Title of Session

Presenter name

CHEST® Congress 2019 | Thailand Bangkok | 10-12 April

The Current State in OSA Diagnosis and Treatment

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Conflicts of Interest

- Symposium Honorarium from ResMed, Respironics, Fisher-Paykel
- Research medical devices from ResMed, Respironics, Fisher-Paykel

Outline

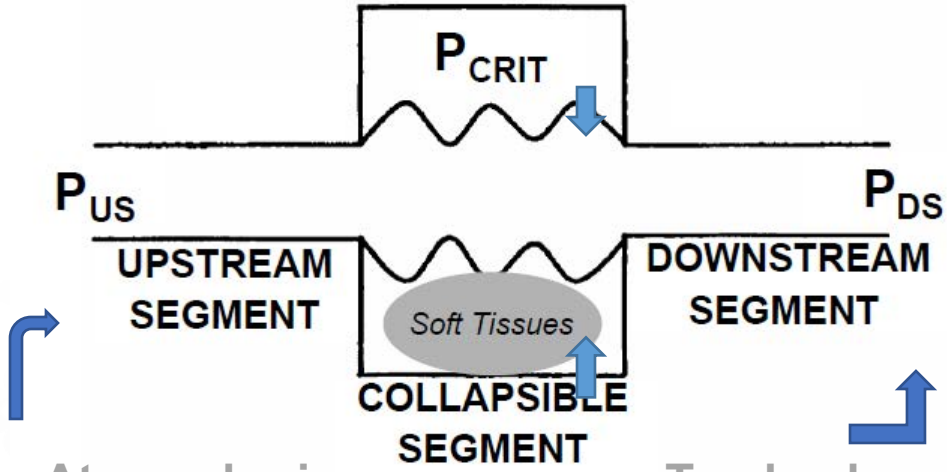
- OSA in brief
- OSA Diagnosis
- OSA treatment

OSA in brief

Obstructive sleep apnea

- “Repetitive upper airway obstruction during sleep resulting in intermittent hypoxia and sleep fragmentation caused by arousals”

Effect of sleep on upper airway collapsibility



Flow proportional to difference between upstream pressure and Pcrit

Effect of sleep on upper airway collapsibility

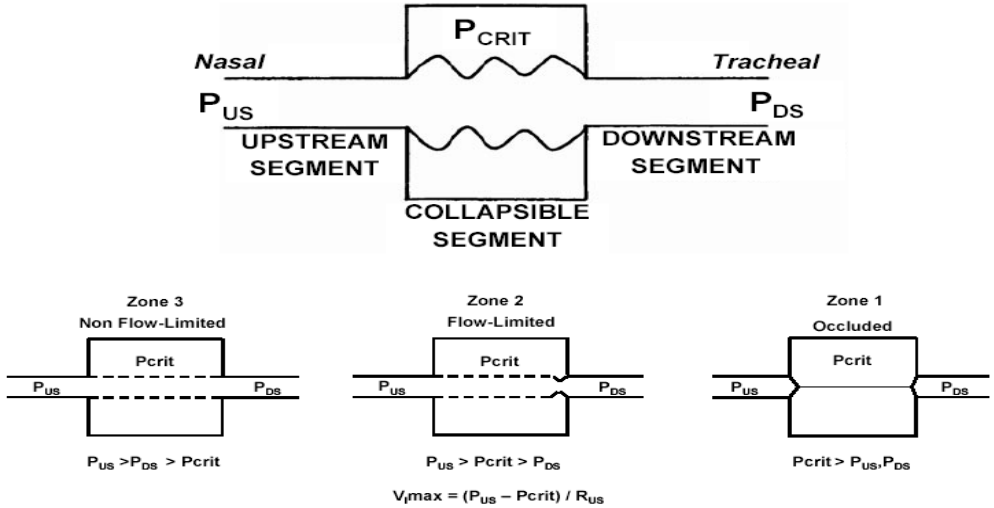
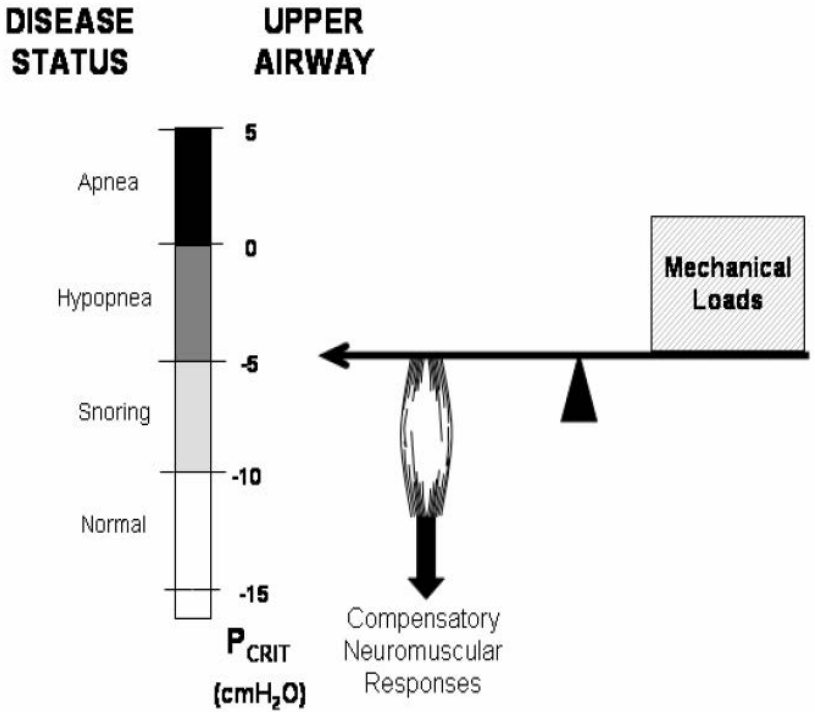


FIGURE 1. In the Starling resistor model, the collapsible segment of the tube is bound by an upstream and downstream segment with corresponding upstream and downstream pressures (Pus and Pds) and resistances (upstream resistance pressure and downstream resistance; data not shown). See text for further explanation (adapted in part from Gleadhill et al[18]). Vtmax = maximal inspiratory flow; Rus = upstream resistance.


DISEASE STATUS
UPPER AIRWAY
Apnea
Hypopnea
Snoring
Normal
5
0
-5
-10
-15
P_{CRIT} (cmH_2O)
Mechanical Loads
Compensatory Neuromuscular Responses

Diagnosis

A. The presence of one or more of the following:

- The patient complains of sleepiness, nonrestorative sleep, fatigue, or insomnia symptoms.
- The patient wakes with breathing holding, gasping, or choking.
- The bed partners or other observer reports habitual snoring, breathing interruptions, or both during the patient's sleep.
- The patient has been diagnosed with hypertension, a mood disorder, cognitive dysfunction, coronary artery disease, stroke, congestive heart failure, atrial fibrillation, or type 2 diabetes mellitus.

B. Polysomnography (PSG) or OCST demonstrates

- Five of more predominantly obstructive respiratory events (obstructive and mixed apneas, hypopneas, or respiratory effort related arousals (RERA)) per hour of sleep during a PSG or per hour of monitoring (OCST).

C. Polysomnography (PSG) or OCST demonstrates

* Fifteen or more predominantly obstructive respiratory events (apneas, hypopneas, or RERAs) per hour of sleep during a PSG or per hour of monitoring (OCST).

International Classification of Sleep Disorders (ICSD)-3 2014

OSA diagnosis

Types of sleep test

- 1. Type 1: full attended polysomnography (≥ 7 channels) in a laboratory setting
- 2. Type 2: full unattended polysomnography (≥ 7 channels)
- 3. Type 3: limited channel devices (usually using 4–7 channels)
- 4. Type 4: 1 or 2 channels usually using oximetry as 1 of the parameters

Collop NA, et al. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. J Clin Sleep Med 2007; 3(7):737-47.

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SPECIAL ARTICLES

Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline

- 1. We recommend that clinical tools, questionnaires and prediction algorithms not be used to diagnose OSA in adults, in the absence of polysomnography or home sleep apnea testing. (STRONG)

Kapur VK, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(3):479–504.

Screening tool

- Berlin Questionnaire
- Sleep Apnea Clinical Score (SACS)
- Epworth Sleepiness Scale Score
- STOP
- STOP-Bang

1. **S**noring Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?	Yes/No
2. **T**ired Do you often feel tired, fatigued, or sleepy during daytime?	Yes/No
3. **O**bserved apnea Has anyone observed you stop breathing during your sleep?	Yes/No
4. Blood **p**ressure Do you have or are you treated for high blood pressure?	Yes/No
5. **B**MI more than 35 kg/m^2?	Yes/No
6. **A**ge Age over 50 yr old?	Yes/No
7. **N**eck circumference Neck circumference greater than 40 cm?	Yes/No
8. **G**ender Gender male?	Yes/No
High risk of OSA: answering yes to three or more items **Low risk of OSA:** answering yes to fewer than three items	

- Seventeen studies including 9,206 patients met criteria for the systematic review
- In the sleep clinic population, the sensitivity was 90%, 94% and 96% to detect any OSA (AHI >5), moderate-to-severe OSA (AHI >15), and severe OSA (AHI>30) respectively
- The corresponding NPV was 46%, 75% and 90%
- Specificity was 49%, 30%, and 25%

Nagappa M, et al. Validation of the STOP-Bang Questionnaire as a Screening Tool for Obstructive Sleep Apnea among Different Populations: A Systematic Review and Meta-Analysis.PLoS One. 2015;10(12):e0143697.

- STOP-Bang may not be good predictor for young and lack of hypertension population
- A prospective cross-sectional study was performed among young doctors <40 years old with HSAT

Table 4 The predictors for obstructive sleep apnea

Predictor of OSA (AHI ≥5/h)	Odds ratio	95 % CI	*p* value
Snoring	34.5	1.92–619.15	0.016
Male gender	18.8	3.10–113.41	0.001
Perception of inadequate sleep	7.4	1.13–48.30	0.037

Yasin R, Muntham D, Chirakalwasan N. Uncovering the Sleep Disorders among Young Doctors. Sleep Breath. 2016 Dec;20(4):1137-44.

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SPECIAL ARTICLES

Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline

- 2. We recommend that polysomnography, or home sleep apnea testing with a technically adequate device, be used for the diagnosis of OSA in uncomplicated adult patients presenting with signs and symptoms that indicate an increased risk of moderate to severe OSA. (STRONG)

Kapur VK, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(3):479–504.

Uncomplicated patients

- 1. Not suspecting non-obstructive sleep-disordered breathing (e.g., central sleep apnea, hypoventilation and sleep related hypoxemia) such as significant cardiopulmonary disease, potential respiratory muscle weakness due to neuromuscular conditions, history of stroke and chronic opiate medication use

Uncomplicated patients

- 2. Not suspecting other sleep disorders e.g. central hypersomnolence, parasomnias, sleep related movement disorders or interfere with accuracy of HSAT (e.g., severe insomnia)

Uncomplicated patients

- 3. Environmental or personal factors that preclude the adequate acquisition and interpretation of data from HSAT

Increased risk of moderate to severe

- Indicated by the presence of excessive daytime sleepiness and at least two of the following three criteria: habitual loud snoring, witnessed apnea or gasping or choking, or diagnosed hypertension

Kapur VK, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(3):479–504.

- A technically adequate HSAT device incorporates a minimum of the following sensors: nasal pressure, chest and abdominal respiratory inductance plethysmography, and oximetry, or else PAT with oximetry and actigraphy
- A technically adequate diagnostic test includes a minimum of 4 hours of technically adequate oximetry and flow data obtained during a recording attempt that encompasses the habitual sleep period

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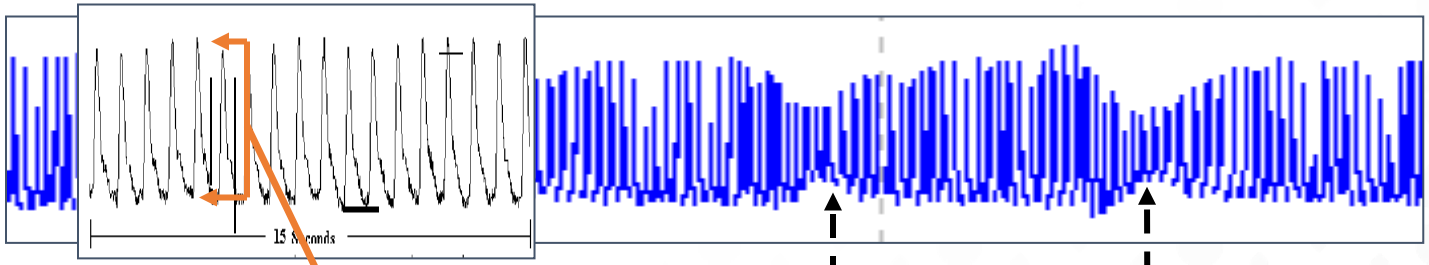
~~฿5,500.00~~ ฿3,900.00

Buy Home Sleep Test
~~฿12,000.00~~ ฿8,900.00

Peripheral Arterial Tone

PAT signal

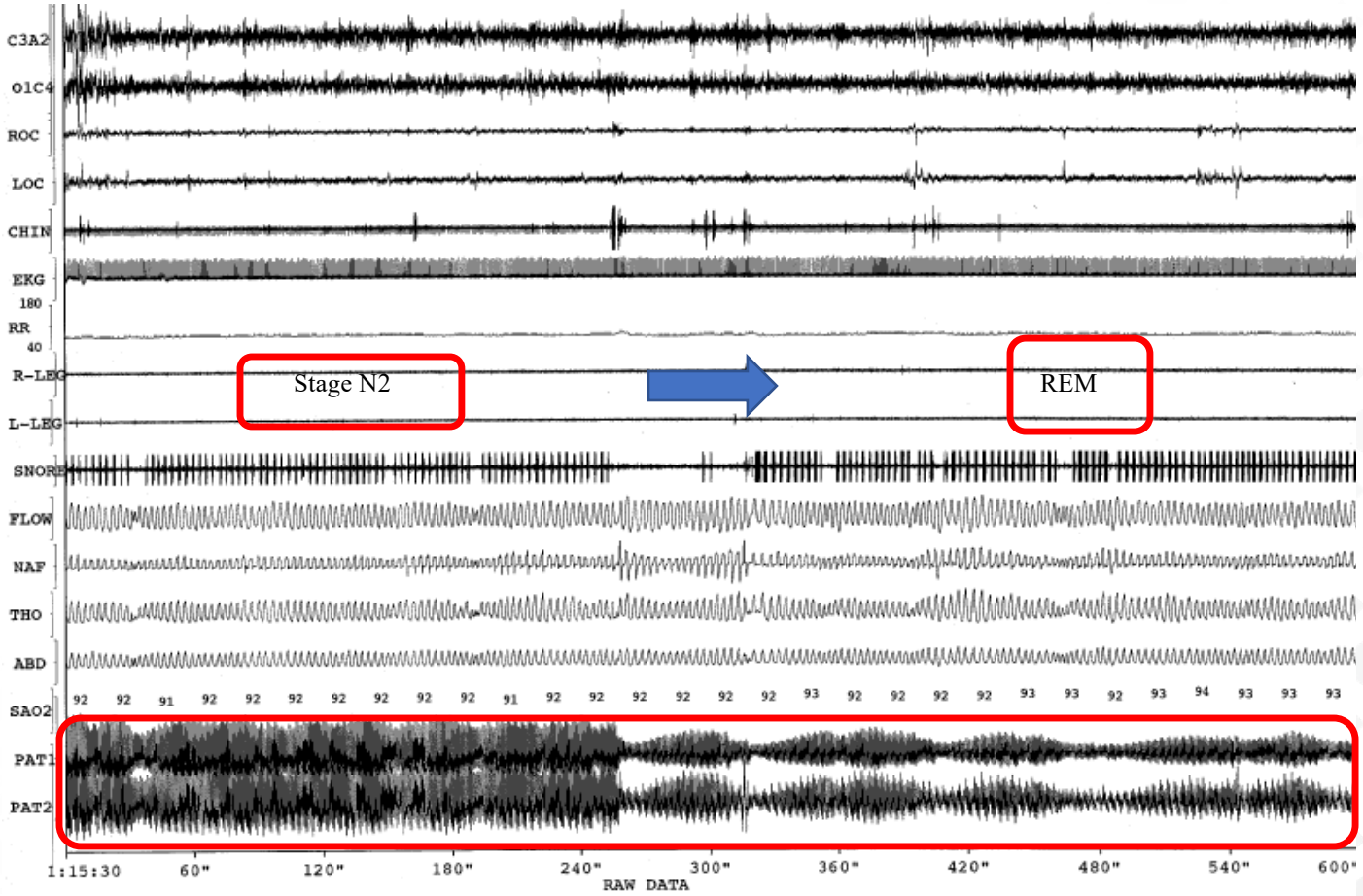


PAT Amplitude

PAT attenuation

α- receptors

Sympathetic activation



Baseline PAT attenuates with transition from stage II to REM

- An HSAT should not be used for general screening of asymptomatic clinical populations
- Diagnosis, assessment of treatment efficacy, and treatment decisions must not be based solely on automatically scored HSAT data
- The raw data from the HSAT device must be reviewed and interpreted by a physician who is either board certified in sleep medicine or overseen by a board certified sleep medicine physician

Rosen IM, et al. Clinical use of a home sleep apnea test: an updated American Academy of Sleep Medicine position statement. J Clin Sleep Med. 2018;14(12):2075–7.

SPECIAL ARTICLES

Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline

- 3. We recommend that if a single home sleep apnea test is negative, inconclusive, or technically inadequate, polysomnography be performed for the diagnosis of OSA. (STRONG)

Kapur VK, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(3):479–504.

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SPECIAL ARTICLES

Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline

- 4. We recommend that polysomnography, rather than home sleep apnea testing, be used for the diagnosis of OSA in patients with significant cardiorespiratory disease, potential respiratory muscle weakness due to neuromuscular condition, awake hypoventilation or suspicion of sleep related hypoventilation, chronic opioid medication use, history of stroke or severe insomnia. (STRONG)

Kapur VK, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(3):479–504.

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Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline

- 5. We suggest that, if clinically appropriate, a split-night diagnostic protocol, rather than a full-night diagnostic protocol for polysomnography be used for the diagnosis of OSA. (WEAK)

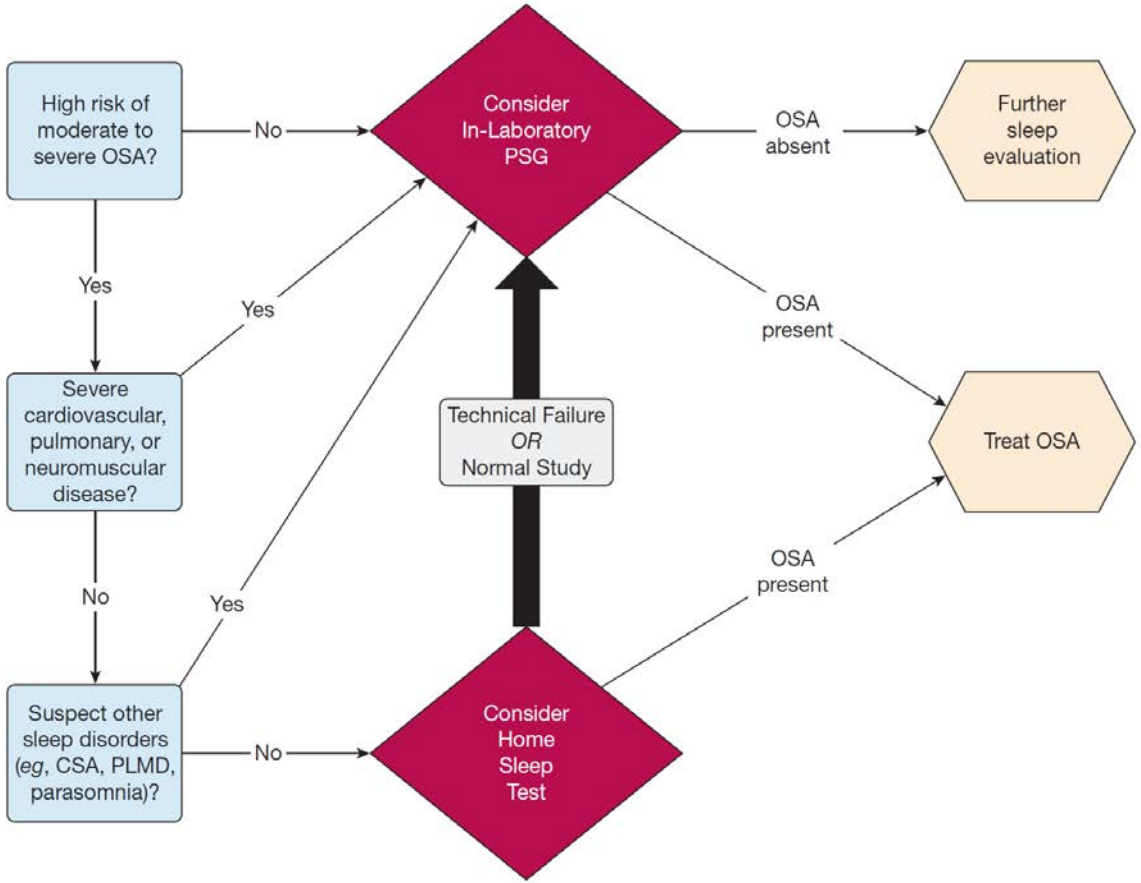
Kapur VK, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(3):479–504.

SPECIAL ARTICLES

Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline

- 6. We suggest that when the initial polysomnogram is negative and clinical suspicion for OSA remains, a second polysomnogram be considered for the diagnosis of OSA. (WEAK)

Kapur VK, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13(3):479–504.



Cooksey JA, et al. Portable Monitoring for the Diagnosis of OSA. Chest. 2016 ;149(4):1074-81.

NEW

1A. Hypopnea

a. The peak signal excursions drop by ≥30%
b. b. The duration of the ≥30% drop in signal excursion is ≥10 seconds
c. There is a ≥3% oxygen desaturation or the event is associated with an arousal

1B. Hypopnea

a. The peak signal excursions drop by ≥30%
b. b. The duration of the ≥30% drop in signal excursion is ≥10 seconds
c. There is a ≥4% oxygen desaturation

Berry RB, et al. The ASSM manual for the scoring of sleep and associated events: rules terminology and technical specifications, Version 2.3. Darien, IL: American Academy of Sleep Medicine, 2016.

APNEA-HYPOPNEA INDICES: IMPACT OF ALTERNATE CRITERIA FOR HYPOPNEAS

Calibration Model for Apnea-Hypopnea Indices: Impact of Alternative Criteria for Hypopneas

Vu Ho, MD[1,2,6]; Ciprian M. Crainiceanu, PhD[3]; Naresh M. Punjabi, MD, PhD[4]; Susan Redline, MD, MPH[5]; Daniel J. Gottlieb, MD, MPH[2,5,6]

[1]Department of Medicine, Division of Sleep Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA; [2]Department of Medicine, The Pulmonary Center, Boston University School of Medicine, Boston, MA; [3]Department of Biostatistics, Johns Hopkins University; [4]Department of Medicine, Johns Hopkins University School of Medicine, Baltimore, MD; [5]Department of Medicine, Division of Sleep Medicine, Brigham and Women's Hospital and Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA; [6]Veterans Affairs Boston Healthcare System, West Roxbury, MA

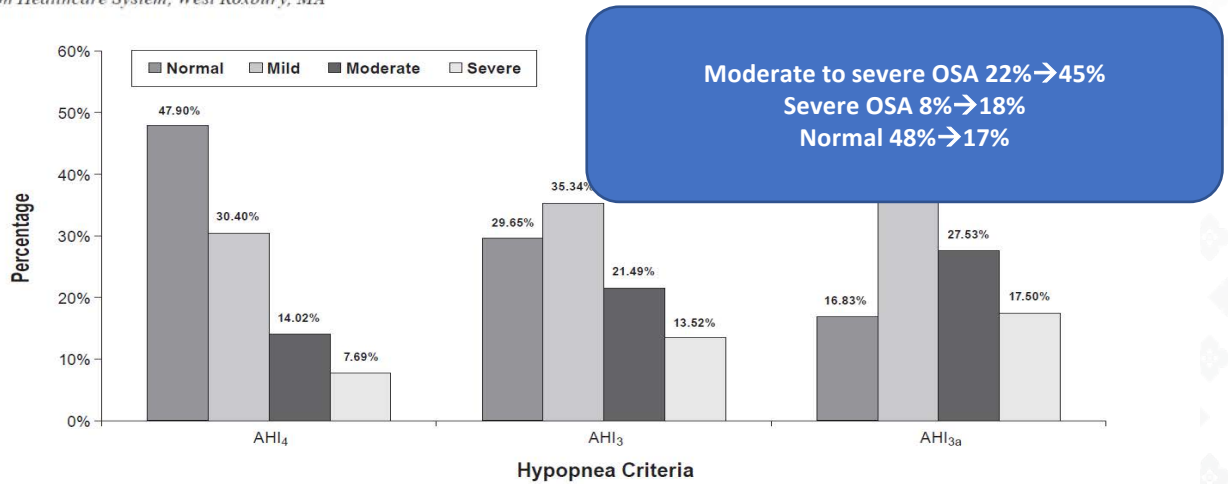
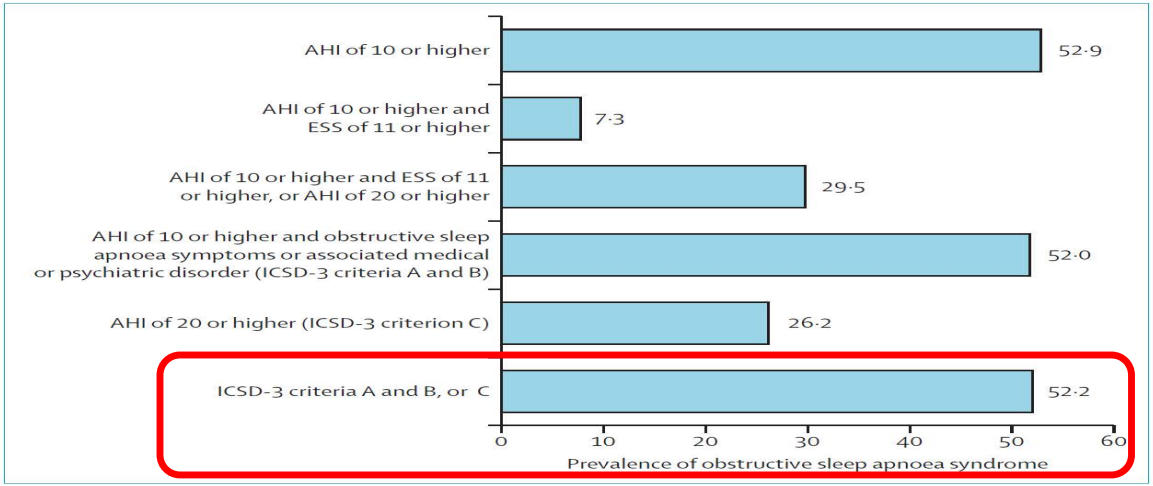


Figure 1—Distribution of obstructive sleep apnea (OSA) severity using different hypopnea criteria to determine apnea-hypopnea index (AHI). OSA classification: normal AHI < 5; 5 ≤ mild < 15; 15 ≤ moderate < 30; severe ≥ 30.

Ho V, et al.SLEEP 2015;38(12):1887–92.

Are the ICSD-3 criteria for sleep apnoea syndrome too inclusive?

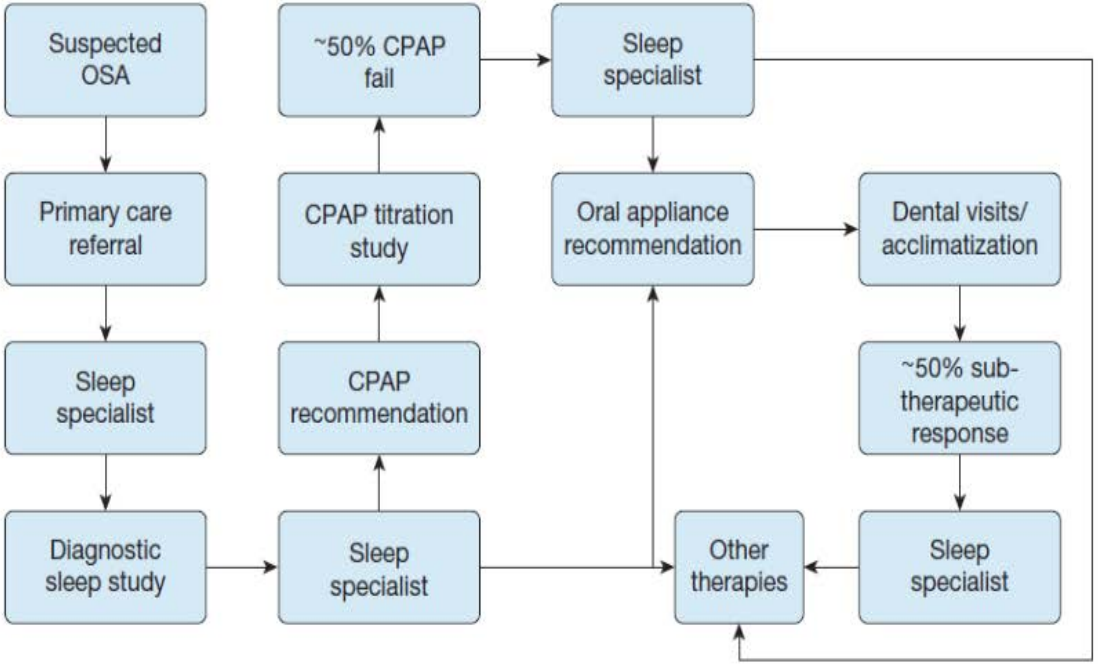


Adams R, et al. Lancet Respir Med. 2016;4(5):e19-20.

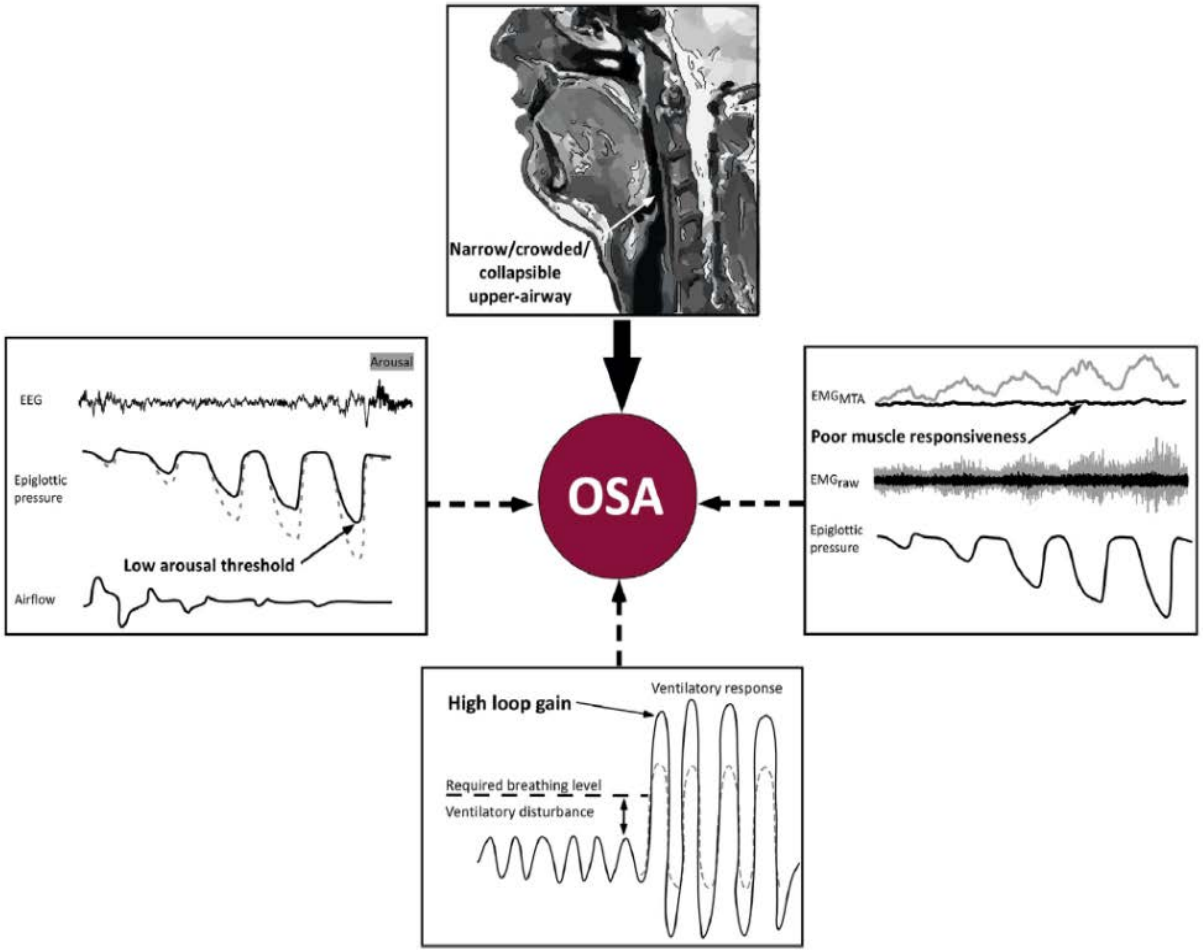
Lancet Respir Med. 2016;4(5):e19-20.

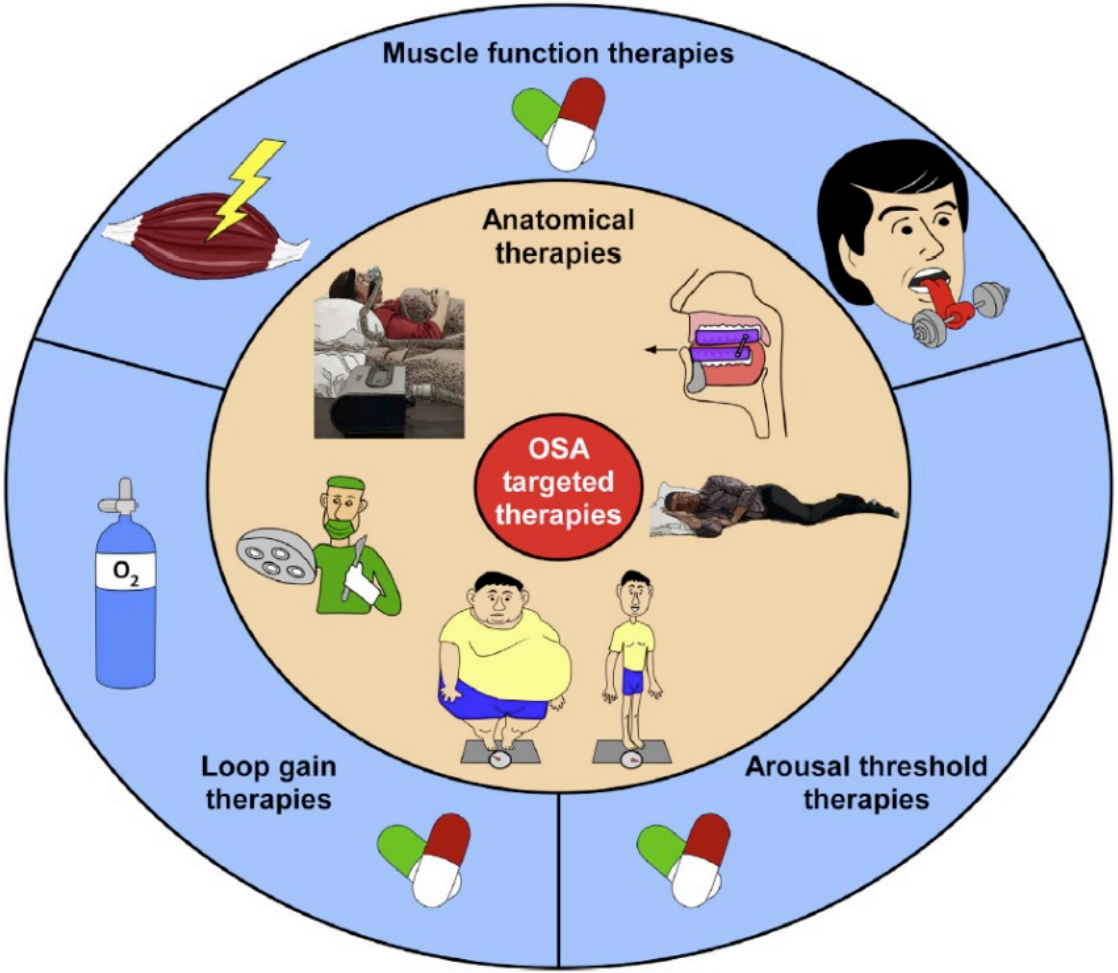
Consistent with the findings of Heinzer and colleagues,[4] the ICSD-3 criteria identified a high prevalence of obstructive sleep apnoea syndrome even though we used a higher AHI cut-off and more conservative hypopnoea scoring criteria. A number of cardiovascular and metabolic disorders included in the ICSD-3 criteria might not be causally related to obstructive sleep apnoea. For many of these disorders, evidence that they improve with treatment of obstructive sleep apnoea is either weak or completely absent. We agree with Heinzer and colleagues that symptoms should only be considered when they cannot be attributed to other factors and that the ICSD-3 criteria need revision.

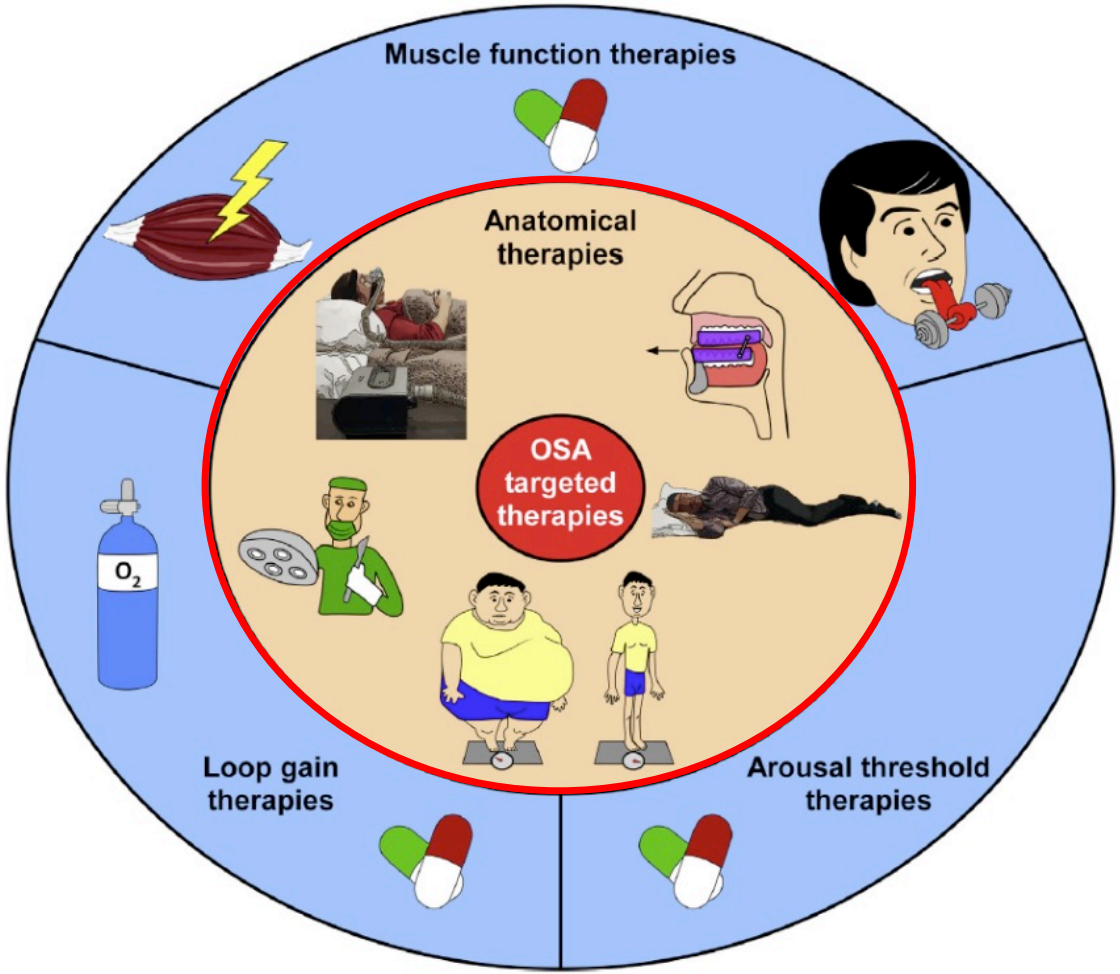
OSA treatment



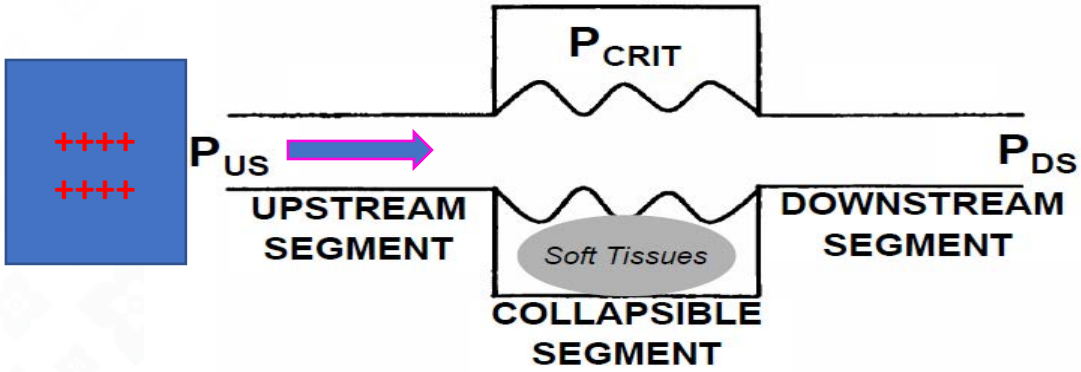
Carberry JC, et al. Personalized Management Approach for OSA. Chest. 2018;153(3):744-55.


Narrow/crowded/
collapsible
upper-airway
Arousal
EEG
Epiglottic
pressure
Low arousal threshold
Airflow
OSA
EMGMTA
Poor muscle responsiveness
EMGraw
Epiglottic
pressure
High loop gain
Ventilatory response
Required breathing level
Ventilatory disturbance


Muscle function therapies
Anatomical therapies
OSA targeted therapies
O_2
Loop gain therapies
Arousal threshold therapies


Muscle function therapies
Anatomical therapies
OSA targeted therapies
O_2
Loop gain therapies
Arousal threshold therapies

Continuous positive airway pressure (CPAP)



First CPAP (1980)

Pressurized airflow is generated with fan-driven or turbine systems, adjustable by varying valve diameter or turbine speed

Nowsaday CPAP

Nowsaday CPAP mask



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SPECIAL ARTICLES

Treatment of Adult Obstructive Sleep Apnea with Positive Airway Pressure: An American Academy of Sleep Medicine Clinical Practice Guideline

- 1. We recommend that clinicians use PAP, compared to no therapy, to treat OSA in adults with excessive sleepiness. (STRONG)
- 2. We suggest that clinicians use PAP, compared to no therapy, to treat OSA in adults with impaired sleep-related quality of life. (CONDITIONAL)
- 3. We suggest that clinicians use PAP, compared to no therapy, to treat OSA in adults with comorbid hypertension. (CONDITIONAL)

Patil SP, et al. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2019;15(2):335–43.

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SPECIAL ARTICLES

Treatment of Adult Obstructive Sleep Apnea with Positive Airway Pressure: An American Academy of Sleep Medicine Clinical Practice Guideline

- 4. We recommend that PAP therapy be initiated using either APAP at home or in-laboratory PAP titration in adults with OSA and no significant comorbidities. (STRONG)
- 5. We recommend that clinicians use either CPAP or APAP for ongoing treatment of OSA in adults. (STRONG)
- 6. We suggest that clinicians use CPAP or APAP over BPAP in the routine treatment of OSA in adults. (CONDITIONAL)

Patil SP, et al. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2019;15(2):335–43.

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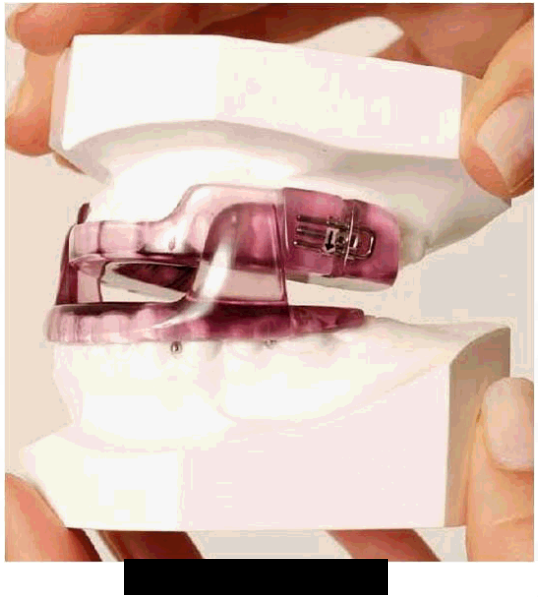
Treatment of Adult Obstructive Sleep Apnea with Positive Airway Pressure: An American Academy of Sleep Medicine Clinical Practice Guideline

- 7. We recommend that educational interventions be given with initiation of PAP therapy in adults with OSA. (STRONG)
- 8. We suggest that behavioral and/or troubleshooting interventions be given during the initial period of PAP therapy in adults with OSA. (CONDITIONAL)
- 9. We suggest that clinicians use telemonitoring-guided interventions during the initial period of PAP therapy in adults with OSA. (CONDITIONAL)

Patil SP, et al. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2019;15(2):335–43.

Mandibular advancement device (MAD)



Mandibular advancement device (MAD)

- Adjustable-MAD is recommended in CPAP/BPAP intolerance or the patients who preferred other treatment options
- May be used in combination with CPAP in CPAP pressure intolerance

Adjustable MAD (duobloc)

Ferguson KA, et al. Oral appliances for snoring and obstructive sleep apnea: a review. Sleep 2006;29:244-62.

Mandibular advancement device (MAD)

- Overall a-MAD is less effective in reducing overall RDI compared to CPAP
- However, in mild OSA, a-MAD may be as effective as CPAP

Ramar K, et al. Clinical Practice Guideline for the Treatment of Obstructive Sleep Apnea and Snoring with Oral Appliance Therapy: An Update for 2015. J Clin Sleep Med 2015;11:773-827.
Sharples LD, et al. Meta-analysis of randomised controlled trials of oral mandibular advancement devices and continuous positive airway pressure for obstructive sleep apnoea-hypopnoea. Sleep Med Rev 2016;27:108-24.

Remotely Controlled Mandibular Positioner (RCMP)

Remotely Controlled Mandibular Positioner (RCMP)

- Effective target protrusive position (ETPP) as measured by the use of RCMP was significantly associated with success of MAD therapy
- RCMP might be a promising instrument for predicting MAD treatment outcome and targeting the degree of mandibular advancement needed

Kastoer C, et al. The use of remotely controlled mandibular positioner as a predictive screening tool for mandibular advancement device therapy in patients with obstructive sleep apnea through single-night progressive titration of the mandible: a systematic review. J Clin Sleep Med 2016;12(10): 1411–21.

Uvulopalatopharyngoplasty (UPPP)

- In patients having difficulty with other treatments, surgical procedures for the nose and throat can be a beneficial alternative
- Surgical therapy can also be effective when used as an adjunct to improve tolerance and success with CPAP or an oral appliance

Drug-induced sleep endoscopy (DISE)

- DISE is an additional method to reveal obstruction sites that have not been detected in awake patients
- DISE demonstrated the importance of identifying multilevel obstruction, especially in relation to retrolingual and laryngeal collapse in OSAS

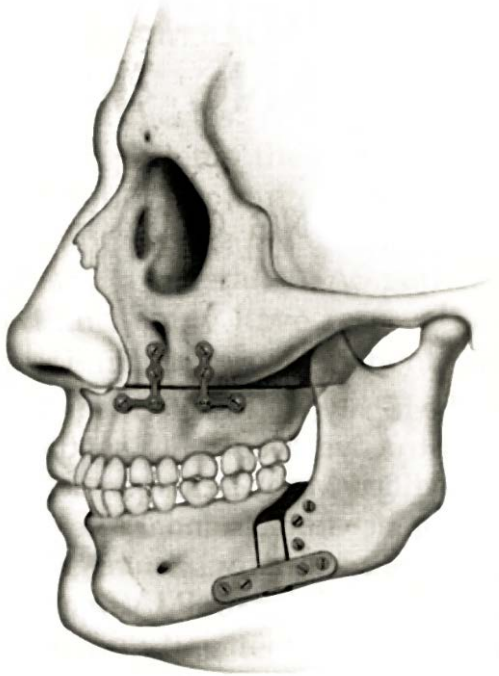
Viana Ada C Jr, et al. Drug-induced sleep endoscopy in the identification of obstruction sites in patients with obstructive sleep apnea: a systematic review. Braz J Otorhinolaryngol. 2015;81(4):439-46.

Drug-induced sleep endoscopy (DISE)

- Greater sedative depth increased upper airway collapsibility under DISE assessment
- DISE under Bispectral Index (BIS)-guided propofol infusion, and especially a level of 65–75, offers an objective and reproducible method to evaluate upper airway collapsibility

Lo YL, et al. Bispectral index in evaluating effects of sedation depth on drug-induced sleep endoscopy. J Clin Sleep Med 2015;11(9):1011–20.

Maxillomandibular advancement surgery (MMA)



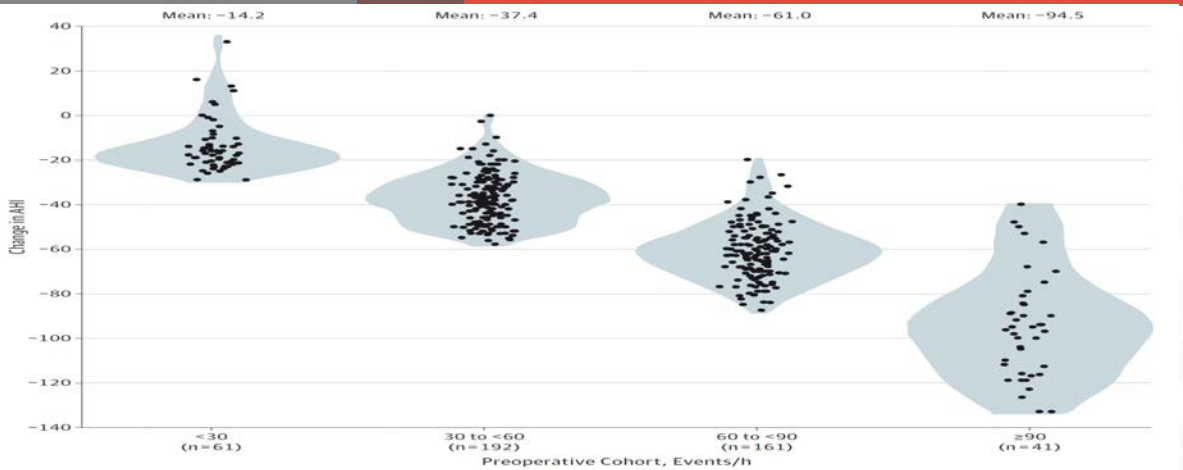


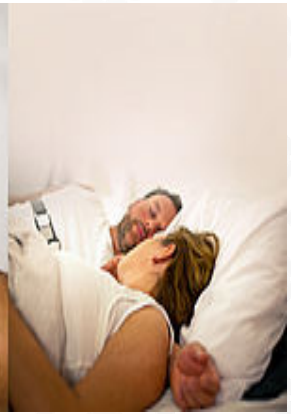
Table 2. Rates of Surgical Success or Cure by Preoperative AHI Severity

Surgical Success[a]	Preoperative AHI Cohort, Events/h			
	<30 (n = 61)	30 to <60 (n = 192)	60 to <90 (n = 161)	≥90 (n = 41)
AHI cure, No. (%)	34 (55.7)[b]	88 (45.8)[b]	45 (28.0)	8 (19.5)
AHI Success-10, No. (%)	47 (77.0)[b]	140 (72.9)[b]	77 (47.8)	24 (58.5)
AHI Success-15, No. (%)	51 (83.6)[c]	169 (88.0)[c]	117 (72.7)	29 (70.7)
AHI Success-20, No. (%)	51 (83.6)[d]	176 (91.7)[d]	130 (80.7)[d]	31 (75.6)

Zaghi S, et al. Maxillomandibular Advancement for Treatment of Obstructive Sleep Apnea: A Meta-analysis. JAMA Otolaryngol Head Neck Surg. 2016;142(1):58-66.

- Preoperative AHI of fewer than 60 events/h was the factor most strongly associated with the highest incidence of surgical cure
- Patients with high residual RDI and AHI scores (despite prior treatments by means of uvulopalatopharyngoplasty, partial glossectomy, and/or nasal surgery) are highly likely to benefit from management of OSA by means of MMA

Positional therapy



- Data from Asians revealed prevalence of positional OSA to be 67% in which almost of these patients (47%), RDI was normalized during non-supine position

Teerapraipruk B, Chirakalwasan N, et al. Clinical and polysomnographic data of positional sleep apnea and its predictors. Sleep Breath. 2012;16(4):1167-72.

- Prior studies demonstrated equal efficacy compared to CPAP in mild positional OSA who demonstrated AHI<5 in non-supine position
- Long term compliance monitoring is a major problem

Permut I, et al. Comparison of positional therapy to CPAP in patients with positional obstructive sleep apnea. J Clin Sleep Med 2010;6:238-43.

- However; recent study up to 1 year follow up demonstrated mean usage of 7.3 ± 0.9 h/night and 69 ±26% of the nights
- Furthermore, 75% of the patients reported a better sleep quality since the start of SPT treatment

Beyers J, et al. Treatment of sleep-disordered breathing with positional therapy: long-term results. Sleep Breath. 2019 Feb 18.

Weight reduction

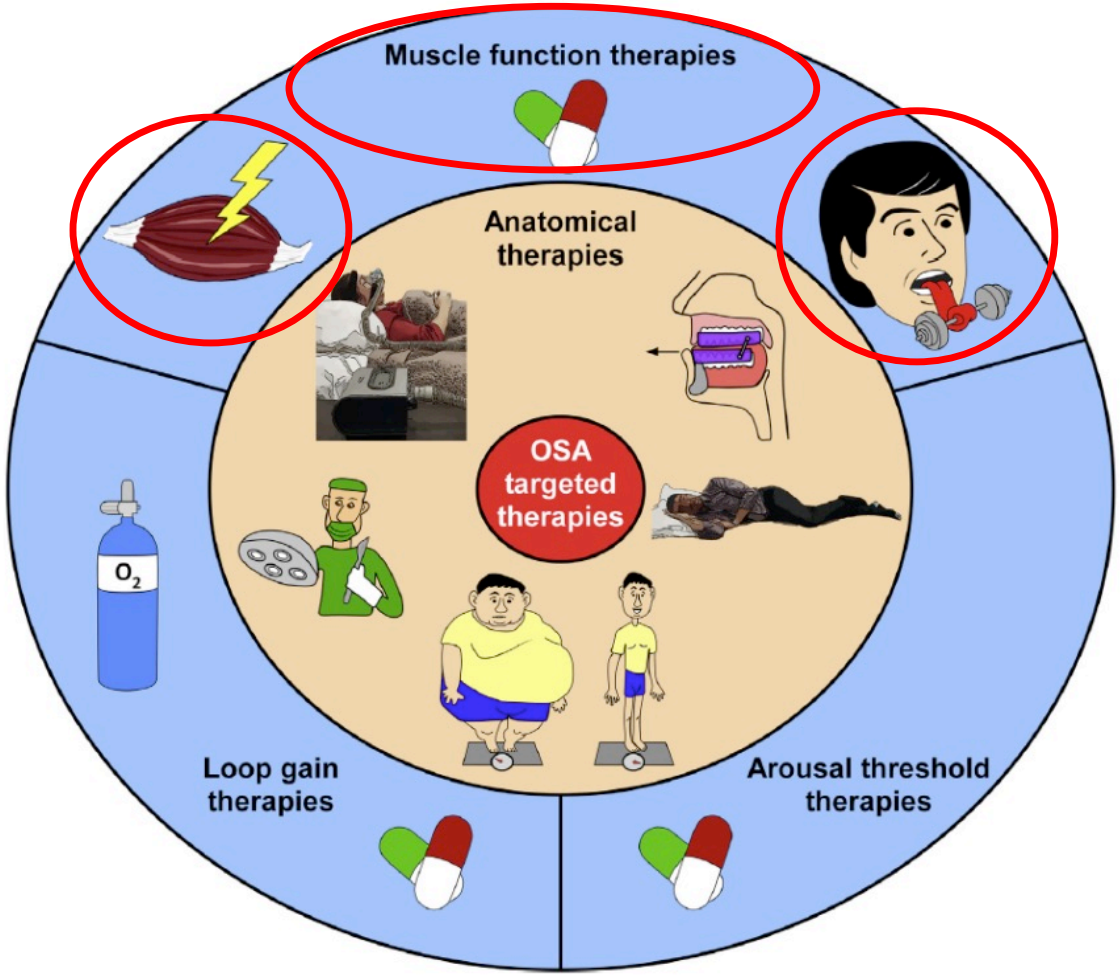
- Weight reduction in recommended in ALL OSA patients who are overweight or obese
- However, current evidence demonstrated that in moderate to severe OSA, weight reduction should not be the sole treatment for OSA
- Scarce data was observed with resolution of OSA in mild group with weight reduction

Morgenthaler TI, et al. Practice parameters for the medical therapy of obstructive sleep apnea. Sleep 2006;29:1031-5.
Tuomilehto H, et al. The impact of weight reduction in the prevention of the progression of obstructive sleep apnea: an explanatory analysis of a 5-year observational follow-up trial. Sleep Med 2014;15:329-35.

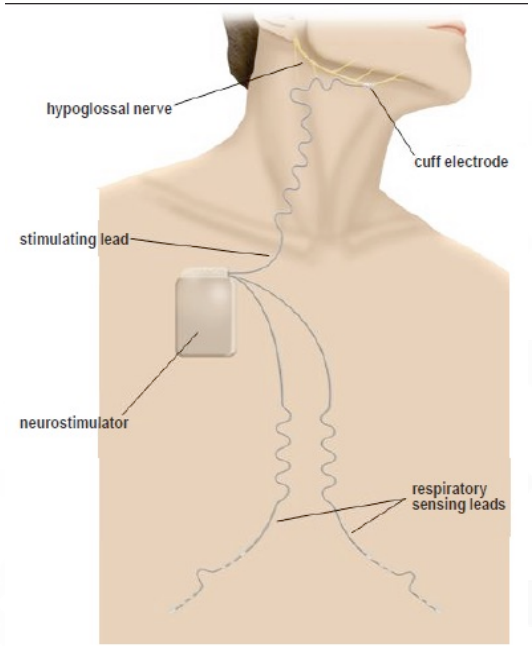
	Mean (95% CI)				
	Surgical Treatment (n = 30)	Conventional Weight Loss Program (n = 30)	Between-Group Difference	No. (%) Missing at 2 y	*P* Value
Weight, kg	107 (99 to 116)	121 (113 to 129)			
Change in weight, kg	−27.8 (−34.7 to −20.9)[a]	−5.1 (−9.3 to −0.8)[a]	−22.7 (−31.1 to −14.3)	2 (3)	<.001
Apnea-hypopnea index, events/h	39.5 (28.4 to 50.5)[a]	43.2 (34.9 to 51.9)[a]			
Change in apnea-hypopnea index, events/h	−25.5 (−36.7 to −14.2)	−14.0 (−24.6 to −3.3)	−11.5 (−28.3 to 5.3)	6 (10)	.18
Total sleep time, min	373 (348 to 399)	333 (297 to 370)			
Change in total sleep time, min	22.0 (−5.5 to 46.5)	10.5 (−25.5 to 46.4)	11.5 (−39.0 to 62.1)	6 (10)	.65
Sleep latency, min	18.6 (11.3 to 26)	24.5 (15.0 to 34.1)			
Change in sleep latency, min	−6.3 (−13.7 to 1.0)	4.2 (−4.4 to 12.8)	−10.6 (−24.4 to 2.3)	6 (10)	.11
Sleep efficiency, %	79.8 (75.8 to 83.8)	72.4 (65.3 to 79.6)			
Change in sleep efficiency, %	1.6 (−3.4 to 6.6)	−3.04 (−9.70 to 3.70)	4.7 (−4.6 to 13.9)	6 (10)	.32
Supine sleep, %	47.1 (35.5 to 58.6)	37.0 (25.1 to 48.8)			
Change in supine sleep, %	2.9 (−7.6 to 13.4)	−1.7 (11.5 to 8.0)	4.6 (−11.3 to 20.5)	6 (10)	.57
Slow wave sleep, %	15.3 (10.5 to 20.1)	21.1 (13.1 to 29.1)			
Change in slow wave sleep, %	0.7 (−2.7 to 4.1)	2.6 (−3.5 to 8.7)	−1.9 (−10.0 to 6.3)	7 (12)	.65
Rapid eye movement sleep, %	15.5 (12.8 to 18.2)	11.3 (8.4 to 14.2)			
Change in rapid eye movement sleep, %	2.6 (−1.1 to 6.3)	−1.6 (−4.7 to 1.5)	4.2 (−1.1 to 9.5)	7 (12)	.12

- Bariatric surgery in superior to conventional therapy in terms on weight loss
- There was also a trend towards greater reduction in AHI

Dixon JB, et al Surgical vs conventional therapy for weight loss treatment of obstructive sleep apnea: a randomized controlled trial. JAMA. 2012;308(11):1142-9.


Muscle function therapies
Anatomical therapies
OSA targeted therapies
O_2
Loop gain therapies
Arousal threshold therapies

Hypoglossal nerve stimulation



Strollo PJ Jr, et al. Upper-airway stimulation for obstructive sleep apnea. N Engl J Med. 2014;370(2):139-49.
Mwenge GB, et al. Targeted hypoglossal neurostimulation for obstructive sleep apnoea: a 1-year pilot study. Eur Respir J. 2013;41(2):360-7.

Table 2. Primary and Secondary Outcome Measures.*

Outcome	Baseline	12 Months	Change	P Value
Primary outcomes				
AHI score†	32.0±11.8	15.3±16.1	−16.4±16.7	<0.001
Median	29.3	9.0	−17.3	
Interquartile range	23.7 to 38.6	4.2 to 22.5	−26.4 to −9.3	
ODI score‡	28.9±12.0	13.9±15.7	−14.6±15.8	<0.001
Median	25.4	7.4	−15.7	
Interquartile range	19.5 to 36.6	3.5 to 20.5	−24.0 to −8.6	
Secondary outcomes				
FOSQ score§	14.3±3.2	17.3±2.9	2.9±3.1	<0.001
Median	14.6	18.2	2.4	
Interquartile range	12.1 to 17.1	16.2 to 19.5	0.7 to 4.7	
Epworth Sleepiness Scale score¶	11.6±5.0	7.0±4.2	−4.7±5.0	<0.001
Median	11.0	6.0	−4.0	
Interquartile range	8.0 to 15.0	4.0 to 10.0	−8.0 to −1.0	
Percentage of sleep time with oxygen saturation <90%	8.7±10.2	5.9±12.4	−2.5±11.1	0.01
Median	5.4	0.9	−2.2	
Interquartile range	2.1 to 10.9	0.2 to 5.2	−6.6 to −0.3	

Strollo PJ Jr, et al. Upper-airway stimulation for obstructive sleep apnea. N Engl J Med. 2014;370(2):139-49.

- Upper airway stimulation maintained a sustained benefit on patient-reported outcomes (ESS, FOSQ, snoring) at 48 months in select patients with moderate to severe OSA
- However, prior studies utilized rigorous inclusion criteria including moderate to severe OSA (AHI, 20-65), failure of CPAP therapy, body mass index (BMI) <32 kg/m2, and absence of complete circumferential palatal collapse on DISE

Gillespie MB,, et al. Upper Airway Stimulation for Obstructive Sleep Apnea: Patient-Reported Outcomes after 48 Months of Follow-up. Otolaryngol Head Neck Surg 2017;156:765-71.

Muscle training

- A systematic review and meta-analysis that includes data from nine studies involving a total of 120 adult patients showed that oropharyngeal training reduces the AHI by approximately 50% and increases nadir oxygen saturation by > 2.5%

Camacho M, et al. Myofunctional therapy to treat obstructive sleep apnea: a systematic review and meta-analysis. Sleep. 2015;38(5):669-75.

Magic pills ?

- Some pre-clinical works identified the main cause of sleep-related hypotonia of the pharyngeal muscles to be the central reduction of norepinephrine from wakefulness to sleep
- Inhibitory effect of acetylcholine through muscarinic receptors was found to be responsible for the REM-related hypotonia

Taranto-Montemurro L, et al. The Combination of Atomoxetine and Oxybutynin Greatly Reduces Obstructive Sleep Apnea Severity: A Randomized, Placebo-Controlled, Double-Blind Crossover Trial. Am J Respir Crit Care Med. 2018

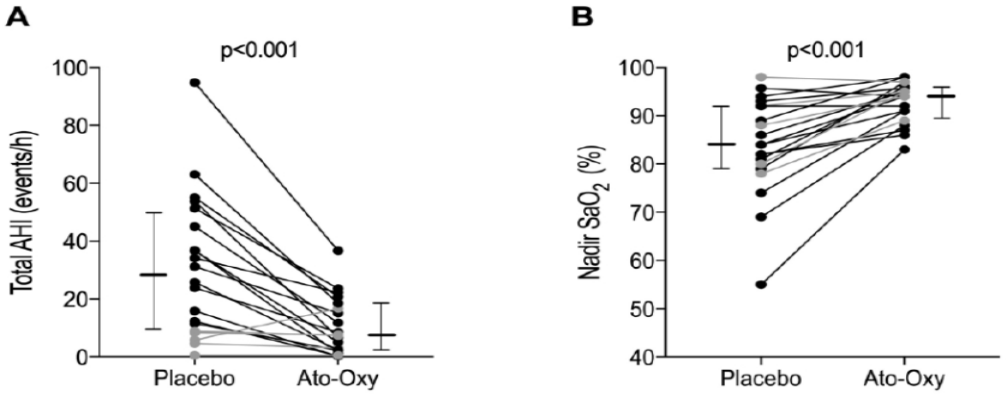
- A trial investigated for the first time the efficacy of the combination of a noradrenergic (atomoxetine) and an antimuscarinic (oxybutynin) on OSA severity and on the responsiveness to esophageal pressure swings of the genioglossus muscle versus placebo

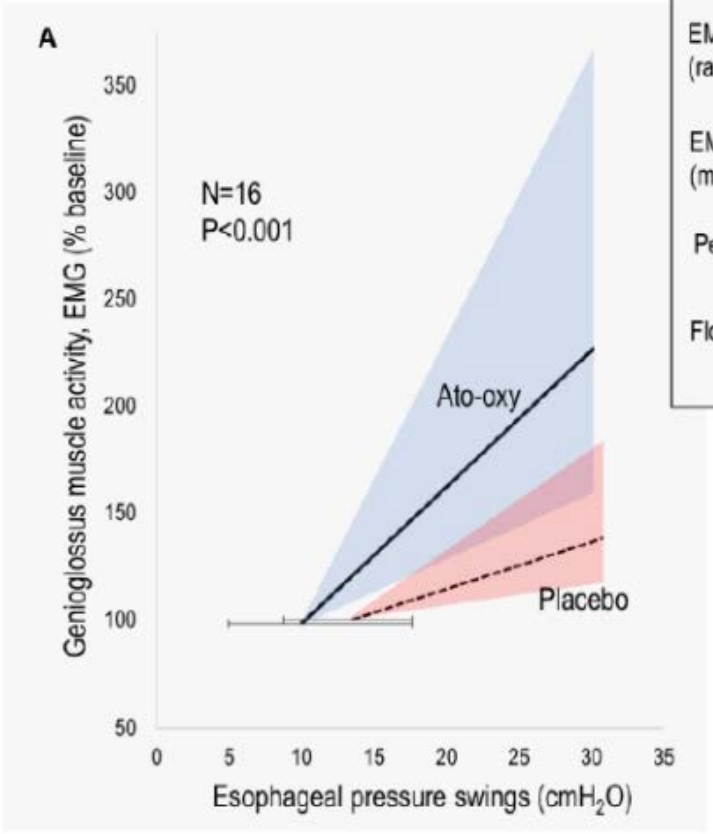
Taranto-Montemurro L, et al. The Combination of Atomoxetine and Oxybutynin Greatly Reduces Obstructive Sleep Apnea Severity: A Randomized, Placebo-Controlled, Double-Blind Crossover Trial. Am J Respir Crit Care Med. 2018

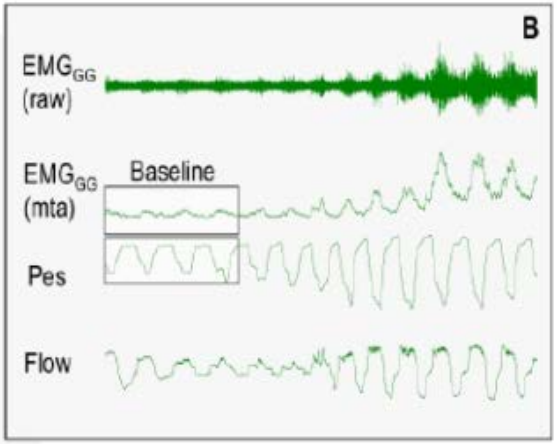
- 20 people completed a randomized, placebo-controlled, double-blind, crossover trial
- comparing one night of atomoxetine 80mg plus oxybutynin 5mg (ato-oxy) to placebo administered prior to sleep

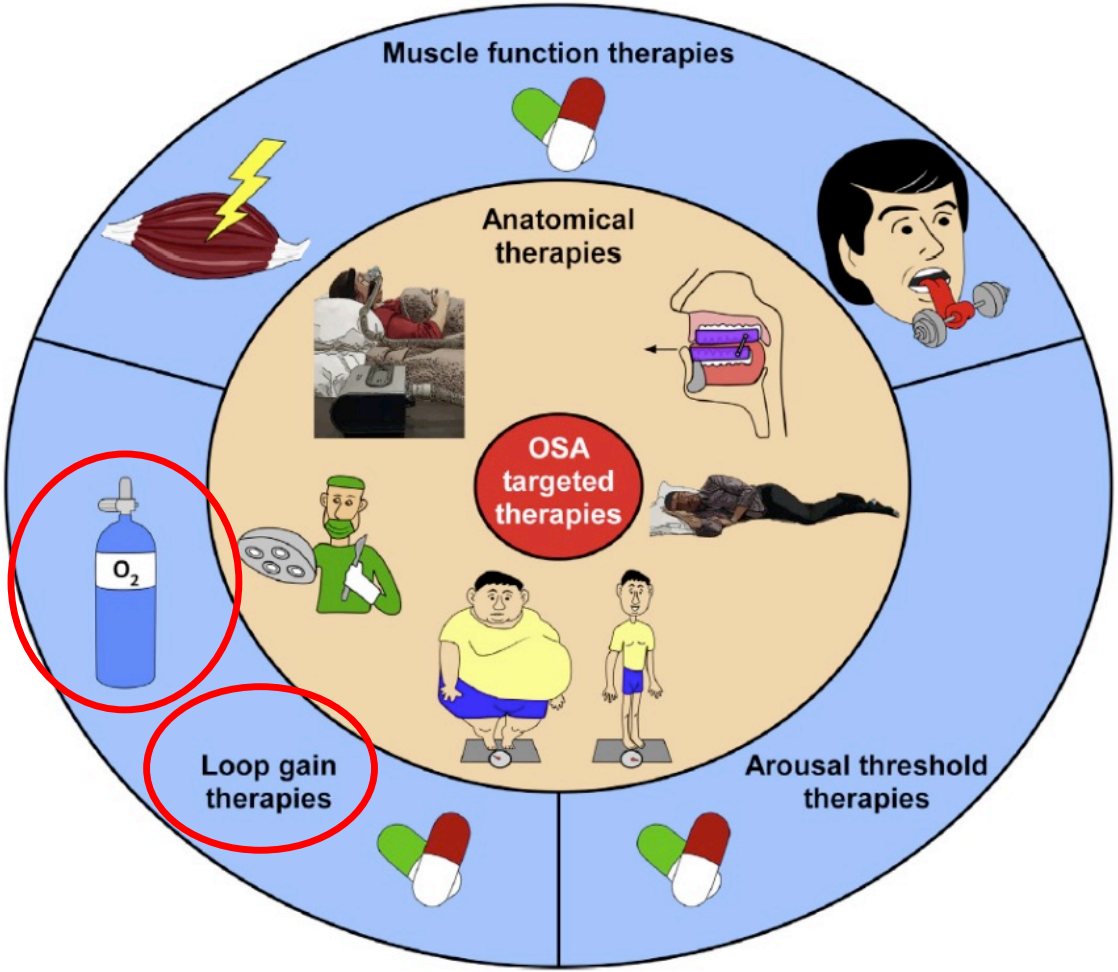
Taranto-Montemurro L, et al. The Combination of Atomoxetine and Oxybutynin Greatly Reduces Obstructive Sleep Apnea Severity: A Randomized, Placebo-Controlled, Double-Blind Crossover Trial. Am J Respir Crit Care Med. 2018

- Ato-oxy lowered AHI by 63% [34-86%], from 28.5 [10.9-51.6] events/h to 7.5 [2.4-18.6] events/h (p<0.001)




A
Genioglossus muscle activity, EMG (% baseline)
350
300
250
200
150
100
50
N=16
P<0.001
Ato-oxy
Placebo
0
5
10
15
20
25
30
35
Esophageal pressure swings (cmH2O)

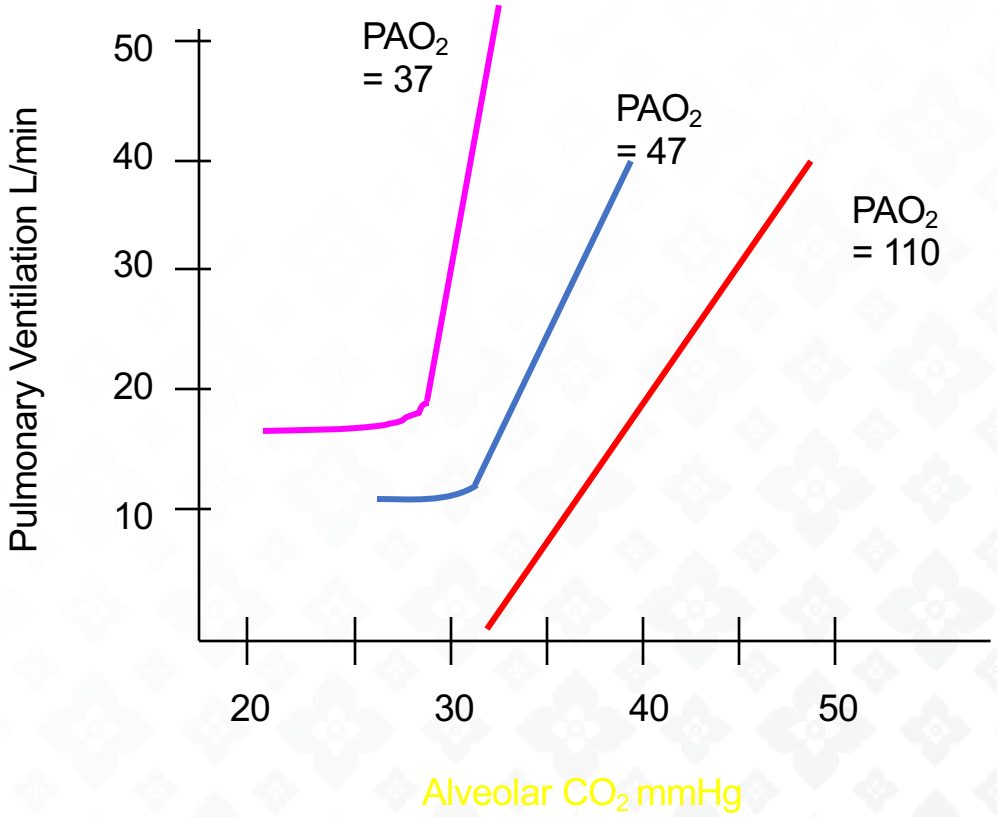

B
EMGGG (raw)
EMGGG (mta)
Baseline
Pes
Flow


Muscle function therapies
Anatomical therapies
OSA targeted therapies
O_2
Loop gain therapies
Arousal threshold therapies

- Excessively large ventilatory response to very small changes in CO2
- This scenario leads to hypocapnia and subsequent reductions in respiratory drive, which can perpetuate recurrent upper airway collapse

Carberry JC, et al. Personalized Management Approach for OSA. Chest. 2018;153(3):744-55.

Ventilatory Response to CO_2

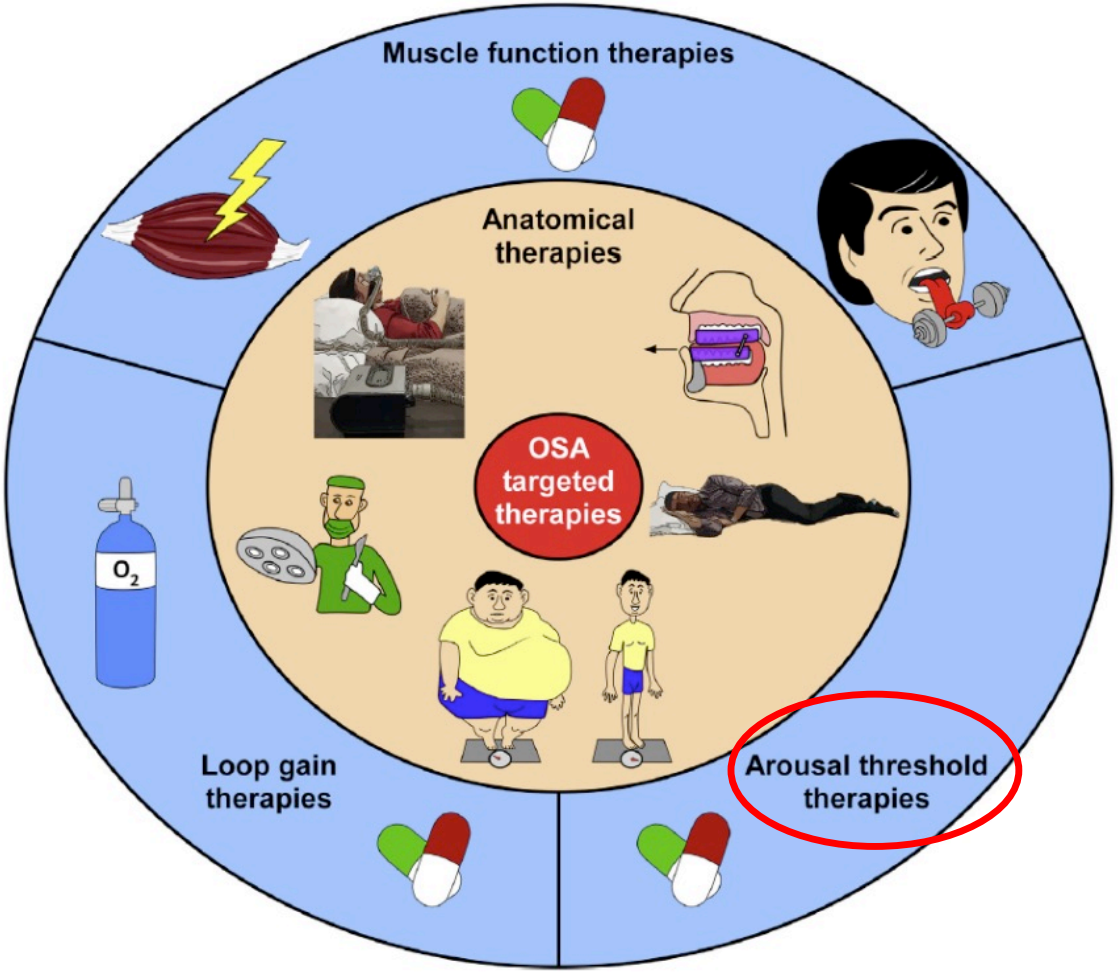


- Oxygen supplementation
- Carbonic anhydrase inhibitor

Carberry JC, et al. Personalized Management Approach for OSA. Chest. 2018;153(3):744-55.

Variable	β	SEM	Odds ratio#	p-value	Interpretation
Constant	−1.97	1.02		0.01	
Loop gain	15.41	7.40	3.7	0.038	Higher loop gain→success
$V_{passive}$	5.27	3.71	4.8	0.15	Reduced collapsibility→success
Compensation	15.09	6.62	45.5	0.023	Greater compensation→success
$V_{passive}$×compensation	−58.53	29.97	0.11	0.036	Poor collapsibility and poor compensation→failure
Loop gain×compensation	−80.34	34.16	0.17	0.019	Low loop gain and poor compensation→failure
Arousal threshold×compensation	−86.43	29.53	0.012	0.003	Low arousal threshold and higher compensation→success

Sands SA, et al. Identifying obstructive sleep apnoea patients responsive to supplemental oxygen therapy. Eur Respir J. 2018 ;52(3).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Arousal threshold therapies

- Hypnotic sleep promotion agents to increase the respiratory arousal threshold (experimental)
- Zopiclone increased the respiratory arousal threshold versus placebo without impairing genioglossus muscle activity or its responsiveness

Carter SG, et al. Zopiclone increases the arousal threshold without impairing genioglossus activity in obstructive sleep apnea. SLEEP 2016;39(4):757–66.

Conclusion

- Polysomnography is still a standard diagnostic tool for OSA
- However; in uncomplicated cases, HSAT may be considered
- CPAP is currently a standard treatment for OSA
- Personalized OSA treatment focusing on anatomical therapies, muscle function therapies, loop gain therapies, and arousal threshold therapies are new targeted therapies for OSA

THANK YOU FOR YOUR ATTENTION

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- International Training Program of Sleep Medicine at Chulalongkorn University, Bangkok, Thailand
- https://www.sleepcenterchula.org/index.php/en/curriculumnmenu-2/152-international-training-program-in-sleep-medicine

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