jaw realignment surgery must usually also undergo orthodontic therapy to correct changes in occlusion associated with the surgery.

Tracheostomy, which simply bypasses the obstructing lesion of the upper airways, has been shown to be the most effective and predictable surgical approach to OSA. However, the social and medical morbidities of a permanent tracheostomy and the advent of surgical alternatives have made tracheostomy an unpopular solution to OSA, reserved for those patients with the most severe sleep apnea not manageable by other interventions.

Laser-assisted uvulopalatoplasty (LAUP) is an outpatient surgical procedure, which has been used as a treatment for snoring. LAUP has also been used as a treatment for sleep-related breathing disorders, including obstructive sleep apnea. The American Academy of Sleep Medicine Standards of Practice Committee reviewed the evidence supporting the use of LAUP in obstructive sleep apnea, and found that adequate controlled studies on the LAUP procedure for sleep-related breathing disorders were not found in the peer-reviewed literature (Littner et al, 2001). The AASM concluded that "LAUP is not recommended for treatment of sleep-related breathing disorders."

There is some evidence for the use of uvulectomy or uvuloplasty as a treatment for snoring, but Aetna does not consider treatment of snoring medically necessary because snoring, in itself, is not associated with functional limitations. Most of the published literature on uvulectomy have to do with ritual removal of the uvula at birth in Africa, a practice that is associated with significant complications. Uvulectomy is also performed, again primarily in Africa, as a treatment for recurrent throat infections. However, there is no reliable evidence to support this practice. Acute edema of the uvula causing respiratory distress is an accepted indication for uvulectomy. Hawke and Kwok (1987) reported on uvulectomy in treating a patient with acute inflammatory edema of the uvula (uvulitis) associated with asphyxiation. Waeckerle et al (1976) reported on uvulectomy for hereditary angioneurotic edema. There is no evidence to support the use of uvulectomy as a treatment for gagging. Dawodu (2007) reported that gagging may occur as a complication of uvulectomy.

Radiofrequency ablation may be used to reduce and tighten excess tissues of the soft palate, uvula and tongue base (Somnoplasty) or nasal passages and soft palate (Coblation or Coblation channeling). These procedures are performed in an outpatient setting under local anesthesia.

Current literature does not support their efficacy and applicability for OSA. Most published studies have been nonrandomized and have enrolled highly selected patients. These studies also fail to report long-term outcomes or recurrence rates. Woodson et al (2003) reported on the results of radiofrequency ablation of the turbinates and soft palate in patients with mild to moderate obstructive sleep apnea (AHI of 10 to 30 on screening sleep study). A total of 90 subjects were randomly assigned to radiofrequency ablation, CPAP, or sham-placebo. Subjects assigned to radiofrequency ablation had a moderate decrease in AHI that did not reach statistical significance. The AHI of subjects assigned to radiofrequency ablation decreased by an average of 4.5 events/hour, whereas the AHI of subjects assigned to sham-placebo decreased by an average of 1.8 events/hour, a difference that did not achieve statistical significance. However, compared with sham-placebo, subjects assigned to radiofrequency ablation reported statistically significant improvements in quality of life, airway volume, apnea index and respiratory arousal index. In addition to the modest impact of radiofrequency ablation on AHI, this study has a number of other important limitations. First, it is a relatively small study, and improvements were not consistently seen among each of the measured parameters. Second, a significant number of subjects were lost to follow-up, and data were incomplete on 25 % of study subjects. Third, the study does not report on long-term clinical outcomes or recurrence rates. Fourth, although this study did not involve a direct comparison with UPPP, which is the current surgical standard treatment for OSA, studies of UPPP have reported much more substantial improvements in AHI, AI and other relevant parameters. Finally, this study involved a single investigator group and is the only published randomized clinical study of radiofrequency ablation for OSA; this study needs to be replicated by other investigators and in larger numbers of subjects.

A recent study (Garrigue et al, 2002) reported on the results of an uncontrolled case series examining the impact of atrial overdrive pacing in 15 patients with central or OSA syndrome who had received permanent atrial-synchronous ventricular pacemakers for symptomatic sinus bradycardia. With atrial overdrive pacing, achieved by increasing the atrial base rate, patients had a significantly reduced the number of episodes of central or OSA (from an average AHI of 28 with spontaneous rhythm to an average AHI of 11 with atrial overdrive pacing) without a significant reduction in total sleep time. The authors, however, concluded that further studies are needed to elucidate the mechanisms involved in achieving these reductions and to assess the precise role of cardiac pacing in preventing symptoms, disability, and death in patients with sleep apnea syndrome. In a randomized controlled trial, Luthje et al (2005) aimed to reproduce the finding of a recent study that atrial overdrive pacing markedly improved SDB. These investigators found that neither the primary endpoint AHI, nor the apnea index, oxygen desaturation, ventilation, biomarkers were affected by the nocturnal atrial overdrive pacing. They concluded that the lack of effect on the AHI means that atrial overdrive pacing is inappropriate for treating SDB. This is in agreement with the findings of a randomized controlled study by Pepin et al (2005) who reported that atrial overdrive pacing has no significant effect on OSA.

In a randomized controlled study, Simantirakis et al (2005) reported that atrial over-drive pacing had no significant effect in treating OSA-hypopnea syndrome. In another randomized controlled study, Krahn et al (2006) evaluated the impact of prevention of bradycardia with physiologic pacing on the severity of OSA. The authors concluded that temporary atrial pacing does not appear to improve respiratory manifestations of OSA, and that permanent atrial pacing in this patient population does not appear to be justified.

Upper airway resistance syndrome (UARS) is characterized by a normal AHI, but with sleep fragmentation related to subtle airway resistance. Guilleminault and colleagues (1993) considered UARS clinically significant if it entails greater than 10 episodes of EEG arousals/hour of sleep in patients with a documented history of excessive daytime sleepiness. They described UARS as

multiple sleep fragmentations resulting from very short alpha EEG arousals, which in turn are related to an increase in resistance to airflow. According to Guilleminault et al (1993), the resistance to airflow is subtle enough that it is not detected by routine sleep analysis, but can be detected with esophageal pressure tracings. In addition, UARS may not be associated with snoring, the classic symptom of OSA. However, there is no consensus on the criteria for diagnosis or indications for treatment of UARS. Neither the American Sleep Disorders Association nor any other professional medical organization has issued guidelines for the diagnosis and treatment of UARS.

Cautery-assisted palatal stiffening operation (CAPSO) is an office-based procedure performed with local anesthesia for the treatment of palatal snoring. A midline strip of soft palate mucosa is removed, and the wound is allowed to heal by secondary intention. The flaccid palate is stiffened, and palatal snoring ceases. Wassmuth et al (2000) evaluated the ability of CAPSO to treat OSA syndrome (OSAS). A total of 25 consecutive patients with OSAS underwent CAPSO. Responders were defined as patients who had a reduction in AHI of 50 % or more and an AHI of 10 or less after surgery. By these strict criteria, 40 % of patients were considered to have responded to CAPSO. Mean AHI improved significantly from 25.1 +/- 12.9 to 16.6 +/- 15.0. The Epworth Sleepiness Scale improved significantly from 12.7 +/- 5.6 to 8.8 +/- 4.6. Mair and Day (2000) analyzed data on CAPSO with regard to extent of surgery, need for repetition of procedure, results, complications, predictors of success. A totalof 206 consecutive patients underwent CAPSO over an 18-month period, followed by office examination and telephone evaluation. The success rate was initially 92 % and dipped to 77 % after 1 year. CAPSO eliminates excessive snoring caused by palatal flutter and has success rates that were comparable with those of traditional palatal surgery. The authors stated that CAPSO is a simple and safe office procedure that avoids the need for multiple-stage operations and does not rely on expensive laser systems or radiofrequency generators and hand pieces. The results of these studies appear to be promising; however their findings need to be verified by randomized controlled studies.

In a prospective, non-randomized study, Pang and Terris (2007) evaluated the effectiveness of CAPSO in treating snoring and mild OSA. A total of 13 patients with simple snoring and mild OSA underwent the modified CAPSO under local anesthesia. Patients had pre-operative polysomnography and at 3 months post-operatively; they were Friedman stage II and III, with tonsil size 0, 1, or 2. All patients had improvement in their snoring; 84 % had improvement in the Epworth Sleepiness Scale, from 12.2 to 8.9. Objective success on the polysomnogram was noted in 75 % of patients (6/8) with mild OSA. The AHI improved from 12.3 % to 5.2 % (p < 0.05), and the lowest oxygen saturation improved from 88.3 % to 92.5 % (p < 0.05). The authors concluded that the modified CAPSO is a simple, low-cost, and effective office-based method to treat snoring and mild OSA. The findings of this small study are promising. Randomized controlled trials with larger sample size and longer follow-up are needed to ascertain the clinical value of CAPSO.

The Pillar Palatal Implant System (Restore Medical, Inc.) is intended as a treatment option for snoring and OSA. The System consists of an implant and a delivery tool. The implants are designed to stiffen the tissue of the soft palate reducing the dynamic flutter which causes snoring. According to the manufacturer, the implants reduce the incidence of airway obstruction caused by the soft palate. The implant is a cylindrical shaped segment of braided polyester filaments. The delivery tool is comprised of a handle and needle assembly that allows for positioning and placement of the implant submucosally in the soft palate. The implant is designed to be permanent while the delivery tool is disposable.

Clinical information on Restore's website reported that with the Pillar Procedure, AHI was reduced in 13 of 16 patients (81.3 %) with a 53.4 % mean decrease for those 13 patients. Six of the 13 patients (46.2 %) experienced an AHI decrease of greater than 50 % along with a 90-day AHI of

less than 10. Ten of the 13 patients (76.9 %) decreased to an AHI less than 10. While these data appeared promising, larger prospective clinical studies with longer follow-up are needed in the peer-reviewed published literature to validate the effectiveness of this procedure for OSA.

In a retrospective review of 125 patients who underwent the Pillar implant for snoring and obstructive sleep apnea/hypopnea syndrome (OSAHS), Friedman and colleagues (2006) found that the Pillar implant is an effective treatment for snoring and OSAHS in selected patients and can be combined with adjunctive procedures to treat OSAHS. The major drawback of this study was that it was a short-term study. Well-designed studies with long-term follow-up are needed to determine the real value of this technique.

A structured assessment of the evidence for the Pillar procedure by Adelaide Health Technology Assessment for the Australian Department of Health and Ageing (Mundy et al, 2006) concluded: "Further investigation is required to establish which patients (mild or moderate obstructive sleep apnoea) would benefit the most from this procedure, and whether greater success would be achieved in conjunction with more invasive surgical procedures. In addition, long-term follow-up of obstructive sleep apnoea patients may indicate whether or not the observed reductions in AHI delivered a clinical benefit to these patients".

This is in agreement with the conclusions of an assessment by the Canadian Agency for Drugs and Technologies in Health (CADTH, 2007), which stated that there is currently insufficient published evidence to ascertain if palatal implants (e.g., the Pillar System) are an effective treatment option for patients with mild to moderate OSA due to palatal obstruction. The CADTH report further stated that larger, randomized controlled studies are needed to determine the long-term safety and effectiveness of the implants in a more diverse patient population, including those who are obese or those with co-morbid medical conditions. Comparisons with existing treatments for OSA are also needed.

An assessment by the National Institute for Health and Clinical Excellence (NICE, 2007) reached similar conclusions about the lack of reliable evidence of the effectiveness of palatal implants as a treatment for obstructive sleep apnea. The assessment concluded: "Current evidence on soft-palate implants for obstructive sleep apnoea (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 this condition".

In a prospective study, Nordgard et al (2007) assessed the long-term effectiveness of palatal implants for treatment of mild-to-moderate OSA. A total of 26 referred patients with a pre-treatment AHI of 10 to 30 and a BMI of less than or equal to 30, representing an extended follow-up of a subset of 41 patients enrolled in previous short-term trials were included. Twenty-one of 26 patients (80.8 %) experienced a decrease in AHI. Fifteen of 26 patients (57.7 %) had a follow-up AHI less than 10 at 1 year, whereas 13 patients (50 %) had a 50 % or greater reduction to an AHI less than 10 at 1 year. Mean AHI was reduced from 16.5 +/- 4.5 at baseline to 12.5 +/- 10.5 at 3 months (p < 0.014) and to 12.3 +/- 12.7 at 1 year (p < 0.019). The authors concluded that patients initially responding to palatal implants with improved AHI maintained improvement through long-term follow-up at 1 year. The main drawback of this study was its small sample size. The authors noted that additional studies with longer follow-up would be appropriate.

In a continuation of a prospective case series, Walker et al (2007) assessed the long-term safety and outcomes of palatal implants for patients with mild-to-moderate OSA. Polysomnography, daytime sleepiness, and snoring intensity were measured at baseline, 90 days, and extended follow-up. A total of 22 (42 %) patients from the previous study were followed for a median of 435.5

days. Thirteen were classified as responders, based on their 90-day evaluation; 76.9 % of initial responders maintained improvements in AHI, daytime sleepiness, and snoring at extended follow-up. Nine patients were initial non-responders for AHI and daytime sleepiness and remained unchanged at extended follow-up. However, snoring for these 9 patients initially improved, and the improvement continued through extended follow-up. The authors concluded that initial response or non-response to palatal implants remains stable over an extended period. However, they noted that the generalizability of these results is unknown because of significant loss to follow-up (31 of 53 or 58 %). Other drawbacks of this study were small sample size, lack of randomization, as well as selection bias that can occur among patients who chose to participate in a follow-up study.

In a multi-institution, randomized, placebo-controlled study, Steward and colleagues (2008) examined the effectiveness of Pillar palate implants for OSA. A total of 100 patients with mild-to-moderate OSA and suspected retropalatal obstruction were randomly assigned treatment with three palatal implants or sham placebo. Final AHI increased for both groups at 3 months, correlating with increased percentage of supine sleep but was less in the implant group (p = 0.05). A clinically meaningful reduction in AHI (greater than or equal to 50 % reduction to less than 20) was more common in the implant group (26 % versus 10 %, p = 0.05). Significant differences were noted for changes in lowest oxyhemoglobin saturation (p = 0.007) and Functional Outcomes of Sleep Questionnaire (p = 0.05). Improvement in Epworth Sleepiness Score did not differ from that of sham (p = 0.62). Partial implant extrusion occurred in 2 patients (4 %). The authors concluded that palate implants for mild-to-moderate OSA showed effectiveness over placebo for several important outcomes measures with minimal morbidity, but overall effectiveness remains limited. They stated that further study is needed.

In a randomized, double-blind, placebo-controlled study, Gillespie et al (2011) examined if the Pillar palatal implant system reduces CPAP pressure and improves patient compliance with CPAP therapy. Subjects with mild-to-moderate sleep apnea dissatisfied with CPAP because of pressure-related complaints were randomized to receive Pillar implants or a sham procedure performed in double-blind fashion. Active and sham groups were compared for changes in therapeutic CPAP pressures (primary outcome) with a 90-day follow-up sleep study and CPAP compliance (secondary outcome) with a 90-day smart card report. A total of 26 subjects were randomized to Pillar implants and 25 to a sham implant procedure. There were no differences between groups with regard to demographics and baseline parameters. Both sham and active groups had reduced mean CPAP pressure (-1.1 versus -0.5 cm H(2)O) with no difference between groups (p = 0.32) at 90-day follow-up. In addition, there was no difference in average daily CPAP use between groups (p = 0.80). Both groups experienced improvements in Epworth sleepiness scores and Functional Outcome of Sleep Questionnaire scores at 90 days with no differences between groups. The active group reported significantly higher CPAP satisfaction scores than the sham group (p = 0.04). The authors concluded that Pillar implants do not significantly reduce CPAP pressure or increase CPAP compliance compared to sham controls but marginally improve subjective CPAP satisfaction (but the reason for this is unclear). These findings do not presently support the use of Pillar implants as an adjunctive treatment to improve CPAP compliance.

In a Cochrane review, Smith et al (2006) ascertained the effectiveness of drug therapies in the treatment of OSA. The authors concluded that there is insufficient evidence to recommend the use of drug therapy in the treatment of OSA. They noted that small studies have reported positive effects of certain agents on short-term outcome. Certain agents have been shown to reduce the AHI in largely unselected populations with OSA by between 24 and 45 %. For fluticasone, mirtazipine, physostigmine and nasal lubricant, studies of longer duration are needed to establish if this has an impact on daytime symptoms. Individual patients had more complete responses to

particular drugs. It is likely that better matching of drugs to patients according to the dominant mechanism of their OSA will lead to better results and this also requires more investigation.

Transpalatal advancement pharyngoplasty (TAP) changes the retro-palatal airway by advancing the palate forward without excising the soft palate. The TAP procedure has been employed alone or in combination with other soft tissue surgeries for patients with narrowing in the retro-palatal airway, in particular, narrowing proximal to the point of palatal excision using traditional UPPP techniques. A transpalatal approach and advancement has also been advocated for individuals with obstructions in the nasopharynx that can not be accessed through traditional techniques. However, to date, there is very little published outcomes data for patients with OSA. Woodson (2005) described the findings of 30 subjects who underwent TAP; 20 of them also had various tongue-base procedures performed at the same time as TAP. Only 10 had TAP alone. Post-operative AHI in these 30 patients was better than a comparable group of 44 patients undergoing UPPP, 26 of whom had UPPP as the sole procedure. In addition, for the patients in each group who did not have additional tongue base surgery, the AHI improved significantly more in the TAP-treated subjects (n = 10) than the UPPP-treated subjects (n = 26). Larger studies are needed to establish the safety and effectiveness of the TAP procedure, together with prospective comparisons with established palate-based surgical techniques.

It has been suggested that nasal surgery may improve subjective daytime complaints in patients with OSA. However, published reports have not demonstrated that reducing nasal obstruction and resistance from various causes and using various methods, (e.g., polypectomy, septoplasty, turbinectomy, and radiofrequency ablation of inferior nasal turbinates) correlates with a significant reduction in objective OSA indicators (e.g., AHI or nocturnal oxygen desaturation). In this regard, Kohler and colleagues (2007) stated that the impact of treating nasal obstruction in patients with snoring and OSA on long-term outcome remains to be defined through randomized controlled studies of medical as well as surgical treatments.

Koutsourelakis et al (2008) stated that although nasal surgery has limited effectiveness in OSA treatment, some patients experience improvement. These researchers tested the hypothesis that post-surgery improvement is associated with increased nasal breathing epochs. A total of 49 OSA patients (mean AHI 30.1 +/- 16.3 events x h(-1)) with symptomatic fixed nasal obstruction due to deviated septum were randomly assigned to either septoplasty (surgery group; n = 27) or sham surgery (placebo group; n = 22). The breathing route was examined during over-night polysomnography. All patients in the placebo group were non-responders, whereas in the surgery group 4 (14.8 %) patients were responders and exhibited considerable increase in nasal breathing epochs (epochs containing more than 3 consecutive phasic nasal signals), and 23 patients were non-responders, presenting a modest increase in nasal breathing epochs. The change in AHI was inversely related to the change in nasal breathing epochs, with responders exhibiting among the greatest increases in nasal breathing epochs. Baseline nasal breathing epochs were positively related to percent change in AHI. Responders had among the lowest baseline nasal breathing epochs; a cut-off value of 62.4 % of total sleep epochs best separated (100 % sensitivity, 82.6 % specificity) responders/non-responders. The authors concluded that nasal surgery rarely treats OSA effectively; but baseline nasal breathing epochs can predict the surgery outcome.

Lin and associates (2008) provided an overview of the literature on multi-level surgery for patients with OSA/hypopnea syndrome (OSAHS) patients. Articles were included only if the surgical intervention involved at least two of the frequently involved anatomical sites: nose, oropharynx, and hypopharynx. After applying specific inclusion criteria, 49 multi-level surgery articles (58 groups) were identified. There were 1,978 patients included in the study. The mean minimal follow-up time was 7.3 months (range of 1 to 100 months). A meta-analysis was performed to re-define the

success rate to be consistent with the commonly agreed upon criteria, namely "a reduction in the AHI of 50 % or more and an AHI of less than 20". "Success" implies an improved condition and is not meant to imply cure. The re-calculated success rate was 66.4 %. The overall complication rate was 14.6 %. The evidence-base medicine (EBM) level of these 49 studies revealed that only 1 study was EBM level 1, 2 papers were EBM level 3, and the other 46 papers were ranked as level 4 evidence. The authors concluded that multi-level surgery for OSAHS is associated with improved outcomes, although this benefit is supported largely by level 4 evidence. They stated that future research should focus on prospective and controlled studies. This is in agreement with the observation of Randerath et al (2007) who noted that combined surgeries in the sense of multi-level surgery concepts are of increasing interest in the secondary treatment of OSA following failure of nasal ventilation therapy although more evidence from prospective controlled trials are needed.

In a prospective, randomized cross-over study, Thomas et al (2003) compared the effectiveness of 2 tongue-base surgical procedures in the treatment of patients with moderate-to-severe sleep-disordered breathing. A total of 17 patients with moderate-to-severe sleep-disordered breathing and Fujita type II upper airway collapse for whom conservative treatment failed were enrolled in this study. They were randomly assigned to undergo palatopharyngoplasty combined with either tongue advancement (mandibular osteotomy) or tongue suspension. Parameters assessed included severity of sleep-disordered breathing (polysomnography), sleepiness (Epworth Sleepiness Scale [ESS]), and anatomic changes (upper airway endoscopy), as well as demographic factors. Patients not achieving satisfactory improvement in their condition were offered non-surgical management or additional surgical treatment that varied based on the post-operative assessment but included crossing-over to the other tongue surgical procedure. Nine of the 17 patients were randomized to the tongue suspension group, and 8 to the tongue advancement group. In the 9 tongue suspension patients, ESS scores fell from 12.1 to 4.1 (p = 0.007). Airway collapse for all 9 patients measured on Müller maneuver improved, by a mean of 64 % (p = 0.0006) at the palate and 83 % (p = 0.0003) at the base of the tongue. In the 8 tongue advancement patients, ESS scores fell from a mean of 13.3 to 5.4 (p = 0.004). Airway collapse for 5 of 8 patients measured on Müller maneuver improved by a mean of 31 % (p = 0.1) at the palate and 75 % (p = 0.03) at the base of the tongue. The authors concluded that prospective, randomized trials of tongue-base surgery for sleep-disordered breathing are possible. Preliminary findings from the current protocol reveal a slight advantage of tongue suspension over tongue advancement.

In a Cochrane review on surgery for OSA that included tongue advancement and tongue suspension, Sundaram et al (2005) concluded that 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. Subjects 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 individuals who undergo surgical correction of upper airway obstruction is needed. 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.

In a pilot study, Hamans et al (2008) examined the effectiveness of adjustable tongue advancement for the treatment of OSA. A total of 10 patients (mean age of 44 years) with moderate-to-severe OSA, i.e., an AHI between 15 and 50, with CPAP intolerance were included in this prospective, non-randomized, multi-center study to evaluate the feasibility, safety, and effectiveness of this novel procedure, which consists of the implantation of a tissue anchor in the tongue base and an adjustment spool at the mandible. Titration of this tissue anchor results in advancement of the tongue and a patent upper airway. The mean AHI decreased from 22.8 at baseline to 11.8 at the 6-

month follow-up (p = 0.007). The ESS score decreased from 11.4 at baseline to 7.7 at the 6-month follow-up (p = 0.094), and the snoring score decreased from 7.5 at baseline to 3.9 at the 6-month follow-up (p = 0.005). Four technical adverse events were noted, and 1 clinical adverse event occurred. The authors concluded that adjustable tongue advancement is a feasible and relatively safe way to reduce the AHI and snoring in selected patients with moderate-to-severe OSA and CPAP intolerance. Technical improvements and refinements to the procedure are ongoing.

In a phase II, prospective, multi-center, case series study, Woodson and colleagues (2010) examined the safety and effectiveness of a new surgical device for tongue suspension for OSA -- the Advance System (an adjustable tongue-advancement device). Surgically naive patients with moderate-to-severe OSA and tongue base obstruction (BMI less than 32, AHI 15 to 60) underwent surgical insertion of a mid-line tissue anchor into the posterior tongue and connected to an adjustable mandibular bone anchor with a flexible tether. Outcomes included changes in AHI, sleepiness (Epworth Sleepiness Scale), sleep-related quality-of-life (Functional Outcomes of Sleep Questionnaire), snoring, swallowing, speech, and pain (0 to 10 visual analog scale [VAS]). Following implantation of the device, 42 patients (mean age of 50 years, BMI 28) noted improvement at 6 months for AHI (mean [SD]: 35.5 [20.4] to 27.3 [18.8]), Epworth Sleepiness Scale (11.5 [3.9] to 7.8 [4.7]), and Functional Outcomes of Sleep Questionnaire (15.5 [2.6] to 17.5 [2.6], all p < 0.01). Snoring VAS scores improved (7.3 [2.1] to 4.7 [2.9], p < 0.01). Post-implantation pain scores were mild-to-moderate (4.4) at day 1 and resolved by day 5. Post-titration pain scores were mild (less than 2). Device-related adverse events included wound infection (7 %) and edema or seroma (5 %), which resolved. However, in 31 % of patients, asymptomatic tissue anchor barb fractures were observed radiographically. The authors concluded that the tissue anchor failure rate of the tested device precludes its clinical use; however, the study results support that a titratable, tongue-suspension device with low direct surgical morbidity in patients with moderate-to-severe OSA significantly improves multiple measures of sleep apnea. They stated that further investigation is warranted.

Obstructive sleep apnea has been reported to be common in medically refractory epileptic patients. Chihorek and colleagues (2007) examined if OSA is associated with seizure exacerbation in older adults with epilepsy. Polysomnography was performed in older adult patients with late-onset or worsening seizures (group 1, n = 11) and those who were seizure-free or who had improvement of seizures (group 2, n = 10). Patients in group 1 had a significantly higher AHI than patients in group 2 (p = 0.002). Group 1 patients also had higher Epworth Sleepiness Scale scores (p = 0.009) and higher scores on the Sleep Apnea Scale of the Sleep Disorders Questionnaire (p = 0.04). The two groups were similar in age, BMI, neck circumference, number of anti-epileptic drugs currently used, and frequency of nocturnal seizures. The authors concluded that OSA is associated with seizure exacerbation in older adults with epilepsy, and its treatment may represent an important avenue for improving seizure control in this population. Moreover, they noted that large, prospective, placebo-controlled studies are needed to ascertain if treatment of OSA (e.g., CPAP) improves seizures control in patients with epilepsy.

Malow and colleagues (2008) stated that small, uncontrolled case series suggested that treatment of OSA in patients with epilepsy may improve seizure control. These researchers addressed critical design issues in a pilot study before conducting a definitive, randomized, controlled trial.   They identified a cohort of adult patients with medically refractory epilepsy and co-existing OSA, documented by PSG. After an 8-week baseline period, subjects with OSA were randomized to therapeutic or sham CPAP for 10 weeks. Subjects maintained seizure calendars and anti-epileptic drug dosages were held constant. A total of 68 subjects with suspected OSA were enrolled and 35 subjects randomized to therapeutic CPAP (n = 22) or sham CPAP (n = 13). Male gender and an elevated sleep apnea questionnaire score were predictive of OSA on PSG. Nineteen subjects in

the therapeutic group and all 13 subjects in the sham group completed the trial. Baseline AHI and CPAP adherence were comparable between groups. A significant reduction in AHI was observed in the therapeutic CPAP group as compared to the sham group. Subjects, study co-ordinators, and principal investigators were unable to predict treatment allocation. The authors concluded that the findings of this pilot study provided critical information related to study design and feasibility for planning a comprehensive trial to test the hypothesis that treating OSA in patients with epilepsy improves seizure control. They stated that randomized, large-scale, multi-center clinical trials are needed to confirm these results.

The Provent sleep apnea therapy is a non-invasive treatment for OSA. The Provent nasal device uses a novel MicroValve design that attaches over the nostrils and is secured in place with hypo-allergenic adhesive. The MicroValve opens and closes, redirecting air through small holes to create resistance upon breathing out.

In a pilot study, Colrain and associates (2008) tested 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. A total of 30 men and women were recruited from the community and from the Stanford University Sleep Disorders Clinic; 24 had at least mild OSA (AHI greater than 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 counter-balanced across participants. The device consisted of a small valve inserted into each nostril calibrated to provide negligible inspiratory resistance, but increased expiratory resistance with a back pressure between 60 and 90 cm H2O*sec/Liter (at 100 ml/sec flow). Standard PSG was conducted to compare participants' sleep both with and without the device, with the scoring conducted blind to treatment condition. The AHI ($p < 0.001$) and oxygen desaturation (O2DI) ($p < 0.01$) indices both significantly decreased, and the percentage of the night spent above 90 % saturation ($p < 0.05$) significantly increased with device use. The observed amount of snoring ($p < 0.001$) was significantly decreased with device use, and there were no significant changes in measures of sleep architecture. The authors concluded that these findings were suggestive of a therapeutic effect of expiratory nasal resistance for some OSA patients and indicated that this technique is worthy of further clinical study. This trial examined the effect of the device over 1 day, and thus did not provide any information on the durability of the effect of the device in OSA.

In a multi-center study, Rosenthal et al (2009) evaluated the effectiveness of a novel device placed in the nares that imposes an expiratory resistance for the treatment of OSA and assessed adherence to the device over a 30-day in-home trial period. One diagnostic and 3 treatment polysomnograms were administered in a Latin-square design to identify the optimal expiratory resistance to be used during the 30-day in-home trial. Subjects had repeat PSG with the prescribed device at the end of the 30-day trial. Subjects (n = 34; aged 27 to 67 years) with a baseline AHI greater than or equal to 5 were included in this study. The AHI was reduced from 24.5 +/- 23.6 (mean +/- SD) to an average of 13.5 +/- 18.7 ($p < 0.001$) across initial treatment nights. The AHI was 15.5 +/- 18.9 ($p = 0.001$) for the prescribed device at the end of the 30-day trial. Of 24 subjects with an AHI greater than 10 at baseline, 13 achieved an AHI less than 10 on the initial treatment nights; 10 had a similar response on the final treatment night. Percent of the night snoring decreased from 27.5 +/- 23.2 to 11.6 +/- 13.7 ($p < 0.001$) on initial treatment nights and 14.6 +/- 20.6 ($p = 0.013$) at the end of the trial; Epworth Sleepiness scores decreased from 8.7 +/- 4.0 at baseline to 6.9 +/- 4.4 ($p < 0.001$) at the end of the trial; the Pittsburgh Sleep Quality Index improved from 7.4 +/- 3.3 to 6.5 +/- 3.6 ($p = 0.042$). Mean oxygen saturation increased from 94.8 +/- 2.0 to 95.2 +/- 1.9 ($p = 0.023$) on initial treatment nights and 95.3 +/- 1.9 ($p = 0.003$) at the end of the trial. Sleep architecture was not affected. Participants reported using the device all night long for 94 % of nights during the in-home trial. The authors concluded that treatment with this novel device was

well-tolerated and accepted by the participants. An overall reduction in AHI was documented; however, therapeutic response was variable among the participants. They stated that further research is needed to identify the ideal candidates for this new therapeutic option in the management of OSA. This small, uncontrolled trial, which showed a statistically significant impact on one of the primary endpoints, AHI, but a non-significant result for another endpoint, oxygen desaturation index. In addition, Provent has not been either compared to CPAP, or evaluated in persons who have failed CPAP. Although reduction in AHI with Provent was significant, patients on average still had clinically significant OSA (AHI greater than 5); by contrast, studies of CPAP have shown success in getting AHI below 5.

Walsh et al (2011) evaluated the short-term efficacy of and adherence with a convenient expiratory positive airway pressure (EPAP) nasal device was evaluated in OSA patients non-adherent with CPAP. Participants were OSA patients who refused CPAP or used CPAP less than 3 hrs/night. After demonstrating tolerability to the EPAP device during approximately 1 week of home use, patients underwent a screening/baseline polysomnogram (PSG1) and a treatment PSG (PSG2). Patients meeting pre-specified efficacy criteria underwent PSG3 after about 5 weeks of EPAP treatment. Forty-seven of 59 eligible patients (80 %) tolerated the device and underwent PSG1. Forty-three patients (27 males, 16 females; 53.7 ± 10.9 years) met apnea-hypopnea index (AHI) entry criteria and underwent PSG2. Mean AHI decreased from 43.3 ± 29.0 at baseline to 27.0 ± 26.7 (p < 0.001) at PSG2. Twenty-four patients (56 %) met efficacy criteria; their mean AHI was 31.9 ± 19.8, 11.0 ± 7.9, 16.4 ± 12.2 at PSG1, PSG2, and PSG3, respectively (p < 0.001, PSG1 versus both PSG2 and PSG3). Mean Epworth Sleepiness Scale (ESS) scores were 12.3 ± 4.8 at baseline, 11.1 ± 5.1 at PSG1, and 8.7 ± 4.4 at PSG3 (p = 0.001 compared to baseline). Device use was reported an average of 92 % of all sleep hours. The authors concluded that the improvements in AHI and ESS, combined with the high degree of treatment adherence observed, suggested that the convenient EPAP device tested may become a useful therapeutic option for OSA. Limitations of this study included lack of a sham or other comparative treatment, lack of objective method for measuring adherence data, small sample size and short duration of study, as well as frequent interaction by study staff.

Berry et al (2011) examined the efficacy of a novel nasal expiratory positive airway pressure (EPAP) device as a treatment for OSA. Patients were treated with a nasal EPAP device (n = 127) or similar appearing sham device (n = 123) for 3 months. Polysomnography (PSG) was performed on 2 non-consecutive nights (random order: device-on, device-off) at week 1 and after 3 months of treatment. Analysis of an intention- to-treat group (ITT) (patients completing week 1 PSGs) (EPAP n = 119, sham n = 110) was performed. At week 1, the median AHI value (device-on versus device-off) was significantly lower with EPAP (5.0 versus 13.8 events/hr, p < 0.0001) but not sham (11.6 versus 11.1 events/h, p = NS); the decrease in the AHI (median) was greater (-52.7 % versus -7.3 %, p < 0.0001) for the ITT group. At month 3, the percentage decrease in the AHI was 42.7 % (EPAP) and 10.1 % (sham), p < 0.0001. Over 3 months of EPAP treatment the Epworth Sleepiness Scale decreased (9.9 ± 4.7 to 7.2 ± 4.2, p < 0.0001), and the median percentage of reported nights used (entire night) was 88.2 %. The authors concluded that nasal EPAP device significantly reduced the AHI and improved subjective daytime sleepiness compared to the sham treatment in patients with mild to severe OSA with excellent adherence. The results of this study suggested that nasal EPAP is an effective treatment alternative for a substantial percentage of OSA patients. Limitations of this study included large number of exclusion criteria, and lack of objective method for measuring adherence data. Also, no baseline predictors of treatment success were identified by post hoc analysis.

Patel et al (2011) examine characteristics predictive of therapeutic response to the device and provided pilot data as to its potential mechanisms of action. A total of 20 subjects (15 males, 5

females, aged 54 ± 12 years, BMI 33.5 ± 5.6 kg/m²) with OSAHS underwent 3 nocturnal polysomnograms (NPSG) including diagnostic, therapeutic (with a Provent® nasal valve device), and CPAP. Additional measurements included intra-nasal pressures and PCO, closing pressures (Pcrit), and awake lung volumes in different body positions. In 19/20 patients who slept with the device, RDI was significantly reduced with the nasal valve device compared to the diagnostic NPSG (27 ± 29/hr versus 49 ± 28/hr), with 50 % of patients having an acceptable therapeutic response. Among demographic, lung volume, or diagnostic NPSG measures or markers of collapsibility, no significant predictors of therapeutic response were found. There was a suggestion that patients with position-dependent SDB (supine RDI greater than lateral RDI) were more likely to have an acceptable therapeutic response to the device. Successful elimination of SDB was associated with generation and maintenance of an elevated end expiratory pressure. No single definitive mechanism of action was elucidated. The authors concluded that the present study shows that the nasal valve device can alter SDB across the full spectrum of SDB severity. There was a suggestion that subjects with positional or milder SDB in the lateral position were those most likely to respond (but this observation needs to be confirmed in a larger study). An important limitation of this study was that these researchers did not directly assess lung volume during sleep. The authors noted that this pilot study was not able to establish predictors of success or a single definitive mechanism of action; but does help define a restricted list of candidates for further investigation.

Kryger et al (2011) evaluated the long-term durability of treatment response and safety of a nasal EPAP device used to treat OSA. Patients in the EPAP arm of the EPAP versus sham randomized study who used the EPAP device ≥ 4 hrs/night, ≥ 5 nights/week on average during months 1 and 2 of the 3-month trial and had ≥ 50 % reduction in AHI or AHI reduction to < 10 documented by polysomnography, comparing the 3-month device-on PSG to the week-one device-off PSG. Treatment with a nasal EPAP device (n = 41) for 12 months. Polysomnography (PSG) on the patients wearing the device was performed after 12 months of treatment. The month 12 device-on PSG data from the analyzable subject cohort (n = 34) was compared to the week 1 device-off PSG from the EPAP versus sham trial. Of the 51 patients eligible, 34 were still using the EPAP device at the end of 12 months. Median AHI was reduced from 15.7 to 4.7 events/hr (week 1 device-off versus month 12 device-on). The decrease in the AHI (median) was 71.3 % (p < 0.001). The median proportion of sleep time with snoring was reduced by 74.4 % (p < 0.001). Over 12 months of EPAP treatment, the Epworth Sleepiness Scale decreased (11.1 ± 4.2 to 6.0 ± 3.2, p < 0.001), and the median percentage of reported nights used (entire night) was 89.3 %. The authors concluded that nasal EPAP significantly reduced the AHI, improved subjective daytime sleepiness and reduced snoring after 12 months of treatment. Long-term adherence to EPAP was excellent in those who had a positive clinical response at month 3 of the EPAP versus sham study. (This appeared to be the same study as reported by Berry et al, 2011 and exhibited similar limitations as that study).

The Zzoma positional device is a cervical pillow designed to prevent positional sleep apnea patients from rolling onto their backs. The device was cleared by the FDA based upon a 510(k) premarket notification due to its substantial equivalence to another positional device, a Sona pillow, which is one of several cervical pillows that have been cleared for treatment of mild obstructive sleep apnea and snoring.

A number of studies have examined various positioning devices for treatment of positional obstructive sleep apnea. Skinner et al (2008) studied a thoracic anti-supine band (TASB), which mimics the 'tennis-ball technique' in a randomized cross-over trial of 20 adults with mild to moderate positional obstructive sleep apnea. Portable sleep studies measuring AHI were performed at start of treatment and at 1-month follow-up. Mean AHI (+/- SD) was 12.0 +/- 14.5/H for TASB and 4.9 +/- 3.9/H for nasal CPAP (nCPAP). No significant difference was founding sleep efficiency or

subjective responses. The investigators concluded that "control of body position during sleep using an anti-supine device mimicking the so-called 'tennis ball technique' provides benefit in the management of position-dependent [obstructive sleep apnea hypopnea syndrome] in subjects who meet strict inclusion criteria. The overall improvement is, however, less than for nCPAP.

Lee et al (2009) evaluated optimal sleep positions in 16 patients, including lateral position, cervical vertebral support with head tilting (CVS-HT), scapula support (SS), and LP, through use of polysomnography for 2 successive nights. Lateral position was found to have the most dominant effect (p = 0.0319) and SS (p = 0.0265) for AHI. The study did not, however, specify any particular positional device for cervical support.

The Zzoma positional device has been examined in a clinical trial. Permut et al (2010) randomly assigned 38 patients to either the Zzoma positional device (PD) OR CPAP. They found no significant different between PD and CPAP in their ability to normalize their AHI (p = 0.16). However, the mean SaO2 during the night was unchanged compared with baseline with the use of PD but was increased with CPAP therapy from 95 % to 96 % (p < 0.001). The lowest SaO2 increased during the night for both PD and CPAP groups. The investigators concluded that positional therapy is equivalent to CPAP at normalizing the AHI in patients with positional OSA, with similar effects on sleep quality and nocturnal oxygenation. They noted that positional therapy is effective at maintaining sleep in the non-supine position during the night and is similar to CPAP therapy in its effects on sleep quality and nocturnal oxygenation. Whether more prolonged use will maintain these effects and how positional therapy compares with CPAP in regard to cognitive function, compliance, and quality of life awaits further study. Drawbacks of this study included (i) it only studied the acute 1-night effects of the PD, as compared with CPAP. Assessment of effectiveness would require the use of other outcome measures, such as daytime sleepiness, cognitive function, and quality of life, all of which would have to be evaluated in a randomized trial after more prolonged use and would be influenced by compliance, and (ii) this study did not include patients with severe OSA.

No studies were found in the peer-reviewed literature comparing the Zzoma device to other positional devices. The Clinical Guideline for the Evaluation, Management and Long-term Care of Obstructive Sleep apnea in Adults released by the Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine (Epstein et al, 2009) state that "positional therapy, consisting of a method that keeps the patient in a non-supine position, is an effective secondary therapy or can be a supplement to primary therapies for OSA in patients who have a low AHI in the non-supine versus that in the supine position".   The guideline does not, however, specify a particular positional device. The guidelines state "[a] positioning device (e.g., alarm, pillow, back pack, tennis ball) should be used when initiating positional therapy".

Valbuza et al (2010) stated that treatment of OSA using methods for increasing upper airway muscle tone has been controversial and poorly reported. These investigators reviewed the evidence to evaluate the effectiveness of these methods. Data sources are from the Cochrane Library, Medline, Embase and Scielo, registries of ongoing trials, theses indexed at Biblioteca Regional de Medicina/Pan-American Health Organization of the World Health Organization and the reference lists of all the trials retrieved. This was a review of randomized or quasi-randomized double-blind trials on OSA. Two reviewers independently applied eligibility criteria. One reviewer assessed study quality and extracted data, and these processes were checked by a second reviewer. The primary outcome was a decrease in the AHI of below 5 episodes per hour. Other outcomes were subjective sleep quality, sleep quality measured by NPSG, quality of life measured subjectively and adverse events associated with the treatments. Three eligible trials were included -- 2 showed improvements through the objective and subjective analyses, and 1 showed

improvement of snoring, but not of AHI while the subjective analyses showed no improvement. The adverse events were reported and they were not significant. The authors concluded that there is no accepted scientific evidence that methods aiming to increase muscle tone of the stomatognathic system are effective in reducing AHI to below 5 events per hour. They stated that well-designed randomized controlled trials are needed to assess the effectiveness of such methods.

The European Respiratory Society's task force on non-CPAP therapies in sleep apneas (Randerath et al, 2011) summarized the effectiveness of alternative treatment options in OSAS. The task force evaluated the scientific literature according to the standards of evidence-based medicine. Evidence supports the use of mandibular advancement devices in mild-to-moderate OSAS. Maxillo-mandibular osteotomy seems to be as efficient as CPAP in patients who refuse conservative treatment. Distraction osteogenesis is usefully applied in congenital micrognathia or mid-face hypoplasia. There is a trend towards improvement after weight reduction. Positional therapy is clearly inferior to CPAP and long-term compliance is poor. Drugs, nasal dilators and apnea triggered muscle stimulation can not be recommended as effective treatments of OSAS at the moment. Although tongue muscle training improves snoring, it is not efficacious in the treatment of sleep apnoea in general. Nasal surgery, radiofrequency tonsil reduction, tongue base surgery, uvulo-palatal flap, laser mid-line glossectomy, tongue suspension and genioglossus advancement can not be recommended as single interventions. Uvulopalatopharyngoplasty, pillar 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. Multi-level surgery is only a salvage procedure for OSA patients.

Percutaneous submental electrical stimulation during sleep has been suggested as a method for treating patients with OSA. Electrical stimulation to the submental region during OSA is reported to break the apnea without arousal and to diminish apneic index, time spent in apnea, and oxygen desaturation. The mode of breaking the apnea by electrical stimulation has not yet been shown. Moreover, genioglossus is supposed to be the muscle responsible for breaking the apnea by forward movement of the tongue. However, the therapeutic value of transcutaneous electrical stimulation of the genioglossus muscle in patients with OSA to reduce sleep-disordered breathing is still unclear. The European Respiratory Society's task force on non-CPAP therapies in sleep apneas (Randerath et al, 2011) noted that "[t]here are conflicting results on the clinical efficacy of apnoea triggered neurostimulation. Intraneural stimulation of the hypoglossus nerve and transcutaneous electrical stimulation of the genioglossus muscle showed significant improvements of respiratory disturbances and sleep parameters without adverse effects. In contrast, other groups failed to find an enlargement of the upper airways by transcutaneous or intramuscular stimulation during wakefulness or sleep. However, undesirable contractions of the platysma or tongue were observed and arousals were induced".

Multiple Sleep Latency Test (MSLT)

The MSLT, most commonly used in the evaluation of narcolepsy, is also used to document daytime sleepiness in OSA. The MSLT evaluates the rapidity with which a patient falls asleep during daytime nap opportunities at 2-hour intervals throughout the day. The test is typically administered after an overnight polysomnogram. Similar to the polysomnogram, the EEG, EOG and EMG are routinely recorded. A sleep latency of less than 6 mins is considered clinically significant. Although the polysomnogram is always part of the work-up of OAS, the MSLT is considered expensive and time consuming and is infrequently performed. However, with the recent emphasis on excessive daytime sleepiness as an initial symptom of an obstructive sleep disorder, evaluating a patient's daytime sleepiness becomes more important, in order to distinguish true excessive daytime sleepiness from the occasional sleepiness that almost every one experiences.

According to the Standards of Practice Committee of the American Academy of Sleep Medicine (Littner et al, 2005), the MSLT is indicated as part of the evaluation of patients with suspected narcolepsy and may be useful in the evaluation of patients with suspected idiopathic hypersomnia. The MSLT is not routinely indicated in the initial evaluation and diagnosis of OSAS, or in assessment of change following treatment with nasal CPAP. The MSLT is not routinely indicated for evaluation of sleepiness in medical and neurological disorders (other than narcolepsy), insomnia, or circadian rhythm disorders.

Assessment of Adequacy of Response to CPAP

In an article on the use of oral appliance therapy for OSA, Ferguson (2001) used a conservative definition of treatment success. A complete response is defined as a reduction in AHI to less than 5/hour. A partial response was defined as an improvement in symptoms combined with a greater than or equal to 50 % reduction in AHI but the AHI remained greater than 5/hour. Treatment failures were defined as having ongoing symptoms and/or a less than 50 % reduction in AHI. By this definition, a reduction of 55 events/hour of sleep to 33 events/hour of sleep (40 % reduction in AHI) would not be considered as a good response to CPAP.

Wassmuth et al (2000) evaluated the ability of cautery-assisted palatal stiffening operation (CAPSO) to treat OSA syndrome. Twenty-five consecutive patients with OSA syndrome underwent CAPSO. Responders were defined as patients who had a reduction in AHI of 50 % or more and an AHI of 10 or less after surgery.

Furthermore, Heinzer et al (2001) noted that a good response to CPAP treatment is defined as an AHI of less than 10 events/hour.

Javaheri (2000) concluded that an AHI of 4 +/- 3 per hour signifies complete elimination of disordered breathing. The author prospectively studied 29 men with heart failure whose initial polysomnograms showed 15 or more episodes of apnea and hypopnea per hour (AHI). Twenty-one patients had predominately central and 8 patients OSA. All were treated with CPAP during the subsequent night. In 16 patients, CPAP resulted in virtual elimination of disordered breathing. In these patients, the mean AHI (36 +/- 12 [SD] versus 4 +/- 3 per hour, p = 0.0001), arousal index due to disordered breathing (16 +/- 9 versus 2 +/- 2 per hour, p = 0.0001), and percent of total sleep time below saturation of 90 % (20 +/- 23 % to 0.3 +/- 0.7 %, p = 0.0001) decreased, and lowest saturation (76 +/- 8 % versus 90 +/- 3 %, p = 0.0001) increased with CPAP. In 13 patients who did not respond to CPAP, these values did not change significantly. In patients whose sleep apnea responded to CPAP, the number of hourly episodes of nocturnal premature ventricular contractions (66 +/- 117 versus 18 +/- 20, p = 0.055) and couplets (3.2 +/- 6 versus 0.2 +/- 0.21, p = 0.031) decreased. In contrast, in patients whose sleep apnea did not respond to CPAP, ventricular arrhythmias did not change significantly. The author concluded that in 55 % of patients with heart failure and sleep apnea, first-night nasal CPAP eliminates disordered breathing and reduces ventricular irritability. Based on this study, an AHI of 4 +/- 3 per hour signifies complete elimination of disordered breathing.

The SleepStrip is an instrument used for screening of OSA. It incorporates signal detection, acquisition, as well as display in a disposable package. The device is placed on the upper lip at bed-time and adjusted until respiration is detected, as indicated by a flashing light. Two nasal thermistors and 1 oral thermistor produce flow signals that are processed within the SleepStrip's microprocessor. The 5 possible results are as follows: "0" (no apneas); "1" (mild sleep apnea, comparable to sleep laboratory AHI between 15 and 24); "2" (moderate sleep apnea, comparable to

sleep laboratory AHI between 25 and 39); "3" (severe sleep apnea, comparable to sleep laboratory AHI of greater than 40); and "E" (error in measurement).

In a prospective, non-randomized double-blinded single cohort study, Pang et al (2006) examined the role of a portable screening device (SleepStrip) in the diagnosis of OSA. Patients with suspected OSA scheduled for an attended over-night Level I PSG and who consented to participate in the study wore the SleepStrip device at home the night after the PSG. The AHI determined by PSG was compared with the results of the SleepStrip recording. A total of 37 patients with a mean age of 52.1 +/- 12.2 years and mean body mass index of 35.7 +/- 5.2 participated in the study. The overall agreement between the AHI and the SleepStrip results using Cohen's Kappa value was 0.139 (p = 0.19). The sensitivity and specificity of the SleepStrip for diagnosing severe OSA when the AHI was greater than 40 were 33.3 % and 95 % (p = 0.05). When the AHI was greater than 25, the SleepStrip sensitivity and specificity were 43.8 % and 81.3 % (p = 0.26). The sensitivity and specificity of the SleepStrip for diagnosing OSA in patients with an AHI greater than 15 were 54.6 % and 70 %, respectively (p = 0.26). The authors concluded that SleepStrip has a low correlation with the AHI as measured by PSG; they stated that further studies are needed before this device can be recommended as a screening tool for the diagnosis of OSA.

In a prospective, non-randomized, double-blinded single cohort study, Ozmen et al (2011) examined the reliability of SleepStrip as a screening test in OSA syndrome. A total of 72 patients (50 males, 22 females; mean age of 51.4 +/- 11.1 years; range of 20 to 74 years) with OSA syndrome were included in this study between May 2008 and February 2009. Patients who underwent an attended over-night PSG and consented to participate in the study were asked to use SleepStrip device within the week following PSG recording. The AHI was compared with the SleepStrip score (Sscore). The mean BMI of patients was 31.1 +/- 4.3. Both AHI and Sscore were obtained in 64 patients. There was a strong correlation between Sscore and AHI (r = 0.76, p <
0.001). The sensitivity and specificity of the SleepStrip were 94.4 % and 93.5 % when used to diagnose cases with AHI = or > 40. The sensitivity and specificity of the SleepStrip was reduced to 80 % and 87.2 % when AHI threshold was chosen as equal or greater than 25 and 83.3 % and 76. 5 % for AHI equal tor greater than 15, respectively. The authors concluded that there is a strong correlation between SleepStrip and AHI. SleepStrip was found to be effective in diagnosing severe OSAS with AHI equal or greater than 40, however, its diagnostic capability was reduced in patients with lower AHI's who constitute the main target of screening.

The Encore tongue base suspension received FDA 510(k) clearance and is intended to be used for anterior advancement of the tongue base by means of a bone screw threaded with suture. It is indicated for the treatment of mild or moderate OSA and/or snoring. http://www.accessdata.fda.gov/cdrh_docs/pdf11/K111179.pdf. However, there is currently insufficient evidence to support its use.

On behalf of the European Respiratory Society task force on non-CPAP therapies in sleep apnea, Randerath et al (2011) stated that "Evidence supports the use of mandibular advancement devices in mild-to-moderate OSAS. Maxillomandibular osteotomy seems to be as efficient as continuous positive airway pressure (CPAP) in patients who refuse conservative treatment. Distraction osteogenesis is usefully applied in congenital micrognathia or midface hypoplasia. There is a trend towards improvement after weight reduction. Positional therapy is clearly inferior to CPAP and long-term compliance is poor. Drugs, nasal dilators and apnoea triggered muscle stimulation cannot be recommended as effective treatments of OSAS at the moment. Nasal surgery, radiofrequency tonsil reduction, tongue base surgery, uvulopalatal flap, laser midline glossectomy, tongue suspension and genioglossus advancement cannot be recommended as single interventions. Uvulopalatopharyngoplasty, pillar 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".

The Winx therapy system/oral pressure therapy (OPT) is a light, oral vacuum delivered by a quiet console through a slim tube connected to a soft, flexible mouth-piece. The mouthpiece and vacuum work together to gently pull the soft palate forward and stabilize the tongue, increasing the size of the airway and allowing for natural breathing to occur during sleep. Farid-Moayer et al (2013) conducted a proof-of-concept study that suggested that OPT can produce clinically relevant relief of OSA in certain subjects who are readily identified by PSG during trial use of the noninvasive system. In this single-center, proof-of-concept, single-treatment-night study, subjects with OSA underwent a baseline PSG study followed by PSG during use of an OPT system. Fifty-four men and 17 women, aged 53.2 ± 11.5 years (mean $\pm$ SD) had a baseline apnea-hypopnea index (AHI) greater than 5 events per hour. The authors reported that OPT was generally well tolerated with no serious adverse events. The authors found that OPT significantly decreased AHI from 34.4 ± 28.9 events per hour (mean $\pm$ SD) at baseline to 20.7 ± 23.3 ($p < 0.001$). Treatment produced an AHI less than 10 in 48% of the subjects. The authors stated that OPT significantly improved oxygen desaturation index ($p < 0.001$) and increased the percentage of the night with oxygen saturation of 90% or greater ($p = 0.028$). Stage-N1 sleep shifts, total sleep-stage shifts, awakenings and the percentage of sleep time spent in N1 sleep were significantly reduced with treatment. Additional studies of longer duration and larger numbers of patients are necessary, as are studies comparing results of OPT with CPAP as current standard of care.

Colrain et al (2013) evaluated the impact of a novel non-invasive oral pressure therapy (OPT) (Winx®, ApniCure) system on polysomnographic measures of sleep-disordered breathing, sleep architecture, and sleep stability in OSA. A 4-week, multi-center, prospective, open-label, randomized, cross-over, first-night order of control versus treatment, single-arm trial was conducted in 5 AASM-accredited sleep clinics and 1 research laboratory. A total of 63 subjects (analysis cohort) were studied from a screening cohort of 367 subjects. The analysis cohort was 69.8 % men, ages 53.6 ± 8.9 years (mean $\pm$ SD), BMI of $32.3 \pm 4.5 kg/m(2)$, with mild-to-severe OSA. At treatment initiation, subjects received random assignment to 1 night with and 1 without (control) treatment, and they were assessed again following 28 nights of treatment. Breathing and sleep architecture were assessed each night based on blind scoring by a single centralized scorer using AASM criteria. Average nightly usage across the take-home period was 6.0 ± 1.4 hrs. There were no severe or serious device-related adverse events (AEs). Median AHI was 27.5 events/hr on the control night, 13.4 events/hr on the first treatment night, and 14.8 events/hr after 28 days of treatment. A clinically significant response (treatment AHI less than or equal to 10/hr and less than or equal to 50 % of control values) was seen in 20 of the 63 subjects evaluated. Rapid eye movement percentage (REM %) was significantly increased, and N1 %, stage shifts to N1 sleep, overall stage shifts, total awakenings, and arousals/hr were all significantly reduced at both treatment nights compared to controls. Mean ESS score was significantly reduced from 12.1 to 8.6 (Cohen d effect size, 0.68) in those untreated for 2 or more weeks prior to OPT study participation and remained unchanged in subjects who directly switched from CPAP therapy to OPT. The authors concluded that clinically significant improvements in sleep quality and continuity, AHI, oxygen desaturation index (ODI), ESS, and overall clinical status were achieved in an easily identified subgroup; OPT was safe and well-tolerated and nightly usage was high. They stated that these findings suggested that OPT may provide useful therapy for a subset of OSA patients who do not tolerate nasal CPAP.

This study had several drawbacks: (i) treatment efficacy was limited to 2 single-night studies, 1 at the beginning and the other at the end of a 28-day take-home period. Future studies will need to extend the period of use for both safety and long-term efficacy evaluation; (ii) the study should have

had multiple measurement points, if not nightly monitoring of oxygen saturation in the home; (iii) the study was conducted on a highly selected study population; and (iv) the lack of a sham-placebo controlled condition. Furthermore, a review on "Alternative devices for obstructive sleep apnea" (Barone, 2013) states that "the initial data are impressive, and OPT certainly seems safe, but as with all new modalities, real-world experience needs to be ascertained and more extensive clinical trials need to be performed. The manufacturer reports that this promising new device should be widely available this year".

The potential benefits of diagnostic audio recording, used alone or in conjunction with pulse oximetry, has not been demonstrated to provide clinical benefits equivalent to the currently accepted standard of care, PSG. While such methods do potentially identify occurrences of sleep apnea, other aspects of physiological functioning are not recorded simultaneously, thus providing an incomplete clinical picture and allowing the possibility of misdiagnosis.

Dafna et al (2012) described a novel method for sleep quality analysis. Its purpose is to assist an alternative non-contact method for detecting and diagnosing sleep related disorders based on acoustic signal processing. In this study, audio signals of 145 patients with OSA were recorded (more than 1,000 hours) in a sleep laboratory and analyzed. The method is based on the assumption that during sleep the respiratory efforts are more periodically patterned and consistent relative to a waking state; furthermore, the sound intensity of those efforts is higher, making the pattern more noticeable relative to the background noise level. The system was trained on 50 subjects and validated on 95 subjects. The accuracy of the system for detecting sleep/wake state is 82.1 % (epoch by epoch), resulting in 3.9 % error (difference) in detecting sleep latency, 11.4 % error in estimating total sleep time, and 11.4 % error in estimating sleep efficiency. The clinical effectiveness of this novel system needs to be ascertained in well-designed studies.

Yadollahi et al (2013) stated that tracheal respiratory sound analysis is a simple and non-invasive way to study the pathophysiology of the upper airway and has recently been used for acoustic estimation of respiratory flow and sleep apnea diagnosis. However, in none of the previous studies was the respiratory flow-sound relationship studied in people with OSA, nor during sleep. In this study, these researchers recorded tracheal sound, respiratory flow, and head position from 8 non-OSA and 10 OSA individuals during sleep and wakefulness. They compared the flow-sound relationship and variations in model parameters from wakefulness to sleep within and between the 2 groups. The results showed that during both wakefulness and sleep, flow-sound relationship follows a power law but with different parameters. Furthermore, the variations in model parameters may be representative of the OSA pathology. The other objective of this study was to examine the accuracy of respiratory flow estimation algorithms during sleep: these researchers investigated 2 approaches for calibrating the model parameters using the known data recorded during either wakefulness or sleep. The results showed that the acoustical respiratory flow estimation parameters change from wakefulness to sleep. Therefore, if the model was calibrated using wakefulness data, although the estimated respiratory flow follows the relative variations of the real flow, the quantitative flow estimation error would be high during sleep. On the other hand, when the calibration parameters were extracted from tracheal sound and respiratory flow recordings during sleep, the respiratory flow estimation error is less than 10 %.

Eisele et al (1997) examined the motor responses resulting from direct electrical stimulation of the hypoglossal (HG) nerve and correlated these responses to changes in upper airway patency during sleep. The motor effects of direct electrical stimulation of the main trunk of the HG nerve and the branch that supplies the genioglossus muscle during anesthesia and wakefulness were assessed visually. Responses in airflow during sleep to HG nerve stimulation were assessed with standard polysomnographic techniques. A total of 15 patients undergoing a surgical procedure that involved

the neck that exposed the HG nerve and 5 volunteer patients with OSA constituted the study population. The main trunk (n = 3) and genioglossus branch (n = 2) of the HG nerve were stimulated electrically with a half-cuff tri-polar electrode. Stimulation of the branch of the HG nerve that innervates the genioglossus muscle caused protrusion and contralateral deviation of the tongue. Stimulation of the main trunk of the HG nerve caused slight ipsilateral deviation and retrusion of the tongue. The arousal threshold for stimulation exceeded the motor recruitment threshold by 0.8 +/- 0.4 V. Inspiratory airflow increased in all patients by 184.5 +/- 61.7 ml/s (mean +/- SD; p = 0.02, analysis of variance) with stimulation. The authors concluded that direct HG nerve stimulation below the arousal threshold can improve airflow in patients with OSA. The findings of this small study need to be validated by well-designed studies with larger sample size and follow-ups. Eisele et al (2003) noted that the feasibility and potential of upper airway stimulation for the treatment of OSA have been demonstrated. Moreover, they stated that further studies and stimulation-system refinements are presently underway, with hopes of establishing upper airway stimulation as a therapeutic option for this challenging disorder.

Kezirian et al (2010) noted that upper airway occlusion in OSA has been attributed to a decline in pharyngeal neuromuscular activity occurring in a structurally narrowed airway. Surgical treatment focuses on the correction of anatomic abnormalities, but there is a potential role for activation of the upper airway musculature, especially with stimulation of the HG nerve and genioglossus muscle. These investigators presented evidence from research on upper airway neuromuscular electrical stimulation in animals and humans. They also presented results from 8 OSA patients with a fully implanted system for HG nerve stimulation, demonstrating an improvement in upper airway collapsibility and OSA severity. Moreover, they stated that future research, including optimization of device features and stimulation parameters as well as patient selection, is necessary to make HG nerve stimulation a viable alternative to positive airway pressure therapy and upper airway surgical procedures.

Oliven (2011) reviewed a new treatment modality, HG stimulation, recently evaluated by multiple physiological studies and currently assessed by several clinical studies. A phase I, implantable HG nerve stimulation multi-center study was published in 2001. Significant reduction in AHI was reported in 7 of the 8 implanted OSA patients, but technical faults precluded prolonged follow-up. Over the past 2 years, 3 new HG nerve stimulation systems have been evaluated in more than 60 OSA patients. In adequately selected patients, a more than 50 % reduction in AHI was observed. Usually, a decrease in OSA severity from moderate-severe to mild-minimal can be achieved. The author concluded that ongoing research, including recent initiation of a large multi-center phase III study, suggested that HG nerve stimulators are likely to be available as a new treatment modality within a few years. Moreover, they stated that additional data are needed to define which OSA patients are most likely to benefit from HG nerve stimulation. Continuous refinement of electrodes design is likely to improve stimulation efficacy in coming years.

In 2 consecutive open prospective studies, Van de Heyning et al (2012) examined the safety and preliminary effectiveness of the Upper Airway Stimulation (UAS) system, and identified baseline predictors for therapy success. The UAS systems were implanted in patients with moderate-to-severe OSA who failed or were intolerant of CPAP. The study was conducted in 2 parts. In part 1, patients were enrolled with broad selection criteria; AHI was collected using laboratory-based PSG at pre-implant and post-implant visits. Epworth Sleepiness Scale and Functional Outcomes of Sleep Questionnaire (FOSQ) were also collected. In part 2, patients were enrolled using selection criteria derived from the experience in part 1. In part 1, 20 of 22 enrolled patients (2 exited the study) were examined for factors predictive of therapy response. Responders had both a BMI of less than or equal to 32 and AHI less than or equal to 50 (p < 0.05) and did not have complete concentric palatal collapse. Part 2 patients (n = 8) were selected using responder criteria and

showed an improvement on AHI from baseline, from 38.9 ± 9.8 to 10.0 ± 11.0 (p < 0.01) at 6 months post-implant. Both ESS and FOSQ improved significantly in part 1 and 2 subjects. The authors concluded that the current study has demonstrated that therapy with upper airway stimulation is safe and effective in a select group of patients with moderate-to-severe OSA who cannot or will not use CPAP as primary treatment. These preliminary findings need to be validated by well-designed studies with larger sample size and longer follow-up.

Mwenge et al (2013) stated that CPAP is an effective but cumbersome treatment for OSA. Non-compliant patients need alternative therapies. These researchers studied a tongue neurostimulation approach: targeted hypoglossal neurostimulation (THN) therapy with the aura6000™ System. A multi-contact electrode positioned around the main trunk of the 12th nerve connected to an implanted pulse generator stimulates segments of the nerve, activating dilator muscles. The primary objective was to improve the polysomnographically determined AHI at 3 months, and maintain the improvement after 12 months of treatment. Overall, 13 out of 14 operated patients were successfully implanted. At 12 months, the AHI decreased from 45 ± 18 to 21 ± 17, a 53 % reduction (p < 0.001). The 4 % oxygen desaturation index fell from 29 ± 20 to 15 ± 16 and the arousal index from 37 ± 13 to 25 ± 14, both p < 0.001. The ESS score decreased from 11 ± 7 to 8 ± 4 (p = 0.09). Targeted hypoglossal neurostimulation was neither painful nor awakened patients, who all complied with therapy. Transient tongue paresis occurred in 2 subjects. The authors concluded that the present study represented the longest study of any HG nerve neurostimulation reported to date. They stated that THN is safe and effective to treat OSA in patients not compliant with CPAP. The findings of this small study need to be validated by well-designed studies.

The American Academy of Sleep Medicine's review on "Obstructive sleep apnea" (2008) did not mention the use of HG nerve stimulation as a therapeutic option. An UpToDate review on "Management of obstructive sleep apnea in adults" (Kryger, 2013) does not mention the use of HG nerve stimulation as a therapeutic option.

Furthermore, a review on "Alternative devices for obstructive sleep apnea" (Barone, 2013) states that "The future -- Next-generation respiratory-triggered implantable devices have recently been designed and have been engineered to provide intermittent electrical impulses to the hypoglossal nerve via an implanted cuff electrode. These devices monitor respiration, via implanted thoracic leads, by sensing changes in motion of the chest wall. Electrical stimulation to the hypoglossal nerve is then provided cyclically during inspiration (which represents the most vulnerable period with regard to upper airway narrowing and collapse). When stimulated, the hypoglossal nerve causes the genioglossus muscle to contract, which results in an anterior displacement of the base of the tongue and an enlargement of the upper airway. The hypoglossal branches that innervate the genioglossus contain mostly efferent fibers, with minimal afferent input; this allows for activation of the genioglossus with less possibility of arousal. In one study, there was a significant improvement from baseline to 6 months in AHI (43.1 ± 17.5 [severe] to 19.5 ± 16.7 [moderate]) and ESS (12.1 ± 4.7 [excessive sleepiness] to 8.1 ± 4.4 [borderline sleepiness]). Another recent study presented initial data suggesting that upper airway stimulation can be effective and safe in certain patients with moderate to severe OSA who are unable or unwilling to use CPAP. However, like all surgical treatments, this is subject to unpredictable results, potential for adverse events, and likely large expense; fortunately, it will be just one of several alternatives to CPAP available in the near future".

In a prospective, non-randomized trial using historical controls, Lee et al (2012) evaluated the use of transoral robot-assisted lingual tonsillectomy and UPPP for the surgical management of tongue base obstruction in patients with OSA. Patients underwent drug-induced sleep endoscopy, transoral robot-assisted lingual tonsillectomy with UPPP, and pre-operative and post-operative PSG. A total of 20 patients have completed the study to date. The rate of surgical success was 45

%, and the rate of surgical response was 65 %. The mean pre-operative AHI of 55.6 decreased by 56.7 %, to a mean post-operative value of 24.1 (p < 0.001), and the minimum arterial oxygen saturation increased from the mean pre-operative value of 75.8 % to the mean post-operative value of 81.7 % (p = 0.013). The mean ESS score improved from 13.4 to 5.9 (p = 0.003). One patient had post-operative bleeding that required cauterization, resulting in a major complication rate of 4.2 %. The authors concluded that transoral robot-assisted lingual tonsillectomy with UPPP is a novel technique for the surgical management of OSA that results in a significant decrease in the AHI, a significant improvement in minimum arterial oxygen saturation, and a significant improvement in the ESS score and has an acceptable complication rate. The findings of this small, non-randomized study need to be validated by well-designed studies.

In a retrospective case-series review, Suh et al (2013) analyzed the overall success rate of open midline glossectomy with lingual tonsillectomy in the surgical management of OSAS as well as a subset analysis to determine whether certain patient factors influence clinical outcome. A total of 50 consecutive patients who had moderate to severe OSAS with Friedman tongue position III or IV and underwent midline glossectomy with lingual tonsillectomy as part of multi-level sleep apnea surgery and had pre- and post-surgery in-laboratory sleep studies performed. The overall success rate was 56.0 % using success defined as a post-operative AHI less than 20 and a decrease of greater than 50 %. Median AHI decreased from 52.0 to 18.3 with a median change of -26.1 (inter-quartile range, -41.6 and -17.1). Of significance on subset analysis, patients with a pre-operative AHI less than 60 had a 68.8 % success rate (p = 0.02), and patients with Friedman tongue position III had a 75.9 % success rate (p = 0.0009). The authors concluded that the findings of this case series would suggest that multi-level sleep apnea surgery, incorporating midline glossectomy with lingual tonsillectomy, is a valid alternative for managing moderate-to-severe OSAS in patients who do not respond or are resistant to CPAP therapy. In patients with a pre-operative AHI less than 60 or Friedman tongue position III, surgical success rate is significantly improved.

Moreover, an UpToDate review on "Management of obstructive sleep apnea in adults" (Kryger, 2013) states that "Laser-assisted and radiofrequency ablation (RFA) are less invasive variants of UPPP. Other common surgical procedures for OSA include septoplasty, rhinoplasty, nasal turbinate reduction, nasal polypectomy, palatal advancement pharyngoplasty, tonsillectomy, adenoidectomy, palatal implants (i.e., Pillar procedure), tongue reduction (partial glossectomy, lingual tonsillectomy), genioglossus advancement, and maxillomandibular advancement. A systematic review reported that most of the evidence related to such surgical treatments is from case series. Meta-analyses of data extracted from these series suggest that UPPP, laser-assisted uvulopalatoplasty, radiofrequency ablation, and maxillomandibular advancement (MMA) decrease the AHI. MMA is most consistently associated with a decreased AHI, although the morbidity of MMA has not been determined. These meta-analyses were limited by a serious risk for bias and inconsistency among the series …. Only a small number of trials have directly compared surgery to either conservative management or a nonsurgical therapy. Overall, the trials have failed to consistently demonstrate a benefit from surgical therapy. While this could be a true effect, it may also reflect the small sample sizes, the heterogeneous patient populations, or the use of short-term outcome measures".

Expansion sphincteroplasty is a modification of UPPP; it removes the remaining tonsil, creates an incision on the soft palate, pulls the muscles of the back wall of the tonsils forward to increase throat space and pulls stitches to further open the space. This surgery preserves the uvula most of the time.

Pensler and Reich (1991) compared speech results after the pharyngeal flap and the dynamic sphincteroplasty procedures. Eighty-five patients underwent surgery to reduce velopharyngeal

incompetence with either a pharyngeal flap (n = 75) or a dynamic sphincteroplasty (n = 10) performed between April 1958 and August 1989, and were evaluated pre-operatively and post-operatively by a plastic surgeon, speech pathologist, and otolaryngologist. Improvement in speech was noted in 75 % (n = 56) of the patients with pharyngeal flaps and 70 % (n = 7) of the patients with dynamic sphincteroplasties post-operatively; 30 % of the patients in both groups showed no improvement post-operatively in speech; 3 patients (4 %) who underwent pharyngeal flap procedures developed sleep apnea post-operatively. The authors concluded that persistent velopharyngeal incompetence may be treated effectively with either a pharyngeal flap or a dynamic sphincteroplasty. Either procedure appeared to result in improved speech in most patients.

Pang and Woodson (2006) stated that the lateral pharyngeal wall has been known to contribute to the collapse of the upper airway in many patients with obstructive sleep apnea (OSA). It is difficult to create enough tension in the lateral pharyngeal walls to prevent its collapse. To the authors' knowledge, there has not been any surgery that specifically addresses this issue. The lateral pharyngoplasty described by Cahali aims to address the lateral pharyngeal wall collapse in patients with OSA. However, post-operatively, many patients had prolonged dysphagia. The expansion sphincter pharyngoplasty is a simple technique that stiffens the lateral pharyngeal walls and prevents its collapse in patients with OSA. The technique basically consists of a tonsillectomy, expansion pharyngoplasty, rotation of the palatopharyngeus muscle, a partial uvulectomy, and closure of the anterior and posterior tonsillar pillars. This procedure can be performed alone or as part of the multilevel surgical algorithm in the treatment of OSA. Moreover, the authors noted that "This new technique of expansion sphincter pharyngoplasty may offer benefits over traditional methods of UPPP in patients with OSA with small tonsils, Friedman stage II and III, and lateral wall collapse noted on endoscopic examination. The procedure has promising results, is anatomically sound, and has minimal complications".

Mann et al (2011) noted that velopharyngeal dysfunction has been treated with either a pharyngeal flap or sphincteroplasty with varying degrees of success. Both of these entities have their own series of problems, with sleep apnea and nasal mucous flow disruptions at the forefront. The purpose of this study was to review the senior author's (R.J.M.) experience performing the double-opposing buccal flap for palatal lengthening. All patients who were treated with double-opposing buccal flaps between October of 1994 and July of 2007 were reviewed. These patients presented with varying degrees of velopharyngeal dysfunction showing some degree of velar movement at the time of surgery. Pre-operative and post-operative speech results were reviewed for comparison. A total of 27 patients underwent palatal lengthening, with an average length of follow-up of 58 months. Distal flap necrosis occurred in 2 patients. The level of intelligibility (65.4 % versus 95.5 %) and resonance (moderately hyper-nasal versus normal resonance) improved significantly postoperatively (p < 0.0001). Only 1 patient required the addition of a pharyngeal flap for persistent velopharyngeal dysfunction, and there were no post-operative issues with sleep apnea. The authors concluded that the double-opposing buccal flap is an effective technique for lengthening the palate, improving speech, and decreasing the risks of post-operative sleep apnea. All patients experienced a dramatic improvement in their resonance and intelligibility. They stated that this technique appeared most effective in patients with intact velar movement who demonstrate a small-to-moderate posterior velar gap. The double-opposing buccal flap is a useful means of treating velopharyngeal dysfunction, thus serving as an adjunct when improving pharyngeal closure.

Also, and UpToDate review on "Overview of obstructive sleep apnea in adults" (Strohl, 2014) does not mention sphincteroplasty as a management option.

Kitamura et al (2014) evaluated the objective and subjective improvement after multi-level surgery, genioglossus advancement (GA) plus UPPP for the treatment of OSAS. Genioglossus

advancement and UPPP were undertaken in 24 patients with moderate and severe OSAS between January 2006 and December 2011. Epworth Sleepiness Scale score, snoring, the feeling of having slept well and PSG were used for the evaluation of surgical outcomes. In addition, these researchers determined whether baseline PSG, cephalometry, and authropometry data could predict GA and UPPP success or failure. The mean ESS score decreased significantly from 12.96 to 7.08. The mean AHI improved from 37.3 to 19.33. Objective success as evaluated by a 50 % reduction in AHI or by AHI less than 15 was obtained in 16 of 24 patients. The lowest oxygen saturation and stage 1 and stage 2 were also improved significantly. There were no major post-operative complications. There were significant differences in SNA, SNB, FX and PNS-P (length of soft palate) between the success and failure of GA and UPPP. The indication of GA and UPPP were SNA greater than 79.11 degrees, SNB greater than 75.69 degrees, FX greater than 78.67 degrees, and 36.79 mm < PNS-P < 42.29 mm. The authors concluded that GA and UPPP surgeries are effective and safe for patients with moderate and severe OSAS. However, they stated that further studies are needed to decide definitively if GA and UPPP are appropriate treatments for OSAS.

Strollo et al (2014) evaluated the safety and effectiveness of upper-airway stimulation at 12 months for the treatment of moderate-to-severe OSA. Using a multi-center, prospective, single-group, cohort design, these researchers surgically implanted an upper-airway stimulation device in patients with OSA who had difficulty either accepting or adhering to CPAP therapy. The primary outcome measures were the AHI (with a score of greater than or equal to 15 indicating moderate-to-severe apnea) and the ODI (the number of times per hour of sleep that the blood oxygen level drops by greater than or equal to 4 percentage points from baseline). Secondary outcome measures were the ESS, the FOSQ, and the percentage of sleep time with the oxygen saturation less than 90 %. Consecutive participants with a response were included in a randomized, controlled therapy-withdrawal trial. The study included 126 participants; 83 % were men. The mean age was 54.5 years, and the mean BMI was 28.4. The median AHI score at 12 months decreased 68 %, from 29.3 events/hour to 9.0 events/hour (p < 0.001); the ODI score decreased 70 %, from 25.4 events/hour to 7.4 events/hour (p < 0.001). 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 non-randomized phase among the 23 participants in the therapy-maintenance group (8.9 and 7.2 events/hour, respectively); the AHI score was significantly higher (indicating more severe apnea) among the 23 participants in the therapy-withdrawal group (25.8 versus 7.6 events/hour, p < 0.001). The ODI results followed a similar pattern. The rate of procedure-related serious adverse events was less than 2 %. The authors concluded that in this uncontrolled cohort study, upper-airway stimulation led to significant improvements in objective and subjective measurements of the severity of OSA. Moreover, they stated that "Additional objective data on adherence will be required to confirm the findings of the current study".

An UpToDate review on "Management of obstructive sleep apnea in adults" (Kryger and Malhotra, 2014) states that "Hypoglossal nerve stimulation via an implantable neurostimulator device is a novel treatment strategy that may have a role in selected patients with moderate to severe OSA who decline or fail to adhere to positive airway pressure therapy, but further data are required".

Appendix

Table 1: Epworth Sleepiness Scale

Indicate the likelihood of falling asleep in the following commonly encountered situations. Assign the following scores to the patient's responses:

Likelihood of dozing	Score
None	0
Low Chance	1
Moderate Chance	2
High Chance	3

1. Sitting and reading
2. Watching TV
3. Sitting, inactive, in a public place, i.e., theater
4. As a passenger in a car for an hour without a break
5. Lying down to rest in the afternoon when circumstances permit
6. Sitting and talking to someone
7. In a car, while stopped for a few minutes in traffic.

Sum the scores. A total greater than 10 is considered abnormal.

Table 2: Monitoring Devices

Monitoring Devices		
Type I:	Comprehensive standard overnight polysomnography in a sleep center or laboratory with a sleep technician in constant attendance.	Minimum of 7 parameters including EEG, EOG, chin EMG, ECG or heart rate, airflow, respiratory effort, oxygen saturation
Type II:	Comprehensive, portable sleep study	Minimum of 7 parameters including EEG, EOG, chin EMG, ECG or heart rate, airflow, respiratory effort, oxygen saturation
Type III:	Modified portable sleep apnea testing	Minimum of 4 parameters, including ventilation (at least 2 channels of respiratory movement, or respiratory movement and airflow), heart rate or ECG, oxygen saturation)
Type IV(A):	Three or more bioparameters	Airflow and at least 2 other parameters (e.g., EOG, peripheral arterial tonometry (PAT), snoring, actigraphy, pulse oximetry)
Type IV(B):	Continuous single- or dual-bioparameter recording	Minimum of 1 parameter (e.g., overnight oximetry) and does not meet criteria for Types I to III or Type IV(A) device.

Table 3: Usual Medically Necessary Quantities of Positive Airway Pressure Supplies

Supply Description	Quantity
Tubing with integrated heating element for use with positive airway pressure device	1 per 3 months
Combination oral/nasal mask, used with continuous positive airway pressure, each	1 per 3 months
Oral cushion for combination oral/nasal mask, replacement only	2 per 1 month
Nasal pillows for combination oral/nasal mask	2 per 1 month
Full face mask used with positive airway pressure device	1 per 3 months
Full face mask interface, replacement for full face mask	1 per 1 month
Cushion for use on nasal mask interface	2 per 1 month
Pillow for use on nasal cannula type interface	2 per 1 month
Nasal interface (mask or cannula type, used with positive aiway pressure	1 per 3 months
Headgear used with positive airway pressure device	1 per 6 months
Chinstrap used with positive airway pressure device	1 per 6 months
Tubing used with positive airway pressure device	1 per 3 months
Filter, disposable, used with positive airway pressure devcie	2 per 1 month
Filter, nondisposable, used with positive airway pressure device	1 per 6 months
Water chamber for humidifier, used with positie airway pressure	1 per 6 months

CPT Codes / HCPCS Codes / ICD-9 Codes

Diagnosis:

CPT codes covered if selection criteria are met:

70350	Cephalogram, orthodontic
70355	Orthopantogram(eg, panoramic X-Ray)
95800	Sleep study, unattended, simultaneous recording; heart rate, oxygen saturation, respiratory analysis (eg, by airflow or peripheral arterial tone) and sleep time
95801	minimum of heart rate, oxygen saturation, and respiratory analysis (eg, by airflow or peripheral arterial tone)
95805	Multiple sleep latency or maintenance of wakefulness testing, recording, analysis and interpretation of physiological measurements of sleep during multiple trials to assess sleepiness
95806	Sleep study, simultaneous recording of ventilation, respiratory effort, ECG or heart rate, and oxygen saturation, unattended by a technologist
95807	Sleep study, simultaneous recording of ventilation, respiratory effort, ECG or heart rate, and oxygen saturation, attended by a technologist
95808	Polysomnography; any age, sleep staging with 1-3 additional parameters of sleep, attended by a technologist
95810	age 6 years or older, sleep staging with 4 or more additional parameters of sleep, attended by a technologist
95811	age 6 years or older, sleep staging with 4 or more additional parameters of sleep, with initiation of continuous positive airway pressure therapy or bilevel ventilation, attended by a technologist
95951	Monitoring for localization of cerebral seizure focus by cable or radio, 16 or more channel telemetry, combined EEG and video recording and interpretation (e.g., for presurgical localization), each 24 hours [to assist with the diagnosis of paroxysmal arousals or other sleep disruptions thought to be seizure related when EEG is inconclusive]

CPT codes not covered for indications listed in the CPB:

70100	Radiologic examination, mandible; partial, less than 4 views
70110	complete, minimum of 4 views
70240	Radiologic examination, sella turcica
70332	Temporomandibular joint arthrography, radiological supervision and interpretation
76101	Radiologic examination, complex motion (i.e., hypercycloidal) body section (e.g., mastoid polytomography), other than urography; unilateral
76102	bilateral

76536	Ultrasound, soft tissues of head and neck (e.g., thyroid, parathyroid, parotid), real time with image documentation
78300	Bone and/or joint imaging; limited area
92520	Laryngeal function studies (i.e., aerodynamic testing and acoustic testing)
94760 - 94762	Noninvasive ear or pulse oximetry for oxygen saturation; single determination; multiple determinations (e.g., during exercise); or by continuous overnight monitoring (separate procedure) [as a screening method to rule out OSA]
95803	Actigraphy testing, recording, analysis, interpretation, and report (minimum of 72 hours to 14 consecutive days of recording)
95805	

HCPCS codes covered if selection criteria are met:

G0398	Home sleep study test (HST) with type II portable monitor, unattended; minimum of 7 channels: EEG, EOG, EMG, ECG/heart rate, airflow, respiratory effort and oxygen saturation
G0399	Home sleep test (HST) with type III portable monitor, unattended; minimum of 4 channels: 2 respiratory movement/airflow, 1 ECG/heart rate and 1 oxygen saturation
G0400	Home sleep test (HST) with type IV portable monitor, unattended; minimum of 3 channels

HCPCS codes not covered for indications listed in the CPB:

D0320	Temporomandibular joint arthrogram, including injection
D0321	Other temporomandibular joint films, by report
D0322	Tomographic survey
D0330	Panoramic film
D0340	Cephalometric film
E0445	Oximeter device for measuring blood oxygen levels non-invasively [as a screening method to rule out OSA]

ICD-9 codes covered if selection criteria are met:

327.00 - 327.8	Organic sleep disorders
780.50 - 780.59	Sleep disturbances
786.03	Apnea
786.09	Other dyspnea and respiratory abnormality

Other ICD-9 codes related to the CPB:

278.00 - 278.01	Overweight and obesity
278.03	Obesity hypoventilation syndrome
291.82	Alcohol induced sleep disorders (parasomnia)
292.85	Drug induced sleep disorders (parasomnia)
307.47	Other dysfunctions of sleep stages or arousal from sleep [parasomnias]
332.0	Paralysis agitans (Parkinson's disease)
335.20	Amyotrophic lateral sclerosis
345.00 - 345.91	Epilepsy and recurrent seizures
347.00 - 347.11	Narcolepsy
359.21	Myotonic dystrophy
428.0	Congestive heart failure
433.00 - 434.91, 436	Stroke
741.00 - 741.93	Spina Bifida
780.39	Other convulsions
780.79	Other malaise and fatigue
V85.42 - V85.45	BMI greater than 45

Treatment:

Oral Appliances:

HCPCS codes covered if selection criteria are met:

E0485	Oral device/appliance used to reduce upper airway collapsibility, adjustable or non-adjustable, prefabricated, includes fitting and adjustment [covered only for obstructive sleep apnea in persons that meet criteria for CPAP but who are intolerant to positive airway pressure devices]
E0486	Oral device/appliance used to reduce upper airway collapsibility, adjustable or non-adjustable, custom fabricated, includes fitting and adjustment
S8262	Mandibular orthopedic repositioning device, each

ICD-9 codes covered if selection criteria are met:

327.23	Obstructive sleep apnea (adult) (pediatric)

ICD-9 codes not covered for indications listed in the CPB:

327.00 - 327.09	Organic disorders of initiating and maintaining sleep (organic Insomnia)
327.20	Organic sleep apnea, unspecified
327.21	Primary central sleep apnea
327.22	High altitude periodic breathing
327.24	Idiopathic sleep related nonobstructive alveolar hypoventilation
327.25	Congenital central alveolar hypoventilation syndrome
327.26	Sleep related hypoventilation/hypoxemia in conditions classified elsewhere
327.27	Central sleep apnea in conditions classified elsewhere
327.29	Other organic sleep apnea
327.30 - 327.39	Circadian rhythm sleep disorder
780.50 - 780.59	Sleep disturbances [unspecified sleep disorders that remain a general symptom without a specifically identified sleep disorder diagnosis]
786.03	Apnea

Continuous Positive Airway Pressure (CPAP):

CPT codes covered if selection criteria are met:

| 94660 | Continuous positive airway pressure ventilation (CPAP), initiation and management |

HCPCS codes covered if selection criteria are met:

A4604	Tubing with integrated heating element for use with positive airway pressure device [4 per 12 months]
A7027	Combination oral/nasal mask, used with continuous positive airway pressure device, each [4 per 12 months]
A7028	Oral cushion for combination oral/nasal mask, replacement only, each [24 per 12 months]
A7029	Nasal pillows for combination oral/nasal mask, replacement only, pair [24 per 12 months]
A7030	Full face mask used with positive airway pressure device, each [4 per 12 months][replacement device is not covered due to misuse or abuse]
A7031	Face mask interface, replacement for full face mask, each [12 per 12 months] [replacement device is not covered due to misuse or abuse]
A7032	Cushion for use on nasal mask interface, replacement only, each [24 per 12 months] [replacement device is not covered due to misuse or abuse]

A7033	Pillow for use on nasal cannula type interface, replacement only, pair [24 per 12 months] [replacement device is not covered due to misuse or abuse]
A7034	Nasal interface (mask or cannula type) used with positive airway pressure device, with or without head strap [4 per 12 months][replacement device is not covered due to misuse or abuse]
A7035	Headgear used with positive airway pressure device [2 per 12 months] [replacement device is not covered due to misuse or abuse]
A7036	Chinstrap used with positive airway pressure device [2 per 12 months] [replacement device is not covered due to misuse or abuse]
A7037	Tubing used with positive airway pressure device [4 per 12 months] [replacement device is not covered due to misuse or abuse]
A7038	Filter, disposable, used with positive airway pressure device [24 per 12 months] [replacement device is not covered due to misuse or abuse]
A7039	Filter, non-disposable, used with positive airway pressure device [2 per 12 months] [replacement device is not covered due to misuse or abuse]
A7044	Oral interface used with positive airway pressure device, each
A7045	Exhalation port with or without swivel used with accessories for positive airway devices, replacement only
A7046	Water chamber for humidifier, used with positive airway pressure device, replacement, each [2 per 12 months]
E0470	Respiratory assist device, bi-level pressure capability, without back-up rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device) [for OSA members intolerant of CPAP or AutoPAP, or for whom CPAP or AutoPAP is ineffective]
E0472	Respiratory assist device, bi-level pressure capability, with back-up rate feature, used with invasive interface, e.g., tracheostomy tube (intermittent assist device with continuous positive airway pressure device) [for OSA members intolerant of CPAP]
E0561	Humidifier, non-heated, used with positive airway pressure device [replacement device is not covered due to misuse or abuse]
E0562	Humidifier, heated, used with positive airway pressure device [replacement device is not covered due to misuse or abuse]
E0601	Continuous positive airway pressure (CPAP) device

HCPCS codes not covered for indications listed in the CPB:

E0471	Respiratory assist device, bi-level pressure capability, with back-up rate feature, used with noninvasive interface, e.g., nasal or facial mask (intermittent assist device with continuous positive airway pressure device)

ICD-9 codes covered if selection criteria are met [with AHI 15 or >]:

327.23	Obstructive sleep apnea (adult) (pediatric)

ICD-9 codes covered if selection criteria are met [with OSA and AHI 5-14]:

293.83	Mood disorder in conditions classified elsewhere
296.90 - 296.99	Episodic mood disorders
401.0 - 405.99	Hypertensive disease [documented systolic blood pressure > 140 mmHg and/or diastolic blood pressure > 90 mm Hg]
410.00 - 414.9	Ischemic heart disease
438.0 - 438.9	Late effects of cerebrovascular disease [history of stroke]
780.79	Other malaise and fatigue [excessive daytime sleepiness by Epworth >10 or Multiple Sleep Latency Test (MSLT) <6]
V12.54	Personal history of transient ischemic attack (TIA), and cerebral infarction without residual deficits
V12.59	Personal history of other diseases of circulatory system [history of stroke]

ICD-9 codes covered [for BIPAP, DPAP, VPAP, VPAP Adapt SV, and AutoPAP] if selection criteria are met [for OSA member intolerant of CPAP]:

327.23	Obstructive sleep apnea (adult) (pediatric)
327.24	Idiopathic sleep related nonobstructive alveolar hypoventilation [nocturnal hypoventilation]
327.26	Sleep related hypoventilation/hypoxemia in conditions classified elsewhere [nocturnal hypoventilation]
358.00 - 358.9	Myoneural disorders [restrictive thoracic disorders]
490 - 496	Chronic obstructive pulmonary disease and allied conditions
738.3	Acquired deformity of chest and rib [restrictive thoracic disorders]
754.89	Other congenital musculoskeletal deformities [chest wall] [restrictive thoracic disorders]

ICD-9 codes not covered for indications listed in the CPB:

345.00 - 345.91	Epilepsy and recurrent seizures [for the improvement of seizure control]
780.39	Other convulsions [for the improvement of seizure control]

There is no specific code for Nasal Dilators:

There is no specific code for Apnea-Triggered Muscle Stimulator:

There is no specific code for SleepStrip:

There is no specific code for Encore Tongue Base Suspension::

There is no specific code for Winx Therapy System/Oral Pressure Therapy::

Uvulopalatopharyngoplasty (UPPP):

CPT codes covered if selection criteria are met:

42145   Palatopharyngoplasty (e.g., uvulopalatopharyngoplasty, uvulopharyngoplasty) [for OSA members who meet criteria for CPAP but are intolerant]

ICD-9 codes covered if selection criteria are met [for OSA members who are intolerant of CPAP]:

327.23   Obstructive sleep apnea (adult) (pediatric)

ICD-9 codes not covered for indications listed in the CPB:

327.00 - 327.09   Organic disorders of initiating and maintaining sleep (organic insomnia)

327.20   Organic sleep apnea, unspecified

327.21   Primary central sleep apnea

327.22   High altitude periodic breathing

327.24   Idiopathic sleep related nonobstructive alveolar hypoventilation

327.25   Congenital central alveolar hypoventilation syndrome

327.26   Sleep related hypoventilation/hypoxemia in conditions classified elsewhere

327.27   Central sleep apnea in conditions classified elsewhere

327.29   Other organic sleep apnea

327.30 - 327.39   Circadian rhythm sleep disorder

780.50 - 780.59   Sleep disturbances

786.03   Apnea

Uvulectomy:

CPT codes covered if selection criteria are met:

42140   Uvulectomy, excision of uvula

Other ICD-9 codes related to the CPB:

782.3   Edema [acute of uvula causing respiratory distress]

786.09   Other dyspnea and respiratory abnormalities [respiratory distress caused by acute edema of the uvula]

Laser Assisted Uvuloplasty (LAUP):

CPT codes not covered for indications listed in the CPB:

42160   Destruction of lesion, palate or uvula (thermal, cryo or chemical)

42890   Limited pharyngectomy

HCPCS codes not covered for indications listed in the CPB:

S2080   Laser-assisted uvulopalatoplasty (LAUP)

ICD-9 codes not covered for indications listed in the CPB:

327.00 - 327.8   Organic sleep disorders

780.50 - 780.59   Sleep disturbances

Somnoplasty and Coblation or Tongue Base Reduction:

CPT codes not covered for indications listed in the CPB:

30801   Cautery and/or ablation, mucosa of inferior turbinates, unilateral or bilateral, any method; superficial [if used to report somnoplasty or coblation]

30802   intramural [if used to report somnoplasty or coblation]

41530   Submucosal ablation of the tongue base, radiofrequency, one or more sites, per session

ICD-9 codes not covered for indications listed in the CPB:

327.00 - 327.8   Organic sleep disorders

780.50 - 780.59   Sleep disturbances

786.03   Apnea

786.09   Other dyspnea and respiratory abnormalities

The Repose System or Advance System:

CPT codes not covered for indications listed in the CPB:

41512   Tongue base suspension, permanent suture technique

Tonsillectomy (adult):

CPT codes covered if selection criteria are met:

42821   Tonsillectomy age 12 and over

CPT codes not covered for indications listed in the CPB:

42870   Excision or destruction lingual tonsil, any method (separate procedure)

ICD-9 codes covered if selection criteria are met:

474.10   Hypertrophy of tonsils with adenoids

474.11   Hypertrophy of tonsils alone

ICD-9 codes not covered for indications listed in the CPB:

327.0 - 327.8   Organic sleep disorders (adult)

Zzoma positional device:

HCPCS codes not covered for indications listed in the CPB:

E0190   Positioning cushion/pillow/wedge, any shape or size, includes all
                        components and accessories [Zzoma positional device]

Jaw Realignment Surgery:

CPT codes covered if selection criteria are met:

21198   Osteotomy, mandible, segmental [for OSA members who fail other treatment
                        approaches]

21199   with genioglossus advancement [for OSA members who fail other
                        treatment approaches]

21208   Osteoplasty, facial bones; augmentation (autograft, allograft, or prosthetic
                        implant) [for OSA members who fail other treatment approaches]

21209   reduction [for OSA members who fail other treatment approaches]

21685   Hyoid myotomy and suspension [for OSA members who fail other treatment
                        approaches]

ICD-9 codes covered if selection criteria are met:

327.23   Obstructive sleep apnea (adult) (pediatric)

Other ICD-9 codes related to the CPB:

756.0   Anomalies of skull and face bones

Tracheostomy:

CPT codes covered if selection criteria are met:

31600 - 31601   Tracheostomy

ICD-9 codes covered if selection criteria are met:

327.23   Obstructive sleep apnea (adult) (pediatric) [for members with the most
                        severe OSA not manageable by other interventions]

Cardiac (Atrial) Pacing:

CPT codes not covered for indications listed in the CPB:

33202 - 33249   Pacemaker procedures

ICD-9 codes not covered for indications listed in the CPB:

327.00 - 327.8   Organic sleep disorders

780.50 - 780.59   Sleep disturbances

786.03   Apnea

786.09   Other dyspnea and respiratory abnormalities

Injection Snoreplasty:

No specific codes

Cautery-Assisted Palatal Stiffening Operation (CAPSO):

CPT codes not covered for indications listed in the CPB:

42950   Pharyngoplasty (plastic or reconstructive operation on pharynx) [if used to report CAPSO]

ICD-9 codes not covered for indications listed in the CPB:

327.00 - 327.8   Organic sleep disorders

780.50 - 780.59   Sleep disturbances

786.03   Apnea

786.09   Other dyspnea and respiratory abnormalities

Pillar™ Palatal Implant System:

HCPCS codes not covered for indications listed in the CPB:

C9727   Insertion of implants into the soft palate; minimum of three implants

ICD-9 codes not covered for indications listed in the CPB:

327.00 - 327.8   Organic sleep disorders

780.50 - 780.59   Sleep disturbances [if used to report OSA]

786.03   Apnea

786.09   Other dyspnea and respiratory abnormalities

Transpalatal Advancement Pharyngoplasty:

CPT codes not covered for indications listed in the CPB:

42145   Palatopharyngoplasty (e.g., uvulopalatopharyngoplasty, uvulopharyngoplasty) [if used to report transpalatal advancement pharyngoplasty]

| 42950 | Pharyngoplasty (plastic or reconstructive operation on pharynx) [if used to report transpalatal advancement pharyngoplasty] |

ICD-9 codes not covered for indications listed in the CPB:

327.00 - 327.8	Organic sleep disorders
780.50 - 780.59	Sleep disturbances [if used to report OSA]
786.03	Apnea
786.09	Other dyspnea and respiratory abnormalities

Nasal Surgery:

CPT codes not covered for indications listed in the CPB:

| 30000 - 30999 | Surgery/Respiratory System, nose/nasal |

ICD-9 codes not covered for indications listed in the CPB:

327.00 - 327.8	Organic sleep disorders
780.50 - 780.59	Sleep disturbances [if used to report OSA]
786.03	Apnea
786.09	Other dyspnea and respiratory abnormalities

Partial Glossectomy:

CPT codes not covered for indications listed in the CPB:

41120	Glossectomy; less than one-half tongue
41130	Hemiglossectomy
41135	Partial; with unilateral radical neck dissection

ICD-9 codes not covered for indications listed in the CPB:

327.00 - 327.8	Organic sleep disorders
780.50 - 780.59	Sleep disturbances [if used to report OSA]
786.03	Apnea
786.09	Other dyspnea and respiratory abnormalities

Provent sleep apnea therapy:

No specific codes

The above policy is based on the following references:

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