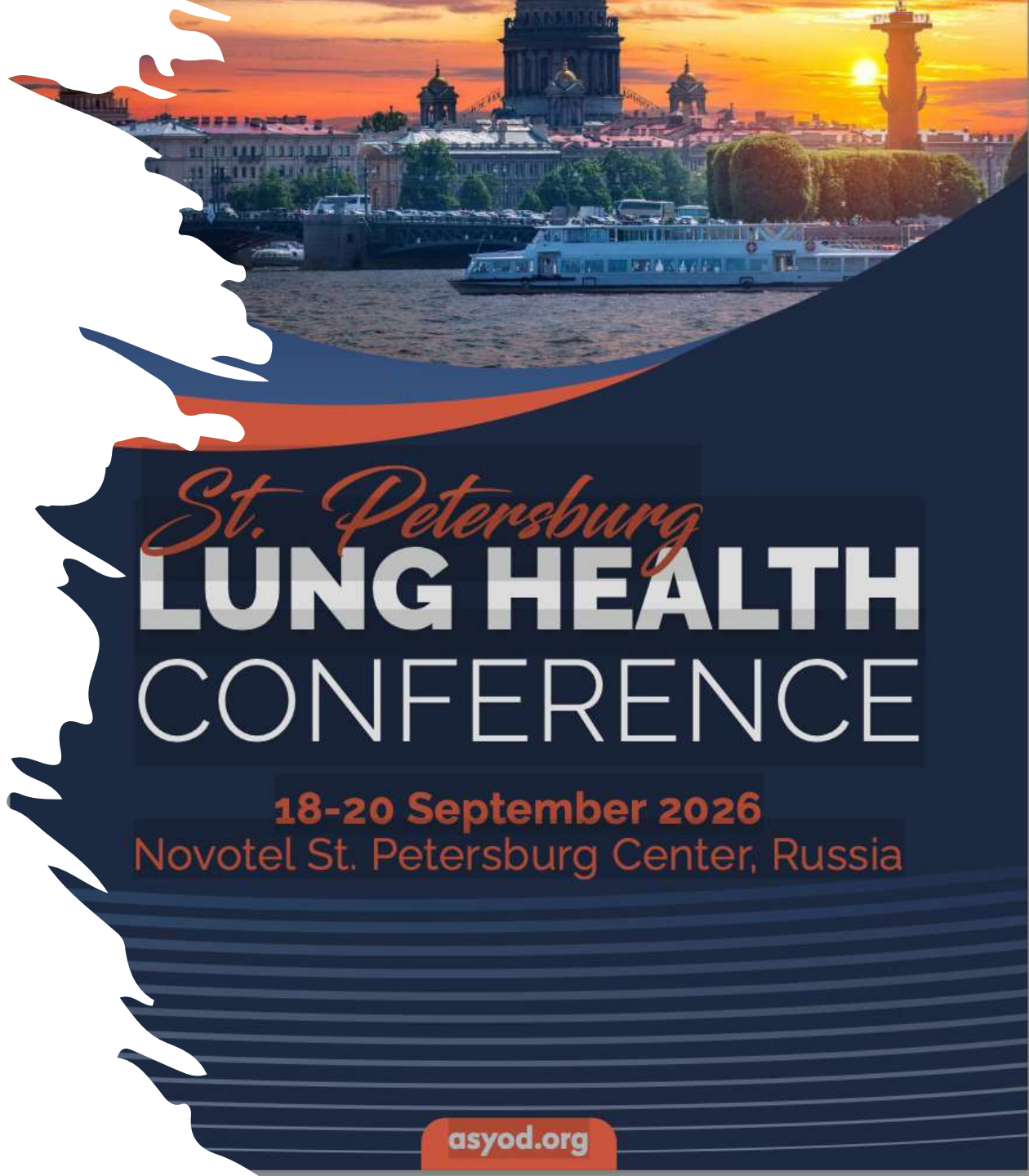


What is the Best Treatment for Sleep Apnea-2026 ?

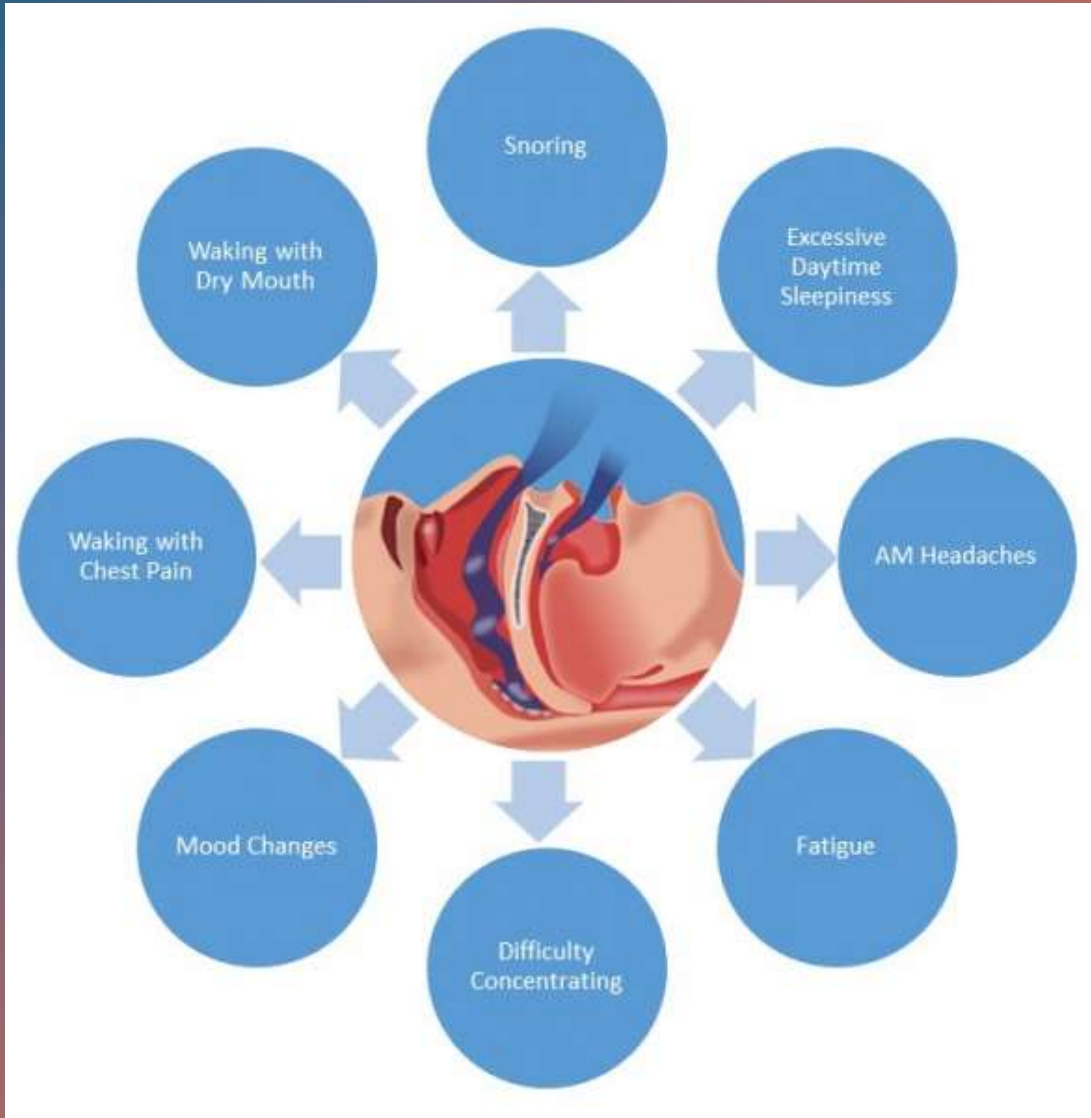
Prof. Dr. Hatice Selimoğlu Şen
Dicle University School of
Medicine Diyarbakır, Türkiye

The banner features a silhouette of a person's head and shoulders on the left side. The background is a scenic view of St. Petersburg, Russia, with the city's architecture and a river visible under a sunset sky. The text "St. Petersburg" is written in a cursive font, while "LUNG HEALTH CONFERENCE" is in a bold, sans-serif font.

St. Petersburg
**LUNG HEALTH
CONFERENCE**

18-20 September 2026
Novotel St. Petersburg Center, Russia

Obstructive Sleep Apnea



- **Obstructive sleep apnea (OSA)** is a disorder that is characterized by obstructive apneas and hypopneas due to repetitive collapse of the upper airway during sleep.

Obstructive Sleep Apnea

American Academy of Sleep Medicine (AASM) Definition

- The obstructive RDI is the number of obstructive apneas, obstructive hypopneas, and RERAs per hour of sleep
- OSA is defined as either of the following:
 - An obstructive respiratory disturbance index (RDI) ≥ 15 events per hour of sleep
 - RDI > 5 and < 15 events per hour that is accompanied by any of the following:
 - *sleepiness,*
 - *fatigue,*
 - *insomnia, or other symptoms leading to impaired sleep-related quality of life*
 - *waking up with breath-holding, gasping, or choking;*
 - *habitual snoring or breathing interruptions during sleep*



Obstructive Sleep Apnea Treatment

- OSA is a prevalent health condition that affects over a billion individuals worldwide.
- The primary physiologic issue is the collapse of the upper airway during sleep.
- However, other pathophysiologic processes beyond airway obstruction can be crucial in treating OSA

What is the best treatment for sleep apnea?



Positive airway pressure (PAP) therapy?



Upper airway surgery



Weight loss?

Diet, exercise, and comprehensive lifestyle intervention

Bariatric surgery

Weight loss pharmacotherapy



Oral Appliances?



Hypoglossal nerve stimulation?



Neuromuscular electrical stimulation (NMES)?



Altered sleep position?



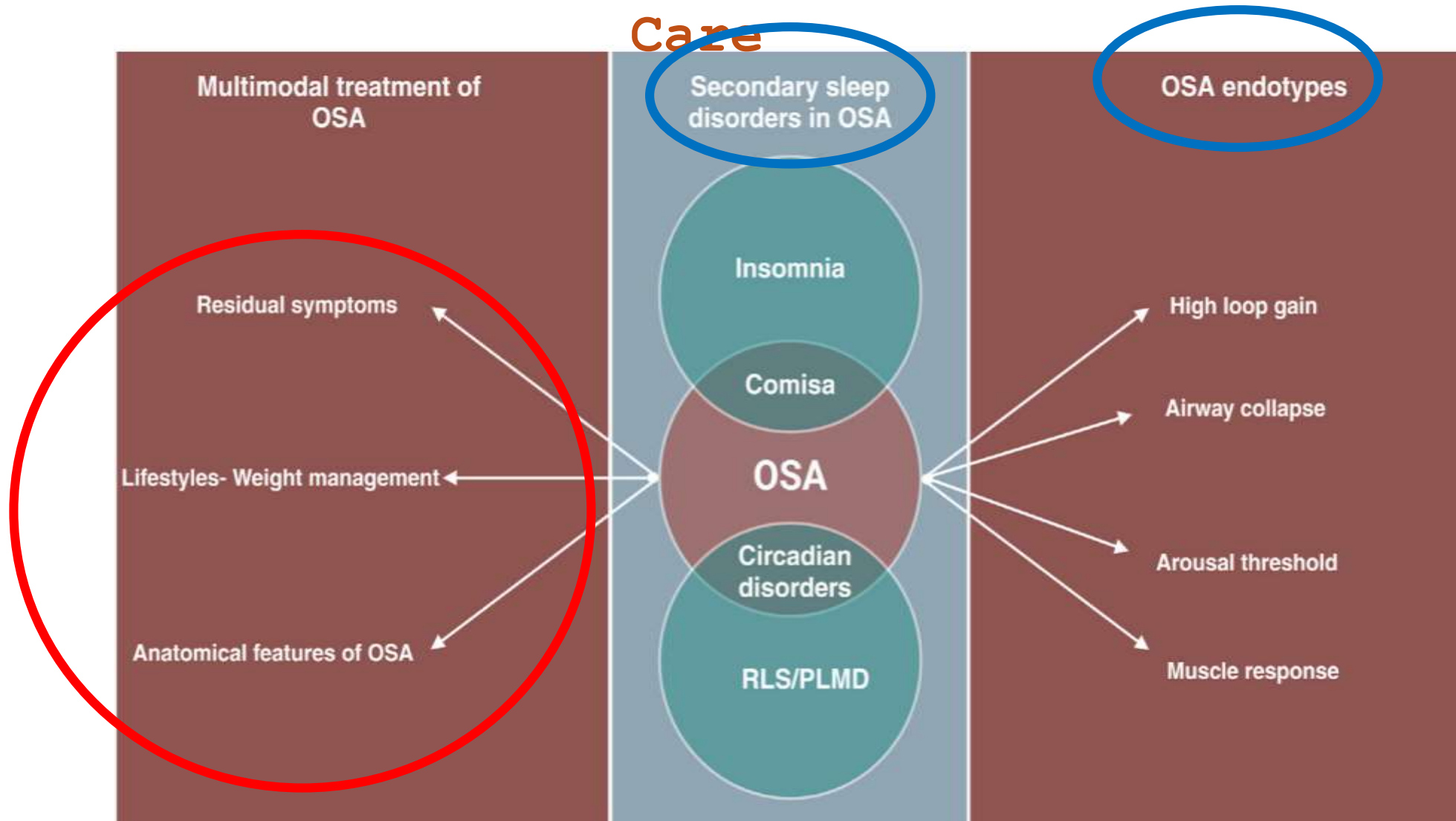
Others (**Pharmacologic**)

Multimodal Treatment Strategy

- A multimodal treatment strategy that targets the specific physiology of OSA and other contributing factors to the patient's symptoms is necessary.
- This may include addressing ;
 - *anatomic abnormalities,*
 - *secondary sleep disorders*
 - *specific OSA-endotyping.*
- Such an approach requires the integration of complementary therapies to ensure a comprehensive treatment plan.

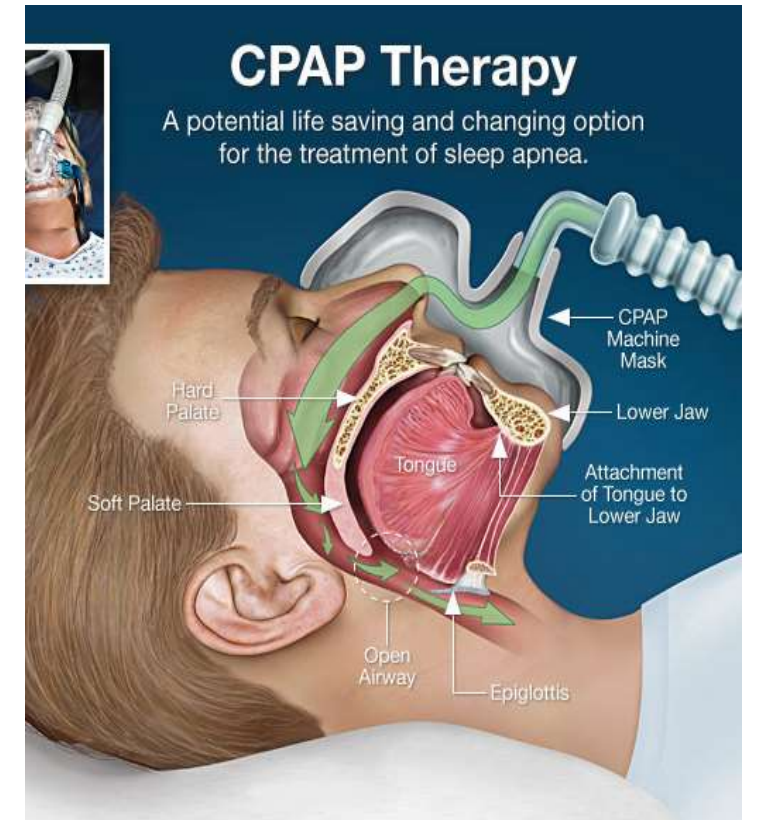
Patient-centric Precision OSA

Care

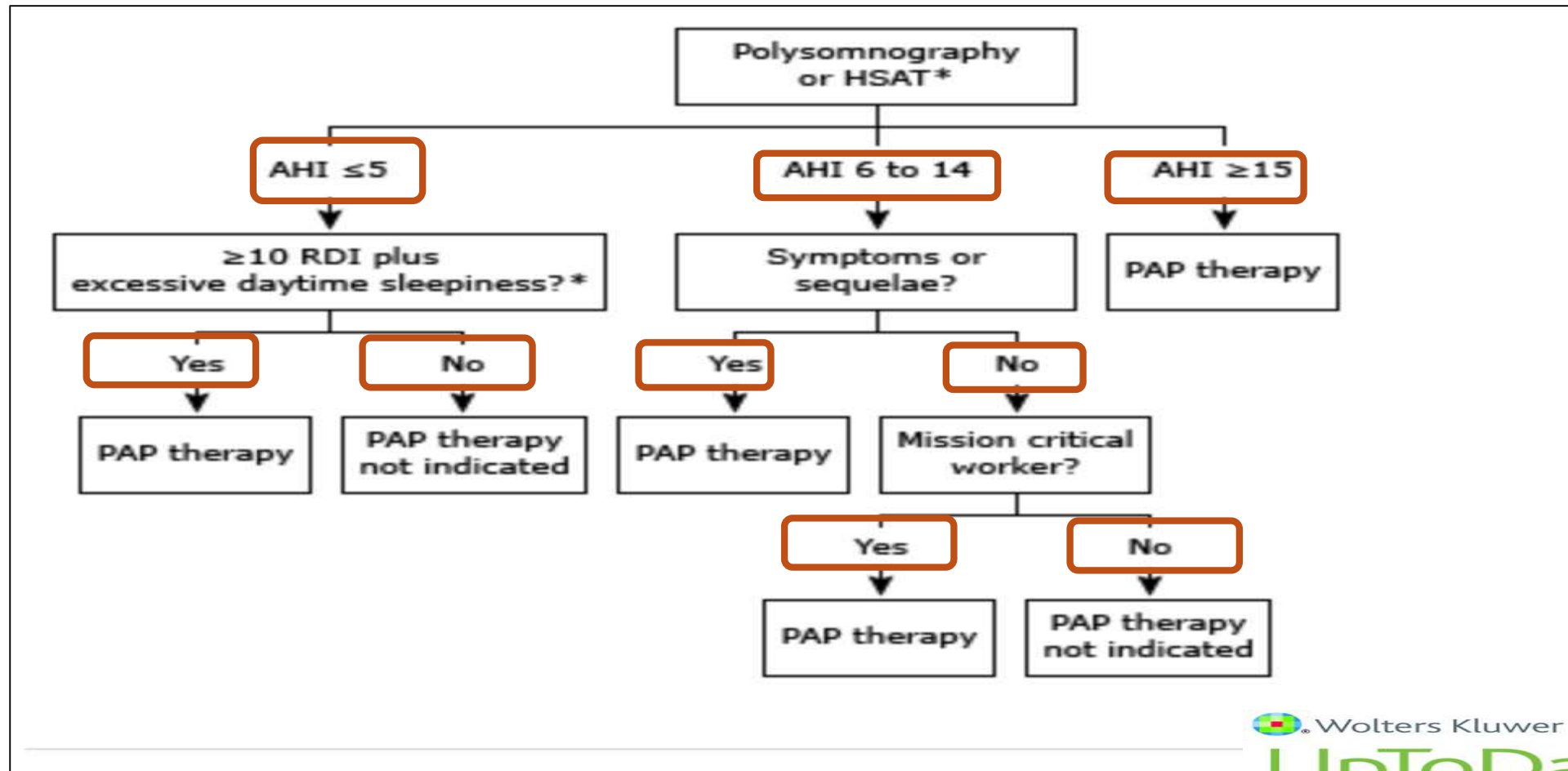


PAP Therapy

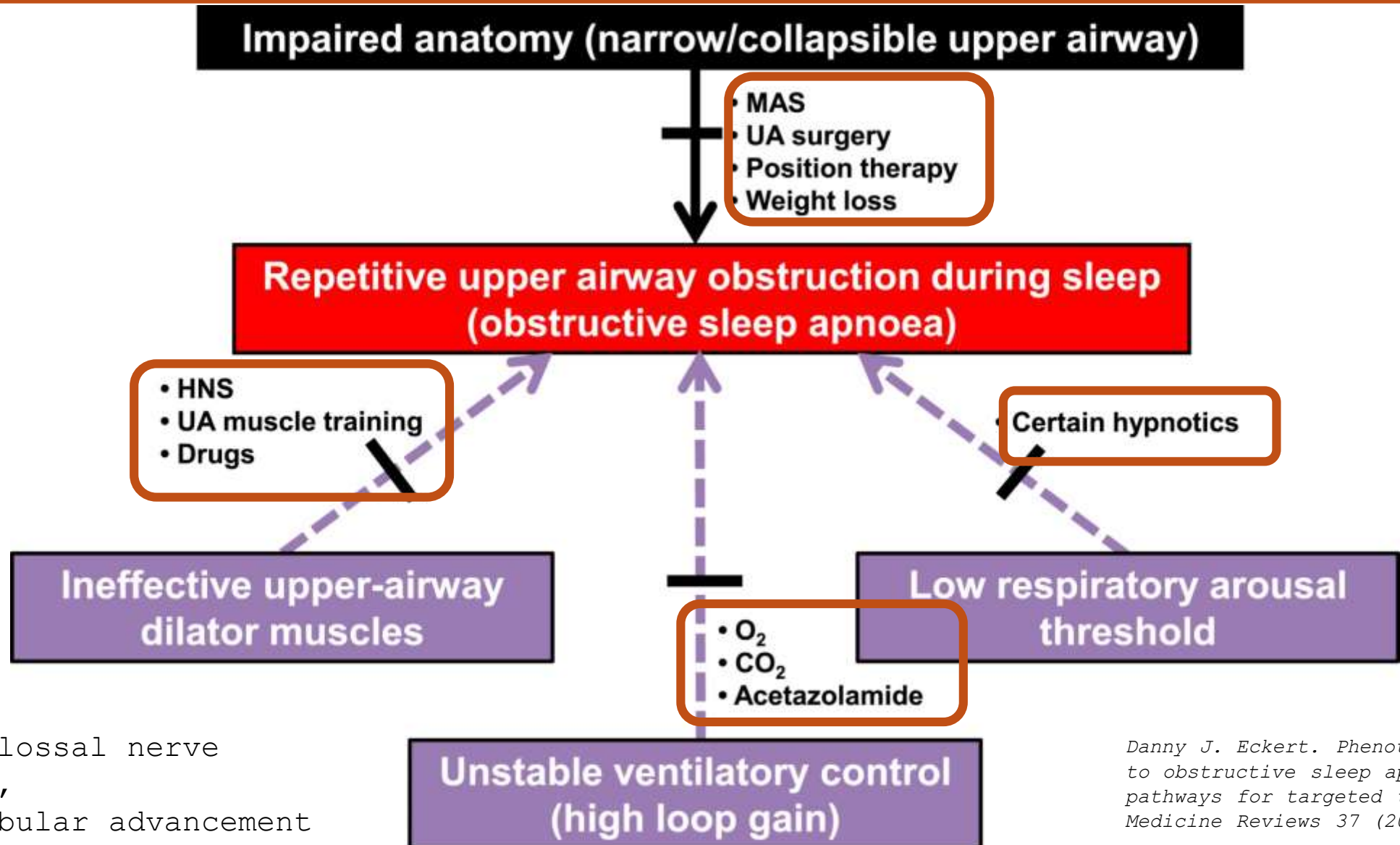
- PAP is an effective therapy for OSA.
- Guidelines generally recommend using PAP devices
- However, residual hypersomnia, poor tolerance, or the emergences of central apneas are important problems.
 - In situations where PAP proves insufficient, a more personalized approach becomes necessary



Indications For PAP Therapy in Adults with OSA



Four Key Phenotypes That Cause OSA and Potential non-CPAP Targeted Therapies



HNS = hypoglossal nerve stimulation,
MAS = mandibular advancement splint,

Danny J. Eckert. Phenotypic approaches to obstructive sleep apnoea. *New pathways for targeted therapy. Sleep Medicine Reviews* 37 (2018) 45e59

PAP Compared with Other Therapies

- Limited studies have compared PAP with other OSA therapies.
- A network meta-analysis of 80 randomized trials reported that:
 - PAP was the most effective therapy for reducing AHI when compared with other OSA therapies including MADs, exercise training, and weight loss.
 - Data on the efficacy of surgical therapy was not included in the analysis.
- CPAP has not been directly compared with HNS or other surgical therapies
- Surgical therapy compared with CPAP.

Comparative Study > Sleep Med. 2017 Feb;30:7-14. doi: 10.1016/j.sleep.2016.06.001.
Epub 2016 Jun 28.

Comparative efficacy of CPAP, MADs, exercise-training, and dietary weight loss for sleep apnea: a network meta-analysis

Imran H Iftikhar ¹, Lia Bittencourt ², Shawn D Youngstedt ³, Najib Ayas ⁴, Peter Cistulli ⁵,
Richard Schwab ⁶, Martin W Durkin ⁷, Ulysses J Magalang ⁸

Affiliations + expand

PMID: 28215266 DOI: 10.1016/j.sleep.2016.06.001

Mode Selection, Titration, Initiation

CPAP

- CPAP (Flex - EPR)
- Oto-CPAP (APAP)

BPAP

- BPAP-S
- BPAP-ST
- Oto-BPAP
- AVAPS - IVAPS
- Servo-Ventilator (ASV)
- ACMV



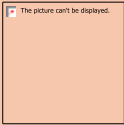
Goals of PAP Therapy

- Resolve signs and symptoms of OSA
- Improve sleep quality
- Normalize the apnea-hypopnea index.
- Normalization of oxyhemoglobin saturation levels

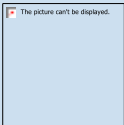
Patients Who Do Not Achieve Goals

- Possible causes of treatment failure include
 - *nonadherence,*
 - *alternate etiology for symptoms,*
 - *inadequate therapy,*

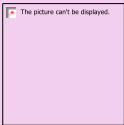
What is PAP Adherence?



Defined as using CPAP for ***more than an average of 4 hours per night and more than 70 percent of nights (ie, more than five nights per week)***.



What goal do we set: ''CPAP should be used for a minimum of 4 hours per night for 5 to 7 nights a week''



Our advice to patients is to use it every night and throughout the night.

- Using less is better than never use
- It has been reported that even 1 hour of CPAP use per night reduces mortality.

PAP Adherence Goals

- **The 4-hour cut-off** is typically used since several studies
- Four or more hours of CPAP use is associated with ;
 - *normalization of daytime sleepiness*
 - *improvement in quality of life,*
 - *improvement in neurocognitive function,*
 - *improvement in cardiovascular disease, and diabetes*
 - *a reduced risk of motor vehicle accidents*

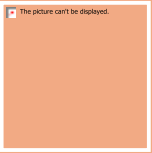
Effects are typically felt within days to weeks of starting CPAP therapy.



PAP Adherence Goals

- **4 hours/ per night**
 - is sufficient to achieve a normal score on the **Epworth Sleepiness Scale**
- **6 hours /per night**
 - to achieve a normal level of objective alertness in the **Multiple Sleep Latency Test**
- **7.5 hours/per night**
 - to normal daytime functioning on the **Functional Outcomes of Sleep Questionnaire**
- **5 hours /per night**
 - improved **neurobehavioral performance**
- **>6 hours/ per night**
 - improves **memory and daily functioning**

Prevalence of Nonadherence



Almost half of patients are nonadherent, (< 4 hours /per night)



The range is broad **(29 to 83 percent)**

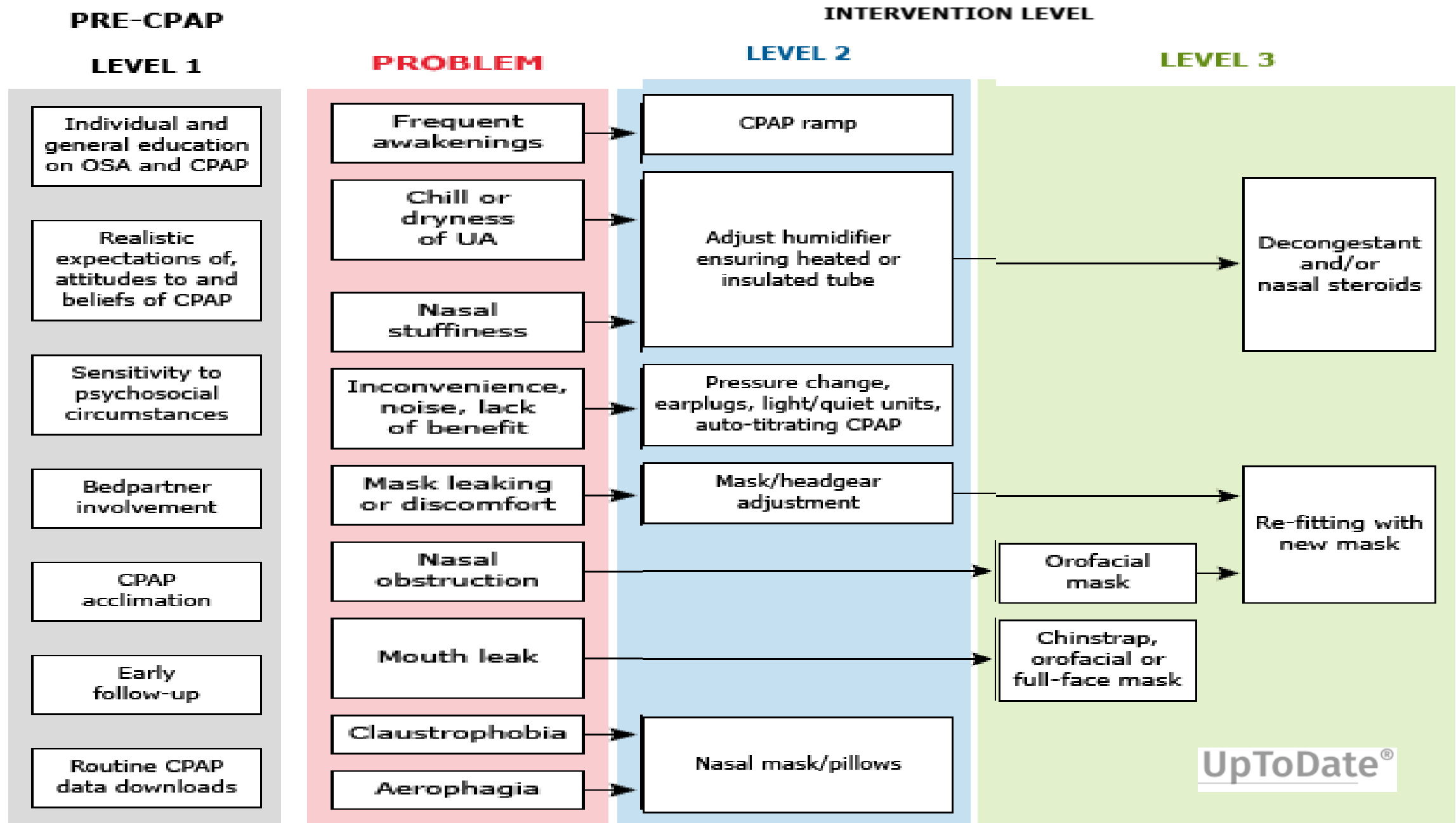
What do we do :
there is no
adherence?



First-Line Intervention For Adherence

- Integrated approach that involves behavioral therapy and prompt management of side effects is useful

Multidisciplinary approach to managing CPAP-related problems



Side Effect Management

- Early troubleshooting of side effects, within **the first few days to two weeks of CPAP use is effective.**
- Prompt intervention should enhance **comfort and self-efficacy**
- The **assessment and troubleshooting** can be done during provider follow-up with the patient at home using **telehealth or in-person visits** with an experienced sleep technician.



Choosing The Correct Patient-Device Interface

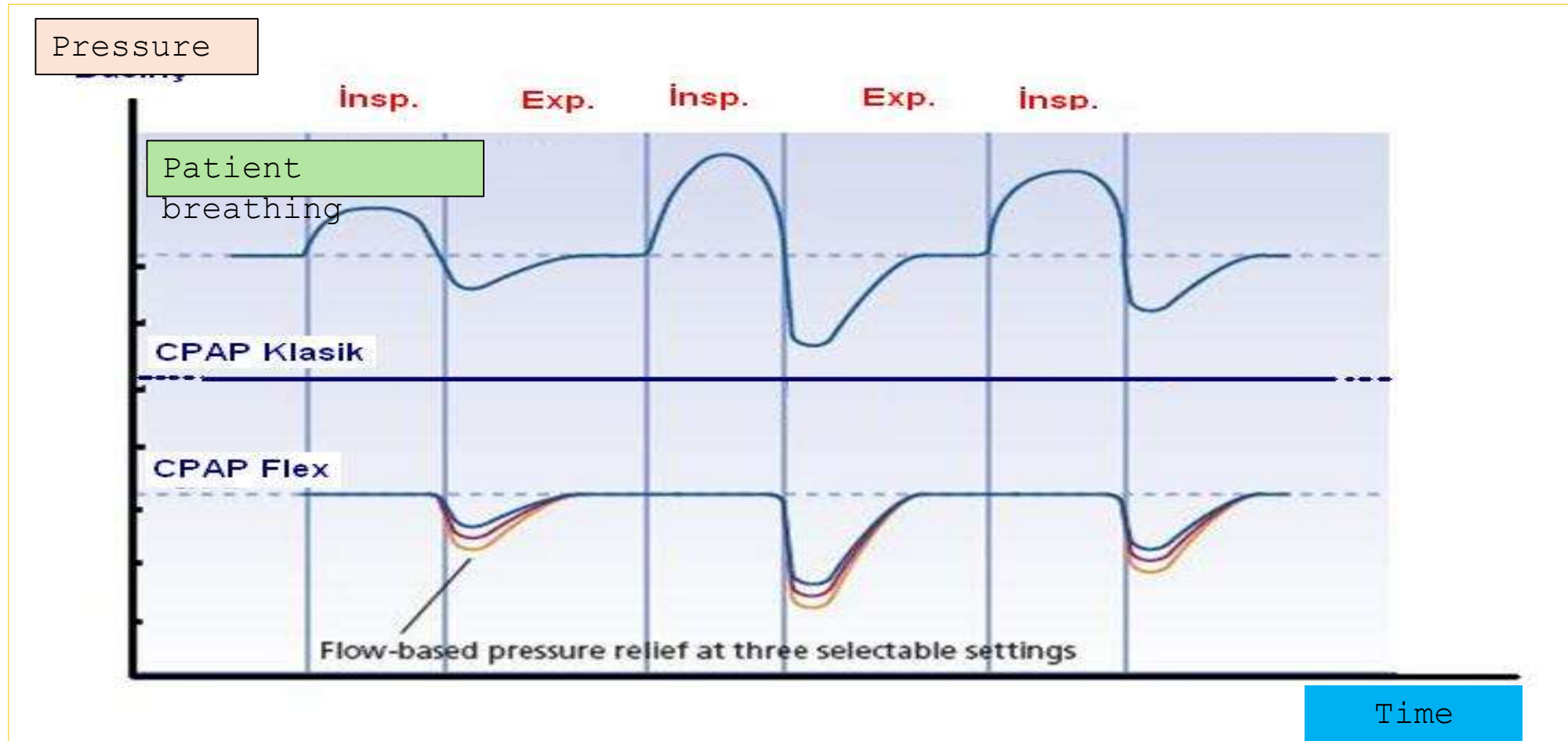
- Advocate for properly fitting interface between the patient and the device to optimize the adherence and efficacy of PAP therapy.
- Options include
 - *nasal masks,*
 - *nasal pillows,*
 - *oronasal masks,*
 - *full facemasks,*
 - *oral interfaces*
- Nasal and oronasal masks are the commonly used interfaces.



Different Methods of PAP Delivery on Adherence

- The impact of different methods of CPAP delivery on adherence has been studied.
- Flexible pressure PAP devices, expiratory pressure relief PAP (EPR) , Auto-titrating CPAP (APAP) are often prescribed in patients when nonadherence is due to **intolerance of positive pressure**,
- Routinely prescribing these measures is not associated with increased adherence rates when compared to **conventional CPAP**.
- Sometimes, switching to a **bilevel device** is needed (**BIPAP**, **BIPAP**

CPAP / Flex / EPR / Smartflex



CPAP vs Flex.



SLEEP DISORDERS

Flexible Pressure Delivery Modification of Continuous Positive Airway Pressure for Obstructive Sleep Apnea Does Not Improve Compliance With Therapy

Systematic Review and Meta-analysis

Jessie P. Bakker, PhD; and Nathaniel S. Marshall, PhD

Background: Continuous positive airway pressure (CPAP) is the first-line therapy for obstructive sleep apnea (OSA), but patient compliance is a major barrier to long-term effectiveness. Flexible pressure delivery of PAP reduces pressure during early exhalation with the aim of improving comfort and, therefore, compliance, leading to subsequent symptoms improvement.

Methods: We undertook a systematic literature search of PubMed (January 1, 2000, to July 11, 2010) to identify all randomized trials comparing flexible and standard CPAP in adult patients with OSA with at least 1-week follow-up. Either we or the original trial investigators extracted means, SEs, and sample sizes for all relevant outcome measures. We then performed meta-analyses quantifying improvements in objective compliance and symptoms as measured by the Epworth Sleepiness Scale (ESS), the Maintenance of Wakefulness Test (MWT), and the Psychomotor Vigilance Task (PVT).

Results

We found 10 relevant trials (599 patients). **Meta-analysis of the seven trials** where we could extract compliance data (514 patients) indicated that flexible pressure did not improve compliance compared with CPAP in either the parallel (0.16 h; 95% CI, -0.09-0.42; $P = .21$) or the crossover trials (0.20 h; 95% CI, -0.26-0.66; $P = .39$). Flexible pressure caused no improvement over CPAP in any secondary outcome (ESS, MWT, PVT, and residual OSA, all $P > .05$).

Conclusions

Flexible pressure modification neither significantly improves compliance with CPAP in patients with OSA nor significantly improves patient outcomes beyond the effects of CPAP. Unfortunately, we were unable to locate compliance data in the correct format for three out of the 10 suitable trials.

No difference in efficacy and compliance

APAP vs. FixCPAP

Sleep

ORIGINAL ARTICLE

Autoadjusted versus fixed CPAP for obstructive sleep apnoea: a multicentre, randomised equivalence trial

Konrad E Bloch,^{1,2} Fabienne Huber,¹ Michael Furian,¹ Tsogyal D Latshang,¹ Christian M Lo Cascio,¹ Yvonne Nussbaumer-Ochsner,¹ Oliver Senn,³ Erich W Russi,^{1,2} Malcolm Kohler,^{1,2} Otto D Schoch,⁴ Alexander Turk,⁵ Edelbert Imhof,⁶ Irène Laube,⁶ Felix Matthews,¹ Robert Thurnheer⁷

► Additional material is published online only. To view please visit the journal online (<http://dx.doi.org/10.1136/thoraxjnl-2016-209699>).

¹Sleep Disorders Center and Pulmonary Division, University Hospital Zurich, Zurich, Switzerland
²Zurich Center for Interdisciplinary Sleep Research,

ABSTRACT
Background The obstructive sleep apnoea syndrome (OSAS) is conventionally treated by continuous positive airway pressure set at a fixed level (fCPAP). Automatic mask pressure adjustment (autoCPAP) is increasingly used during home therapy. We investigated whether autoCPAP is equivalent to fCPAP in improving sleepiness in patients with OSAS in the long-term.
Methods In this multicentre equivalence trial, 208 patients with OSAS, with median Epworth sleepiness

Key messages
What is the key question?
► Is CPAP therapy with continuous automatic mask pressure adjustment (autoCPAP) equivalent to conventional CPAP therapy with fixed mask pressure (fCPAP) in improving sleepiness in patients with obstructive sleep apnoea syndrome (OSAS) in the long term?

Conclusions AutoCPAP and fCPAP are equivalent within prespecified ranges in improving subjective and objective sleepiness in patients with OSAS over the course of 2 years. Costs of these treatments are similar.

 **Cochrane Library**
Cochrane Database of Systematic Reviews

Pressure modification or humidification for improving usage of continuous positive airway pressure machines in adults with obstructive sleep apnoea (Review)

Kennedy B, Lasserson TJ, Wozniak DR, Smith I

A meta-analysis of 64 studies reported that pressure modification by switching to APAP resulted in approximately **13 more minutes of usage per night at six weeks**. However, the

AHI scores were lower in patients on fixed-level CPAP

BPAP vs CPAP

Clinical Trial > Sleep. 2003 Nov 1;26(7):864-9. doi: 10.1093/sleep/26.7.864.

A randomized, double-blind clinical trial comparing continuous positive airway pressure with a novel bilevel pressure system for treatment of obstructive sleep apnea syndrome

Peter C Gay ¹, Daniel L Herold, Eric J Olson

Affiliations + expand

PMID: 14655921 DOI: 10.1093/sleep/26.7.864

Abstract

Study objectives: To obtain efficacy, objective compliance, and self-assessment data from obstructive sleep apnea syndrome (OSAS) patients treated with continuous positive airway pressure (CPAP) or a novel bilevel (NBL) therapy.

Design: Randomized, controlled, double-blind trial.

Setting: Home treatment after diagnosis and titration by split-night polysomnography (PSG) in a sleep laboratory.

Patients: Twenty-seven adults (22 men) newly referred for suspected OSAS but without concomitant medical or sleep disorders.

Interventions: If the subject's apnea-hypopnea index was greater than 10 and less than 100, the CPAP was titrated during PSG and then followed by NBL titration. Treatment was randomly and blindly set to either CPAP or NBL mode for 1 month.

Measurements & results: There were no significant baseline group differences in age, body mass index, apnea-hypopnea index (mean +/- SD, CPAP group vs NBL group of 46.1 +/- 23.1/hour vs 41.8 +/- 25.8), CPAP requirement, or scores on the Epworth Sleepiness Scale and Functional Outcomes of Sleep Questionnaire. Treatment with CPAP and NBL equivalently reduced the apnea-hypopnea index during the laboratory titration (7.6 +/- 11.9/hour vs. 3.7 +/- 4.4, respectively). At 1 month, there were no significant group compliance differences as determined by percentage of nights with at least 4 hours of use (CPAP, 80.5 +/- 24 vs NBL, 77.6 +/- 24.8) and hours of use per night (CPAP, 5.6 +/- 1.4 hours/night vs NBL, 5.6 +/- 1.7). Similar improvements were seen in scores on the Epworth Sleepiness Scale and Functional Outcomes of Sleep Questionnaire.

Conclusions: The NBL appeared to be as effective as CPAP for the treatment of OSAS but offered no advantages in patients receiving first-time therapy for OSAS.

There was no difference between BPAP and Fix CPAP (in terms of compliance, measurements, sleepiness, and quality of life).

Patients who could not tolerate CPAP (OHS, COPD) tolerated BPAP.

AVAPS vs. BPAP

Chest. 2006 Sep;130(3):815-21.

Average volume-assured pressure support in obesity hypoventilation: A randomized crossover trial.

Storre JH¹, Seuthe B, Fiechter R, Milioglou S, Dreher M, Sorichter S, Windisch W.

⊕ **Author information**

Abstract

BACKGROUND: Average volume-assured pressure support (AVAPS) has been introduced as a new additional mode for a bilevel pressure ventilation (BPV) device (BiPAP; Respironics; Murrysville, PA), but studies on the physiologic and clinical effects have not yet been performed. There is a particular need to better define the most efficient ventilatory treatment modality for patients with obesity hypoventilation syndrome (OHS).

- Effective in reducing ventilation quality and CO₂ levels
- There is no difference in terms of quality of sleep and life.

ASV

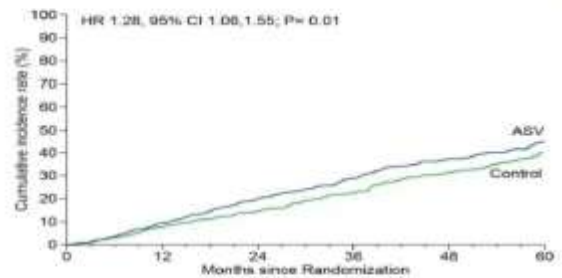
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 17, 2015 VOL. 373 NO. 32

Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure

Martin R. Cowie, M.D., Holger Woehrle, M.D., Karl Wegscheider, Ph.D., Christiane Angermann, M.D., Marie-Pia d'Ortho, M.D., Ph.D., Erland Erdmann, M.D., Patrick Levy, M.D., Ph.D., Anita K. Simonds, M.D., Virend K. Somers, M.D., Ph.D., Faiez Zannad, M.D., Ph.D., and Helmut Teichler, M.D.

All-Cause Death



No. at Risk						
Control	659	563	493	334	213	117
ASV	666	555	466	304	189	97

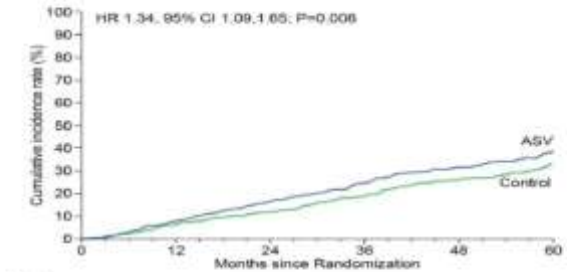
Cowie et al. NEJM 2015, 1 Sep [Epub ahead of print]

ESC CONGRESS
LONDON 2015

Hot Line presentation

www.escardio.org/ESC2015

Cardiovascular Death



No. at Risk						
Control	659	563	493	334	213	117
ASV	666	555	466	304	189	97

Cowie et al. NEJM 2015, 1 Sep [Epub ahead of print]

ESC CONGRESS
LONDON 2015

Hot Line presentation

www.escardio.org/ESC2015

CONCLUSIONS

Adaptive servo-ventilation had no significant effect on the primary end point in patients who had heart failure with reduced ejection fraction and predominantly central sleep apnea, but all-cause and cardiovascular mortality were both increased with this therapy. (Funded by ResMed and others; SERVE-HF ClinicalTrials.gov number, NCT00733343.)

ASV



EUROPEAN RESPIRATORY JOURNAL
ERS OFFICIAL DOCUMENTS
W.J. RANDERATH ET AL.

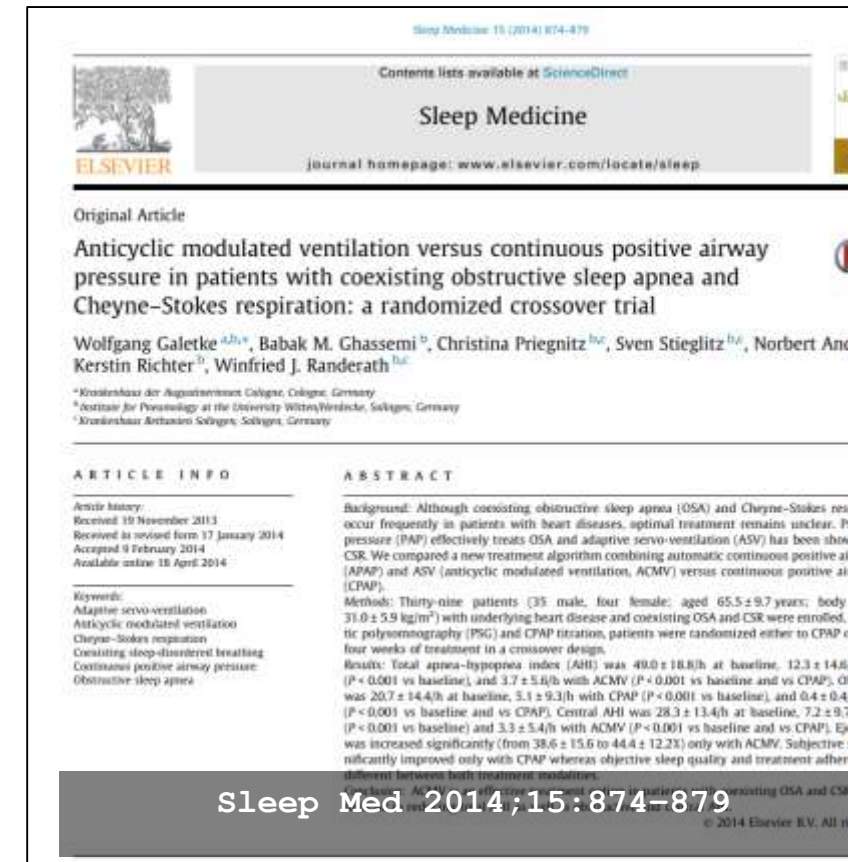
European Respiratory Society and European Sleep Research Society statement on the treatment of central sleep apnoea with adaptive servo-ventilation

Winfried J. Randerath¹, Sophia E. Schiza², Michael Arzt³, Maria Rosaria Bonsignore⁴, Raphael Heinzer⁵, Carolina Lombardi^{6,7}, Robert Lyssens⁸, Gianfranco Parati^{6,7}, Thomas Penzel⁹, Jean Louis Pepin¹⁰, Dirk Pevernagie¹¹, Silke Ryan¹², Luca Vignatelli¹³ and Esther I. Schwarz^{14,15}

The expert group concludes that ASV has positive effects on CSA and QoL in various forms of CSA, that current ASV devices have no negative effect on hard cardiovascular endpoints, and that ASV has positive effects on patient-reported outcomes.

Anti-Cyclic Modulated Ventilation (ACMV)

- Auto-CPAP + ASV
- OSAS + Cheyne Stokes



Patients Who Fail First-Line Interventions

- Pharmacologic therapy in the form of a **sedative-hypnotic sleep aid** is a last resort but may be attempted on a trial basis.
- The routine use of a sedative-hypnotic at the time of CPAP initiation is not recommended.
- **A short-term trial of sedative hypnotic therapy may be tried in those who fail all other options (eg, one to two weeks).**
- Randomized studies have yielded conflicting results



Patients Who Fail First-Line Interventions/ Pharmacologic Therapy

- **Single-Dose Therapy –**

- One trial randomly assigned 117 patients with OSA to receive premedication with **a single dose of eszopiclone (3 mg)** or placebo 30 minutes prior to attended polysomnography (PSG) for CPAP titration 4–6 weeks later, the eszopiclone group used their CPAP on **more nights and for a longer duration** (four versus three hours) than the placebo group.



- **In contrast**, in a second study of 134 patients with OSA undergoing initial split-night PSG, there was no difference in the median daily CPAP use at one month among those who were randomly assigned to receive **a single dose of zaleplon or placebo**

Lettieri CJ, Chest 2009, Park JG, J Clin Sleep Med 2013

Patients Who Fail First-Line Interventions/Pharmacologic Therapy

- **Two Weeks Course of Therapy -**
- Extended dosing was tested in a trial to **zolpidem, placebo, or standard of care for the first 14 days of CPAP therapy**. There was **no difference** in CPAP adherence among the three groups as measured by average nightly CPAP use or total days used.
- In contrast, in a subsequent trial, 160 patients with newly diagnosed OSA were randomly assigned to receive **eszopiclone (3 mg) or placebo** during the initial 14 nights of CPAP therapy. After six months of follow-up, patients who received eszopiclone used their CPAP device for more nights and for a longer duration
- One **meta-analysis included over 1000 patients** with OSA reported that patients who were treated with nonbenzodiazepine sedative hypnotics had **higher rates of adherence** than those who did not receive such medication.

Bradshaw DA Chest 2006, Lettieri CJ Ann Intern Med 2009, Wang D Sleep 2021

Patients Who Fail, Do Not Tolerate or
Decline
PAP Therapy



Targeting Different
Subtypes and Anatomic
Features of
Obstructive
Sleep Apnea



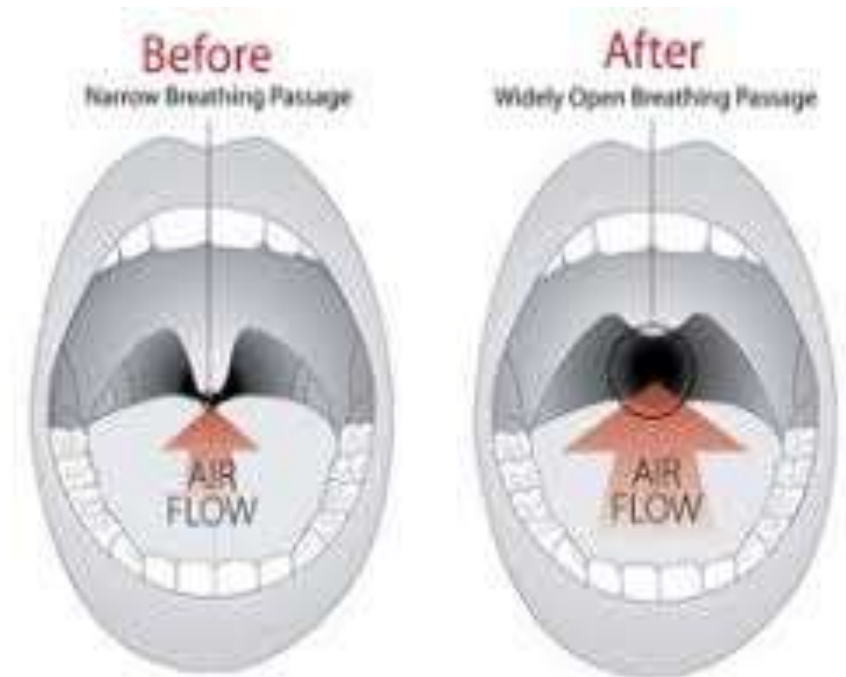
Positional Obstructive Sleep Apnea

- Positional therapy is considered an *alternative therapy according to AASM OSA guidelines,*
- Significantly worsen when the patient is in a specific position, typically lying on their back (supine).
- The primary goal of positional therapy is to encourage patients to **sleep in non-supine positions,**
- Positional therapy can be achieved through various methods,
 - *special pillows,*
 - *positional alarms,*



Upper Airway Surgery

- Ear, nose and throat (ENT) surgery is available treatment option for selected patients.
- The primary goal is to remove or reduce the tissue obstructing the airway,
- The efficacy of surgery for treating OSA varies significantly depending on the type of surgical procedure performed, the individual patient's anatomy, and the severity of the OSA.



- ENT surgery can significantly improve the AHI, and other patient-reported outcome measures such as quality of life and daytime sleepiness.

Upper Airway Surgery

Uvulopalatopharyngoplasty

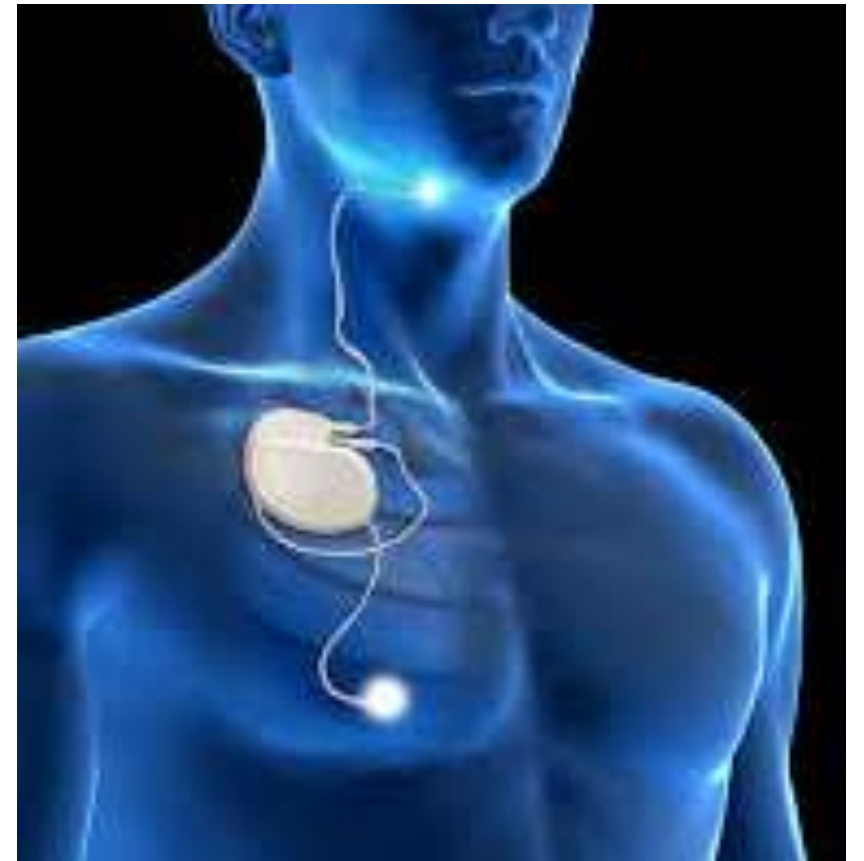
*Advancing the genioglossus
muscle*

*Maxillomandibular advancement
(MMA) .*

- It is essential to note that ENT surgery is usually considered when non-surgical treatments have failed or are not tolerated by the patient.
- Nasal surgery (eg, polypectomy) is sometimes performed to improve the efficacy of PAP therapy

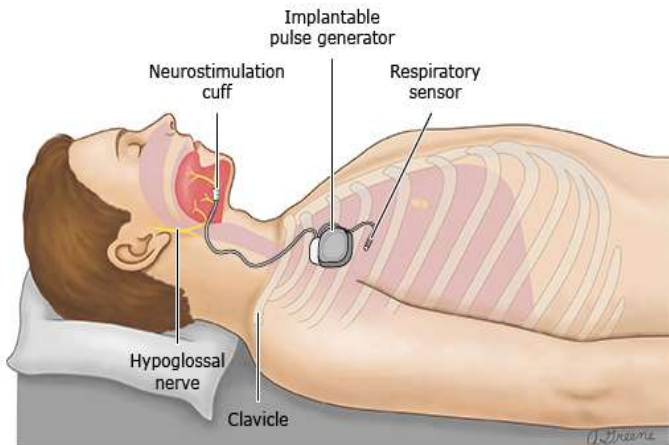
Hypoglossal Nerve Stimulation

- It functions by stimulating the hypoglossal nerve, which is responsible for tongue movements, thus preventing the tongue from obstructing the airway during sleep and reducing apnea episodes.



Hypoglossal Nerve Stimulation (HNS)

Hypoglossal nerve stimulation implant



This image depicts the hypoglossal nerve stimulation device components. A neurostimulation cuff with electrodes is typically placed on the medial branches of cranial nerve 12 through an incision in the submandibular area. The neurostimulation lead is tunneled subcutaneously and connected to the implantable pulse generator. The implantable pulse generator and the respiratory sensor lead are placed through an incision in the anterior chest. The respiratory sensor is placed in the second or third intercostal space.

Patient selection criteria for hypoglossal nerve stimulation therapy

Parameter	Criteria
Age	18 years or older
AHI	15 to 100 events/hour
BMI	40 kg/m ² *
Central and mixed apneas	<25% of total events
Drug-induced sleep endoscopy findings	No complete concentric collapse of the velopharynx or soft palate
Failed or declined PAP therapy	Yes

HNS: hypoglossal nerve stimulation; AHI: apnea hypopnea index; BMI: body mass index; PAP: positive airway pressure.

* Since most trials were conducted in patients with a BMI <32 kg/m², most United States commercial insurances require a BMI <32 kg/m², although Medicare coverage and coverage in Europe extends to patients with BMI <35 kg/m².

Hypoglossal Nerve Stimulation

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Upper-Airway Stimulation for Obstructive Sleep Apnea

Patrick J. Strollo, Jr., M.D., Ryan J. Soose, M.D., Joachim T. Maurer, M.D., Nico de Vries, M.D., Jason Cornelius, M.D., Oleg Froymovich, M.D., Ronald D. Hanson, M.D., Tapan A. Padhya, M.D., David L. Steward, M.D., M. Boyd Gillespie, M.D., B. Tucker Woodson, M.D., Paul H. Van de Heyning, M.D., Ph.D., Mark G. Goetting, M.D., Olivier M. Vanderveken, M.D., Ph.D., Neil Feldman, M.D., Lennart Knaack, M.D., and Kingman P. Strohl, M.D., for the STAR Trial Group*

ABSTRACT

CONCLUSIONS

In this uncontrolled cohort study, upper-airway stimulation led to significant improvements in objective and subjective measurements of the severity of obstructive sleep apnea. (Funded by Inspire Medical Systems; STAR ClinicalTrials.gov number, NCT01161420.)

N ENGL J MED 370;2 NEJM.ORG JANUARY 9, 2014



Journal of
Clinical Medicine



Article

Effect of Upper Airway Stimulation in Patients with Obstructive Sleep Apnea (EFFECT): A Randomized Controlled Crossover Trial

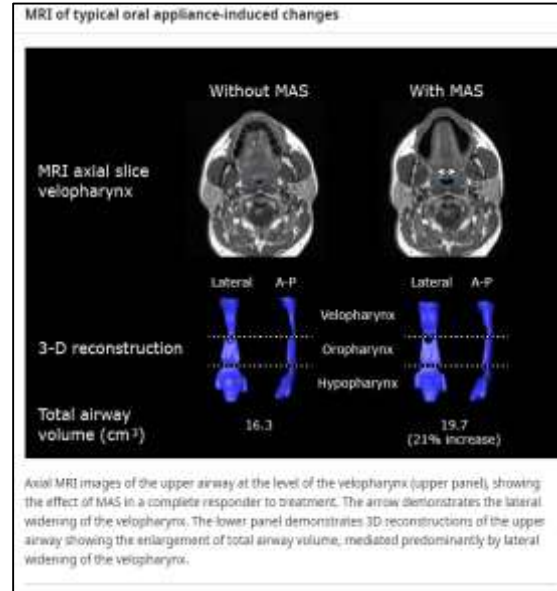
Clemens Heiser ^{1,*}, Armin Steffen ^{2,†}, Benedikt Hofauer ^{1,§}, Reena Mehra ³, Patrick J. Strollo, Jr. ⁴, Olivier M. Vanderveken ⁵ and Joachim T. Maurer ^{6,7}

Conclusions: therapeutic UAS reduced OSA severity, sleepiness symptoms, and improved quality of life among participants with moderate-to-severe OSA

J. Clin. Med. 2021, 10, 2880. <https://doi.org/10.3390/jcm10132880>

Oral Appliances

- Mandibular Advancement Devices
- Tongue Retaining Devices
- The mandibular advancement device (MAD) has been proposed as a standard treatment in mild and moderate OSA



Oral Appliances

- PAP was observed to be more effective than MAD in eliminating respiratory events.
- The evidence suggests that PAP may offer advantages over MAD in treating OSA patients.
- Nevertheless, MAD has been proposed as an alternative therapy for patients with low adherence to PAP or as a first-line treatment for mild to moderate OSA patients.

Oral Appliances

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Mandibular Advancement vs CPAP for Blood Pressure Reduction in Patients With Obstructive Sleep Apnea



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CONCLUSIONS MAD is noninferior to CPAP for reducing 24-hour mean arterial BP in participants with hypertension and increased cardiovascular risk. (Cardiosleep Research Program on Obstructive Sleep Apnea, Blood Pressure Control and Maladaptive Myocardial Remodeling—Non-inferiority Trial [CRESCENT]; [NCT04119999](https://clinicaltrials.gov/ct2/show/study/NCT04119999))
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Continuous Positive Airway Pressure vs Mandibular Advancement Devices in the Treatment of Obstructive Sleep Apnea: An Updated Systematic Review and Meta-Analysis

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Conclusions

CPAP is the most commonly used therapy for OSA, however, the compliance with CPAP is questionable which leads our direction to use MAD as an alternative for CPAP. CPAP still remains the gold standard in the treatment of obstructive sleep apnea and should continue to be recommended as a treatment for OSA. MAD can be used as an adjunctive treatment or as a treatment for those who cannot readily access or do not prefer CPAP.

Targeting the Secondary Sleep Disorder in Obstructive Sleep Apnea





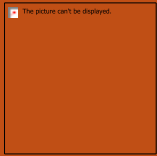
Comorbid Insomnia and Sleep Apnea

Insomnia and OSA are prevalent conditions affecting 1 billion individuals worldwide

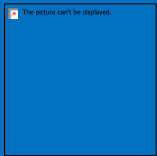
Their coexistence, known as comorbid insomnia and sleep apnea **(COMISA)**, is associated with cortical arousal, a primary factor in insomnia development.

Current treatment approaches for insomnia in patients with OSA are mainly pharmacologic and cognitive behavioral therapy for insomnia **(CBT-I)**.

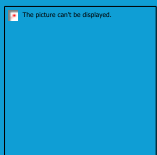
Comorbid Insomnia and Sleep Apnea



Combining CBT-I and CPAP can be more effective in reducing insomnia symptoms and improving sleep quality than using CPAP alone.



Applying CBT-I before initiating CPAP treatment can reduce immediate CPAP rejection and increase long-term CPAP usage.



Pharmacological treatment should be considered in a limited number of selected cases.

Targeting Residual Symptoms



Stimulants/Wake-Promoting Drugs

- *amphetamine (methylphenidate),*
- *modafinil,*
- *armodafinil,*
- *novel drugs such as Solriamfetol and Pitolisant*

Patients Who Are Adherent With Residual Sleepiness

- For patients who are adherent and in whom CPAP is adequate but **who remain sleepy**
 - *evaluate for other etiologies of excessive sleepiness:*
 - *central hypersomnia, insufficient sleep time, circadian misalignment, and sleepiness due to psychiatric or medical causes,*

Modafinil

Start with 100 or 200 mg every morning for the first week → □.

titrate up to 300 -400 mg over the next two to three weeks, as needed.

Armodafinil

Start with 150 mg once daily → □

titrate up to 250 mg once daily as needed.



Targeting Systemic Inflammation



Weight Management

- Lifestyle modification and rehabilitation are crucial in treating OSA.
- OSA can impair cardiovascular health, causing endothelial damage, systemic inflammation, and hypertension.
- OSA is closely linked with overweight or obesity
- A 10% increase in weight predicts a 6-fold increase in developing OSA.

Labarca G, et al Multimodal Treatment of Sleep Apnea. Sleep Med Clin. 2025

Weight Management

- Anthropometric parameters, such as increased neck circumference and cervical fat tissue, contribute to the risk of nocturnal apnea.
- Fat accumulation in the tongue is also linked to higher AHI in OSA patients.
- Weight management is recommended as a treatment strategy.

Weight Management

- Diet,
- Physical activity,
- Behavioral modifications,
- Surgical interventions
- Pharmacotherapy,
 - weight loss drugs could significantly impact the management
 - Tirzepatide has received FDA approval for moderate to severe obstructive sleep apnea (OSA) in adults with obesity (also as Zepbound) in December 2024.

Targeting Obstructive Sleep Apnea Endotypes



Ventilatory Control: High Loop Gain

- **Oxygen Therapy**

- High loop gain signifies a heightened, highly reactive response, which can perpetuate the cycle of apneas and hypopneas.
- Oxygen therapy is a treatment option in OSA patients who exhibit high loop gain.

- **Non-vented mask and dead space:**

- Non-vented masks, also known as non-vented oronasal masks, have emerged as an important option in treating high loop gain OSA (and central sleep apnea/periodic breathing).
- Primary function is to minimize hypocapnia, thus aiding in respiratory control stability.

Ventilatory Control: High Loop Gain

- Carbonic Anhydrase Inhibitors (CAIs):
- *Acetazolamide and Zonisamide* are 2 types of carbonic anhydrase inhibitors (CAIs)
- Carbonic anhydrase, plays a key role in maintaining the acid-base balance in the body.
- CAIs that have shown efficacy in managing OSA.
- CAIs **leads to mild metabolic acidosis**, which stimulates the central respiratory centers, resulting in an increased respiratory drive and improved ventilation during sleep.
- *Buspirone, Sulthiame*: routine clinical use has not yet been published

Ventilatory Control: Targeting arousal threshold

- The respiratory arousal threshold is the amount of ventilatory drive necessary to rouse a person from sleep in response to a breathing disturbance.
- With a low arousal threshold, respiratory events are shorter, which may not allow sufficient pharyngeal neural stimuli to accumulate.
- This is necessary to stabilize airway patency by activating pharyngeal muscles (ie, the threshold for effective recruitment) and prevent event cycling.
- The arousal threshold should be relatively easy to raise with the administration of hypnotics.

Summary

- CPAP is the gold standard therapy for OSA
- There is a high percentage of noncompliance or CPAP failure.
- In this scenario, a multimodal approach combining pharmacologic and non-pharmacologic interventions should improve patient symptoms and reduce the burden of comorbidities associated with untreated OSA.
- A better understanding of OSA endotyping and phenotyping should allow us to identify complementary therapies for individual patients.



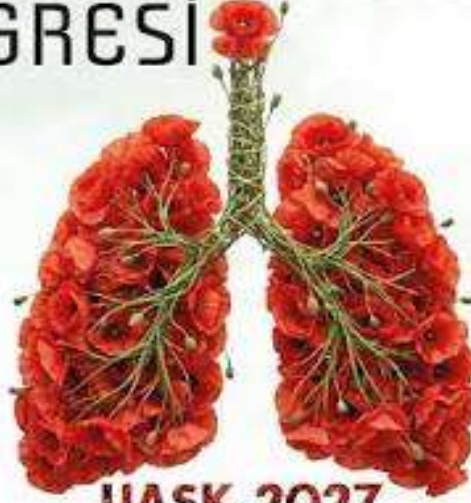






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