UPDATE ON OBSTRUCTIVE SLEEP APNOEA (OSA)

Personalised Interventions for our Patients

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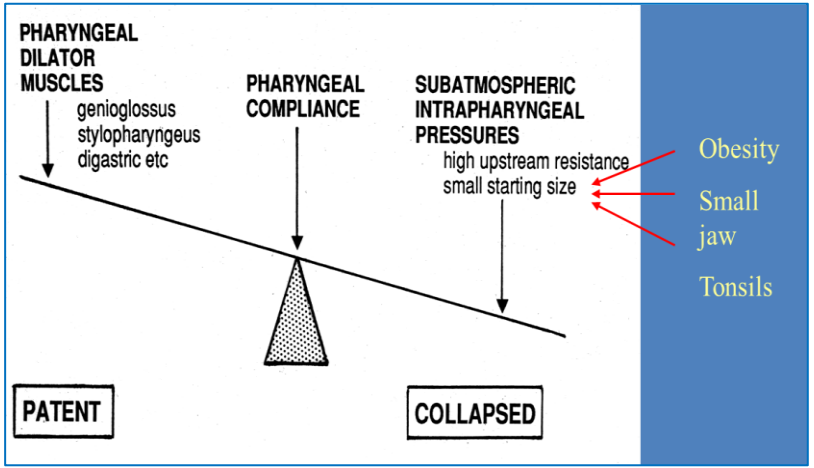
THIS IS MODERN MEDICINE

Obstructive Sleep Apnoea

- Pharyngeal incompetence brought on by sleep
- Recurrent arousals from sleep to clear the airway
- Markedly fragmented sleep
- Excessive daytime sleepiness



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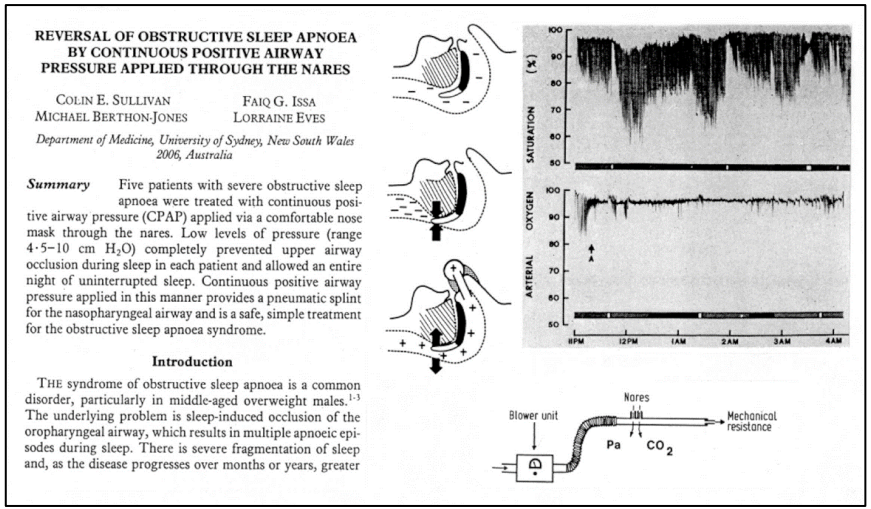
Obstructive Sleep Apnoea

- First described 1960's
- 'Pickwickian Syndrome' linked obesity & sleepiness with periodic breathing (without citing upper airway obstruction as the cause)
- First major breakthrough came in 1981 with CPAP therapy



REVERSAL OF OBSTRUCTIVE SLEEP APNOEA BY CONTINUOUS POSITIVE AIRWAY PRESSURE APPLIED THROUGH THE NARES

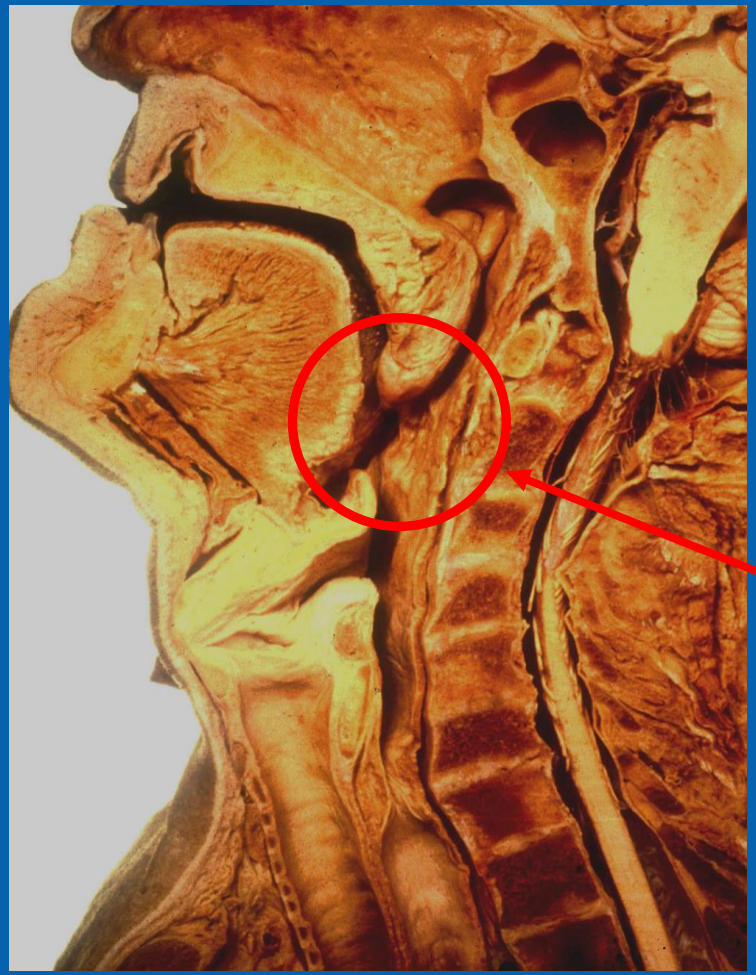
COLIN E. SULLIVAN FAIQ G. ISSA
MICHAEL BERTHON-JONES LORRAINE EVES

Department of Medicine, University of Sydney, New South Wales 2006, Australia

Summary Five patients with severe obstructive sleep apnoea were treated with continuous positive airway pressure (CPAP) applied via a comfortable nose mask through the nares. Low levels of pressure (range 4·5–10 cm H_2O) completely prevented upper airway occlusion during sleep in each patient and allowed an entire night of uninterrupted sleep. Continuous positive airway pressure applied in this manner provides a pneumatic splint for the nasopharyngeal airway and is a safe, simple treatment for the obstructive sleep apnoea syndrome.

Introduction

THE syndrome of obstructive sleep apnoea is a common disorder, particularly in middle-aged overweight males.[1-3] The underlying problem is sleep-induced occlusion of the oropharyngeal airway, which results in multiple apnoeic episodes during sleep. There is severe fragmentation of sleep and, as the disease progresses over months or years, greater

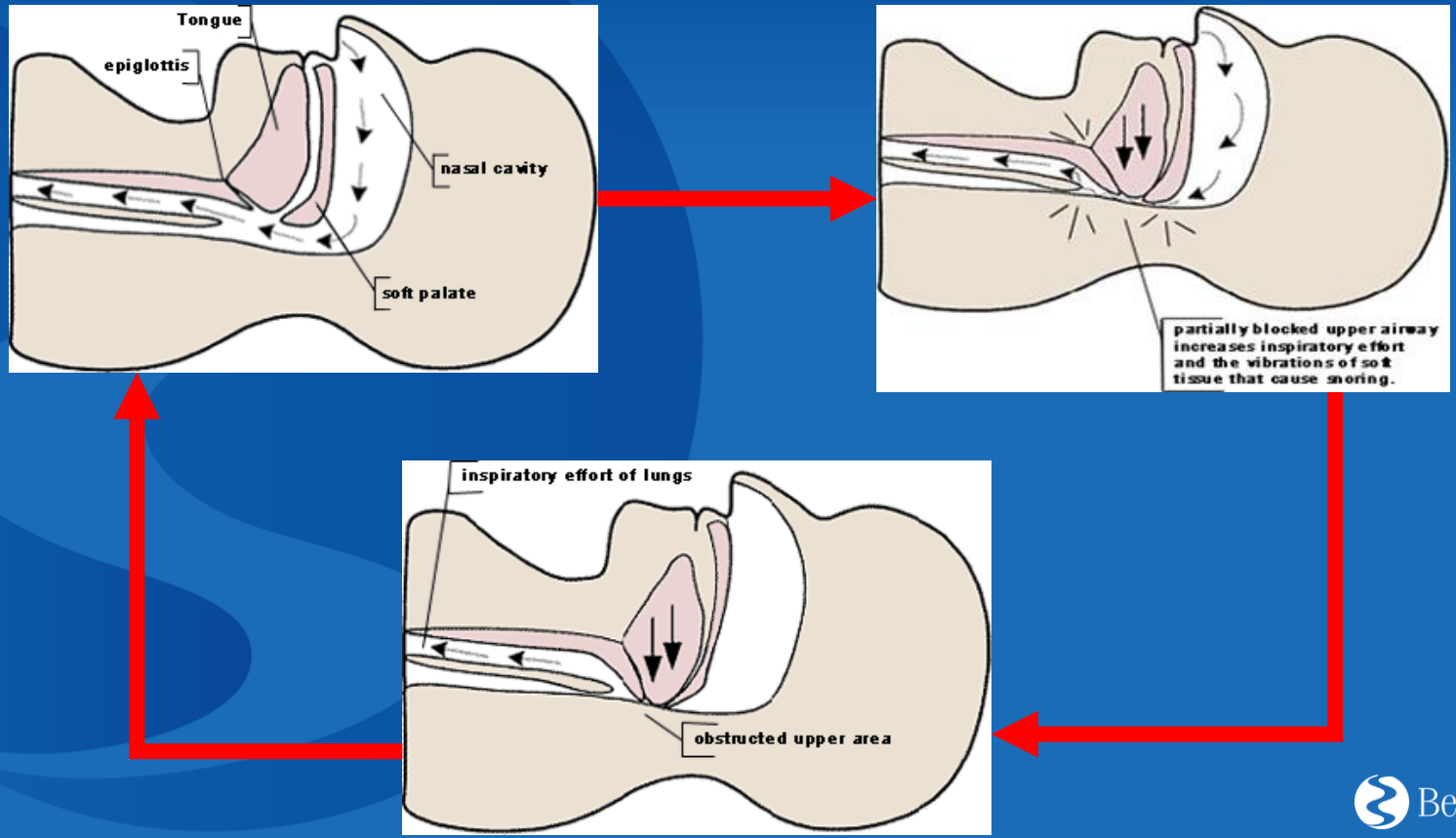


Obstructive Sleep Apnoea

Midline coronal section through the upper airway

Main area of pharyngeal airway collapse in OSA

Apnoea Hypopnoea Cycle



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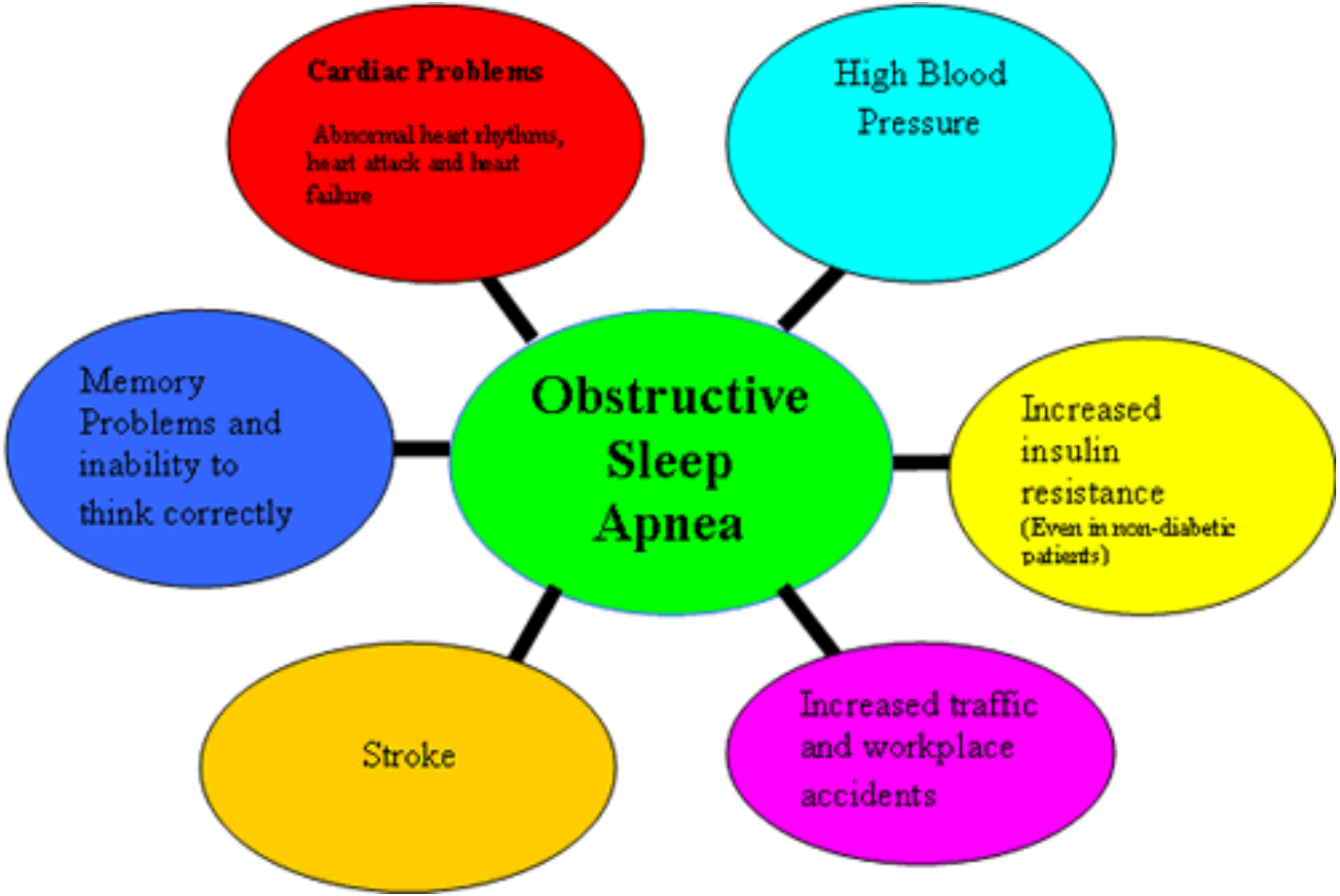

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Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis

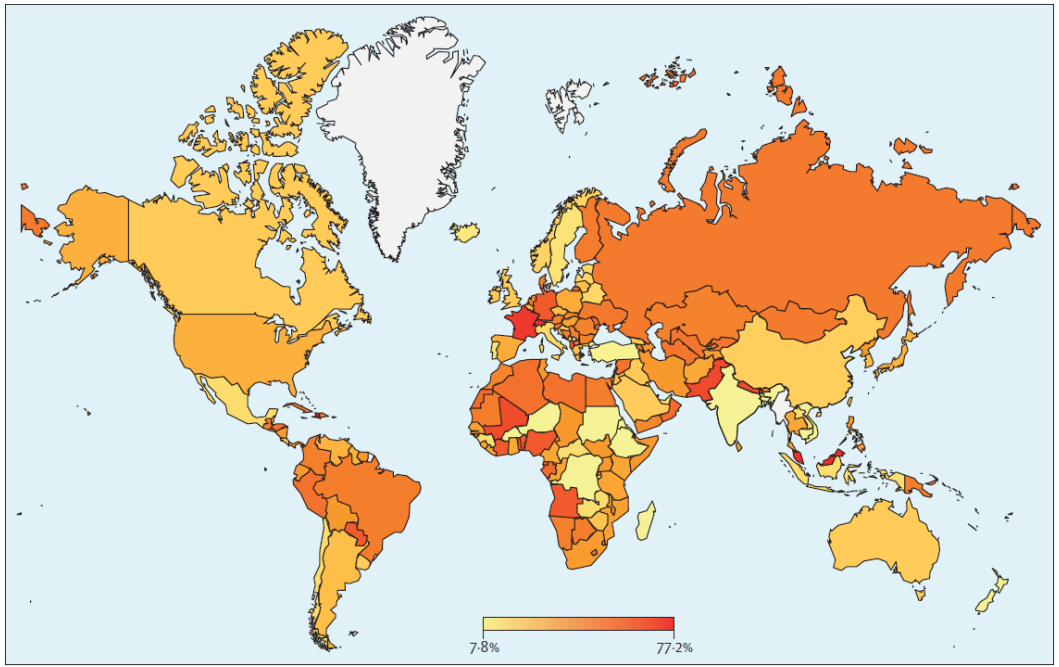
Adam V Benjafield, Najib T Ayas, Peter R Eastwood, Raphael Heinzer, Mary S M Ip, Mary J Morrell, Carlos M Nunez, Sanjay R Patel, Thomas Penzel, Jean-Louis D Pépin, Paul E Peppard, Sanjeev Sinha, Sergio Tufik, Kate Valentine, Atul Malhotra

AHI ≥ 5

936,360,689

AHI ≥ 15

424,630,028



Lancet Respiratory Medicine 2019

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How do we diagnose and manage a problem in 1 billion people?

- Scalable models
- Stratify patients based on risk of complications
- Not everybody is going to get a full PolySomnoGraphy (PSG)
- Personalized wearable technologies with Home Sleep Apnoea Testing (HSAT)


Somfit® PRO


PAT signal
Actigraphy
Heart rate
Body position
Oximetry
Chest motion
Snoring

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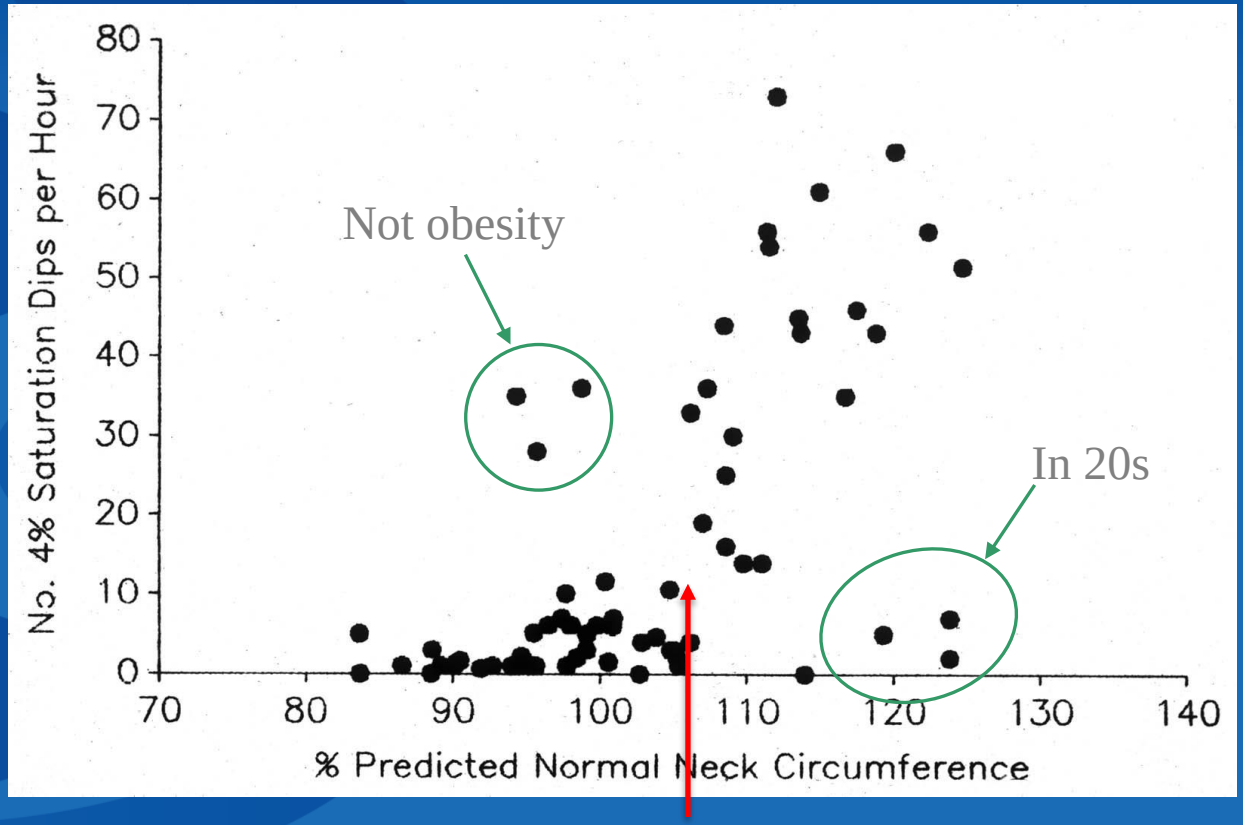
Effect of Neck Circumference on OSA



Neck size approx 17 inches

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Personalised Interventions for our Patients

- Patients do not all get OSA for the same reason and vary in clinical expression.
- There are likely to be multiple mechanistic pathways which may help guide individualized therapy.

The different clinical faces of obstructive sleep apnoea: a cluster analysis

Lichuan Ye[1], Grace W. Pien[2], Sarah J. Ratcliffe[3], Erla Björnsdottir[4,5], Erna Sif Arnardottir[4,5], Allan I. Pack[6], Bryndis Benediktsdottir[4,5] and Thorarinn Gislason[4,5]

Clusters:

1. Disturbed sleep group 33%
2. Minimally symptomatic 25%
3. Severe excessive daytime sleepiness 43%

Differential susceptibility that may help guide personalised interventions

ERJ 2014
AJRCCM 2019

Interfaces for CPAP











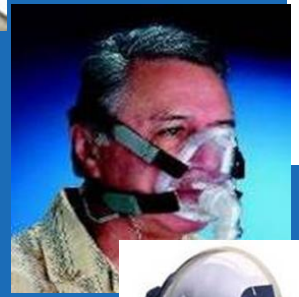






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OSA Underlying Mechanisms (Endotypes) that guide Personalised Interventions

- **Pharyngeal Anatomy**
- Pharyngeal dilator muscle control during sleep
- Low Arousal Threshold
- High Loop gain

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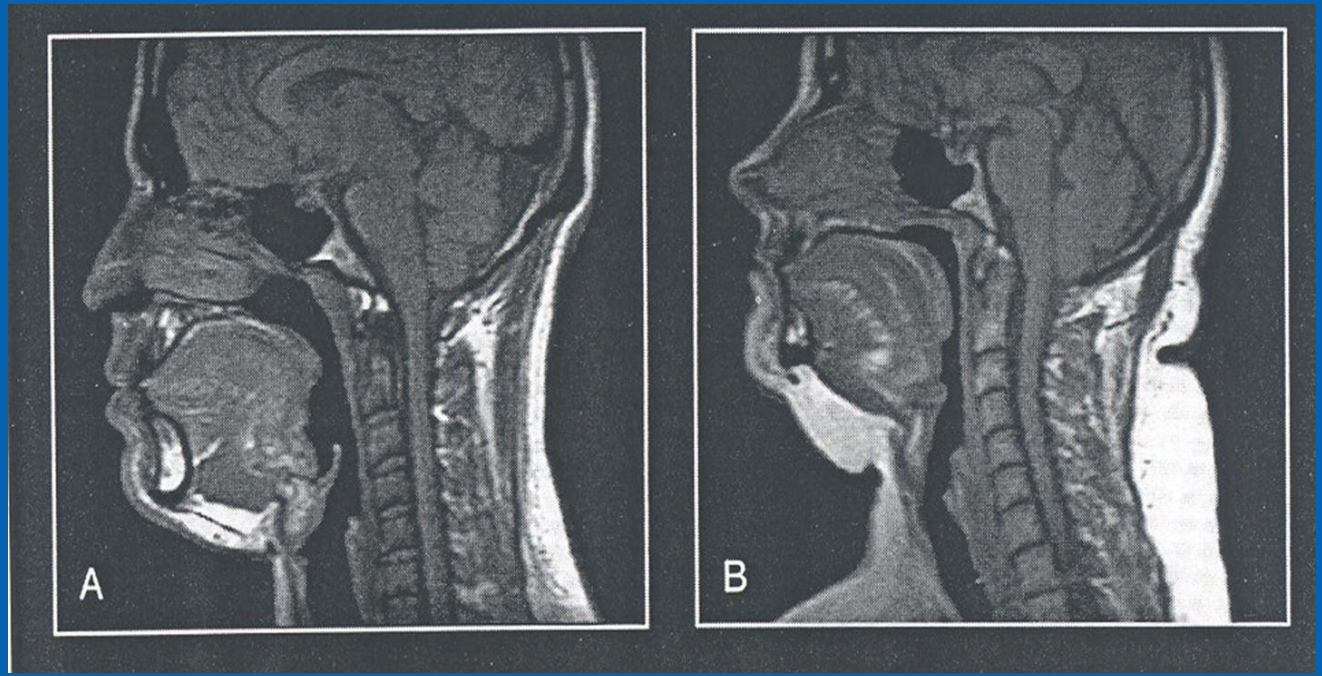
Pharyngeal Anatomy



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Positional Devices

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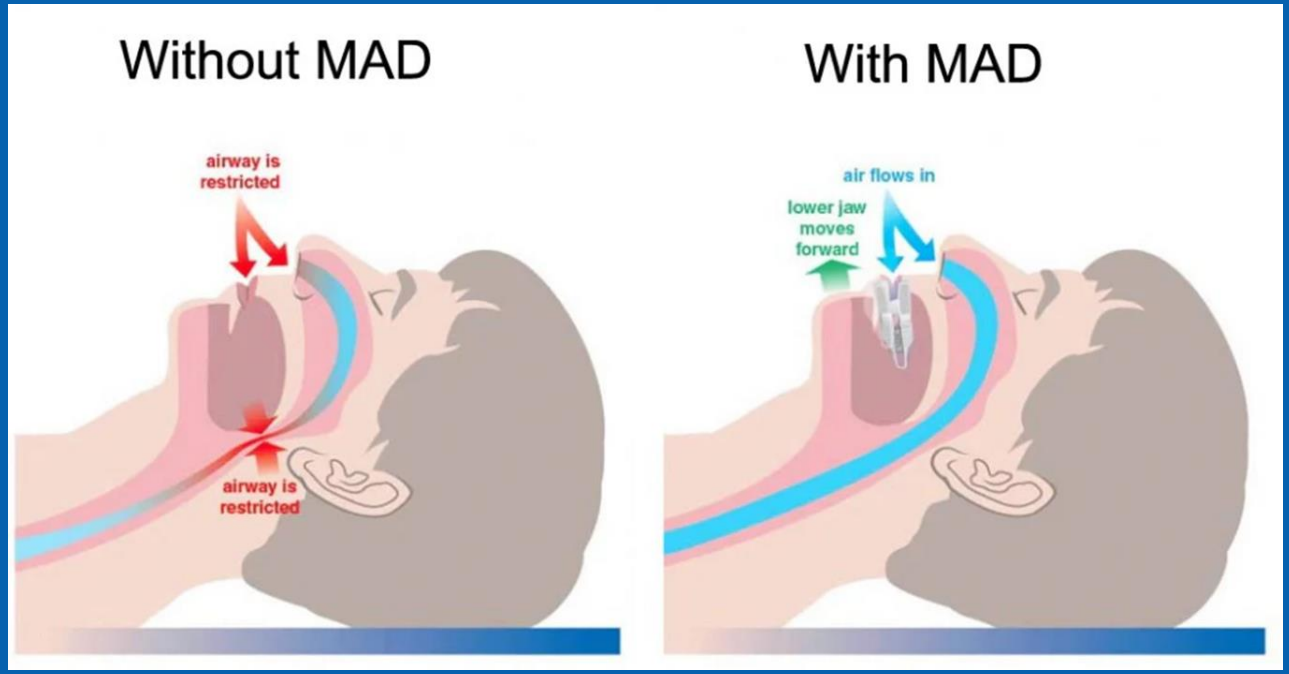
Mandibular Advancement Device (MAD)



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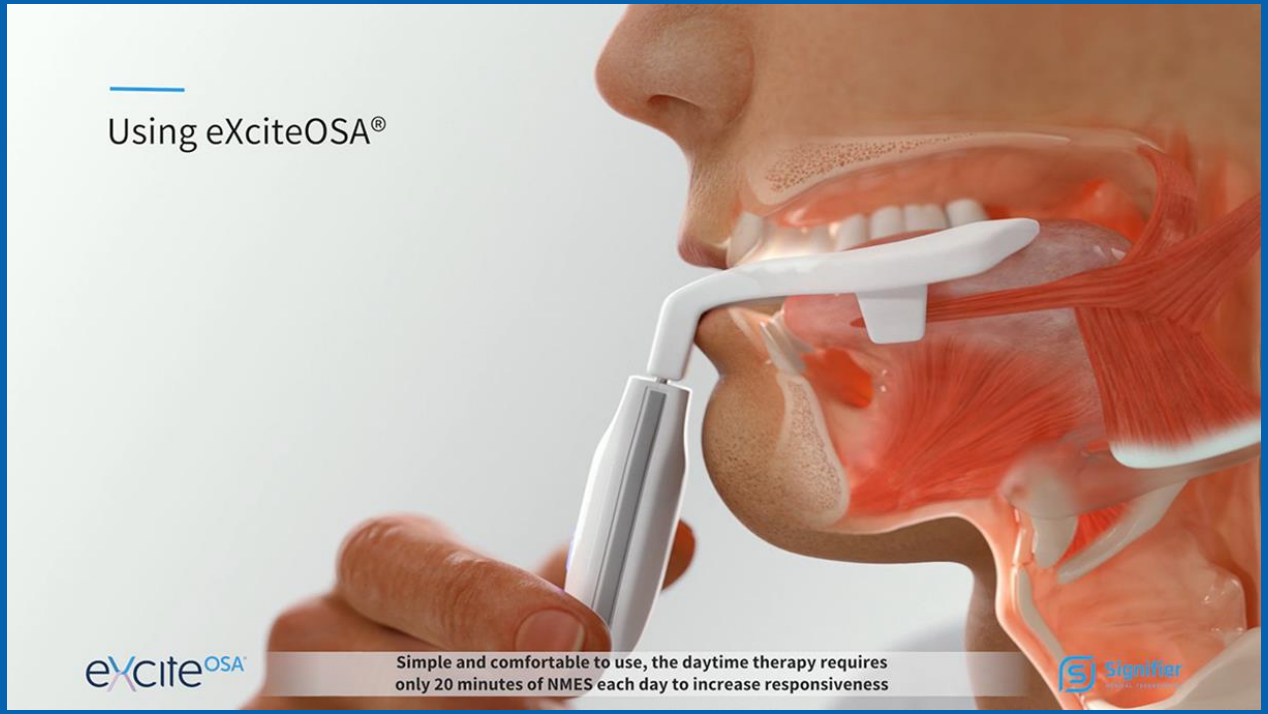
Neuromuscular Electrical Stimulation



Promotes endurance of the tongue muscles

OSA Underlying Mechanisms (Endotypes) that guide Personalised Interventions

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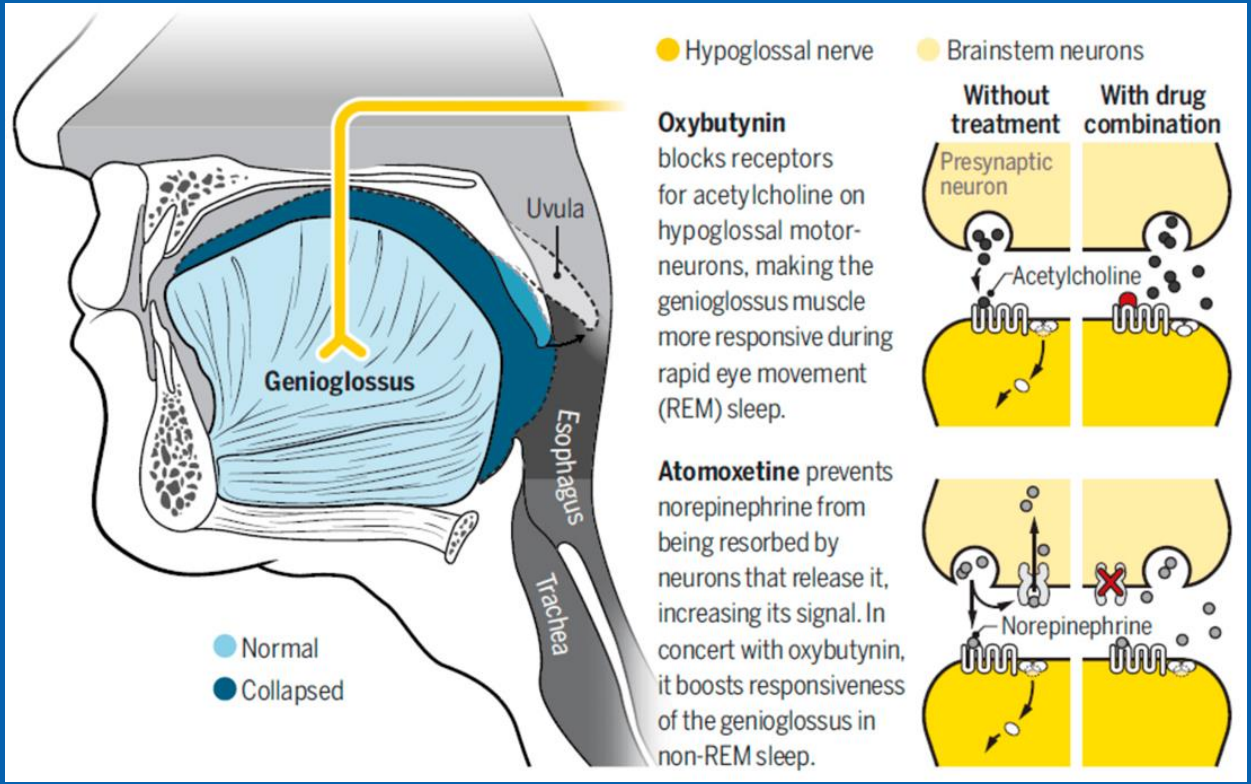
Oral antimuscarinic & noradrenergic agents as therapy for OSA



Mediano O et al. J Clin Med. 2019

Hypoglossal Nerve Stimulation Devices

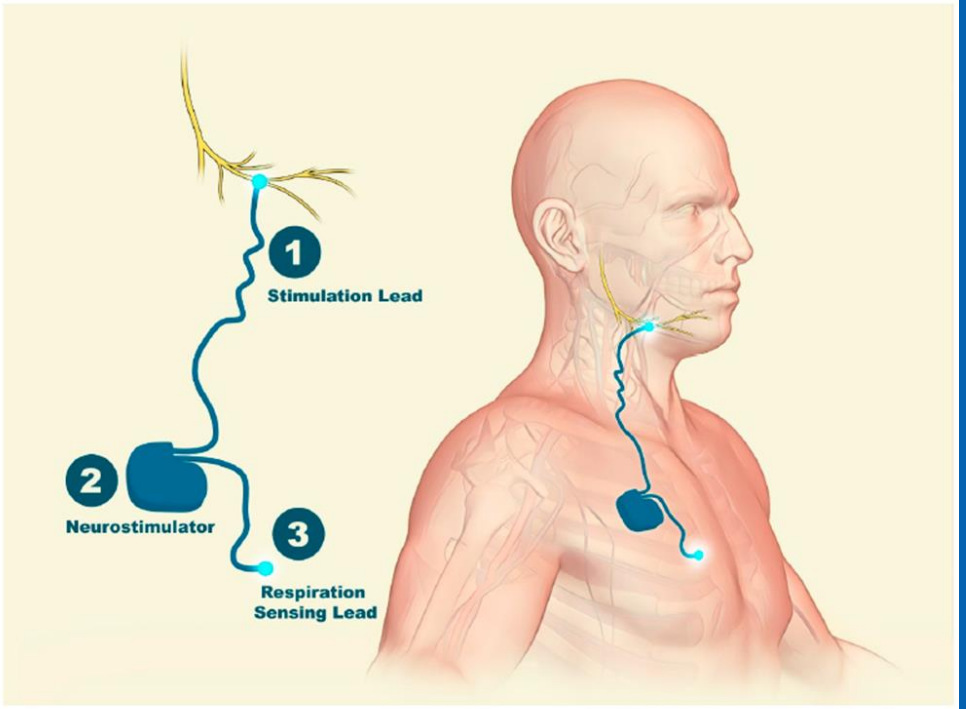


Figure 6. Hypoglossal nerve stimulation devices. (1) An electrode cuff wrapped around the hypoglossal nerve attached to (2) an implantable pulse generator (IPG) surgically placed in a subcutaneous pocket; the IPG is attached to a respiration-sensing lead (3).

OSA Underlying Mechanisms (Endotypes) that guide Personalised Interventions

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- Pharyngeal dilator muscle control during sleep
- **Low Arousal Threshold**
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Low Arousal Threshold

- A low Arousal Threshold (AT) could lead to premature arousals with inadequate time to accumulate respiratory stimuli
- A high AT could lead to substantial hypoxaemia and hypercapnia with end-organ impact
- Therapies to manipulate AT are likely to benefit some patients and theoretically hurt others

Clinical SCIENCE

www.clinsci.org

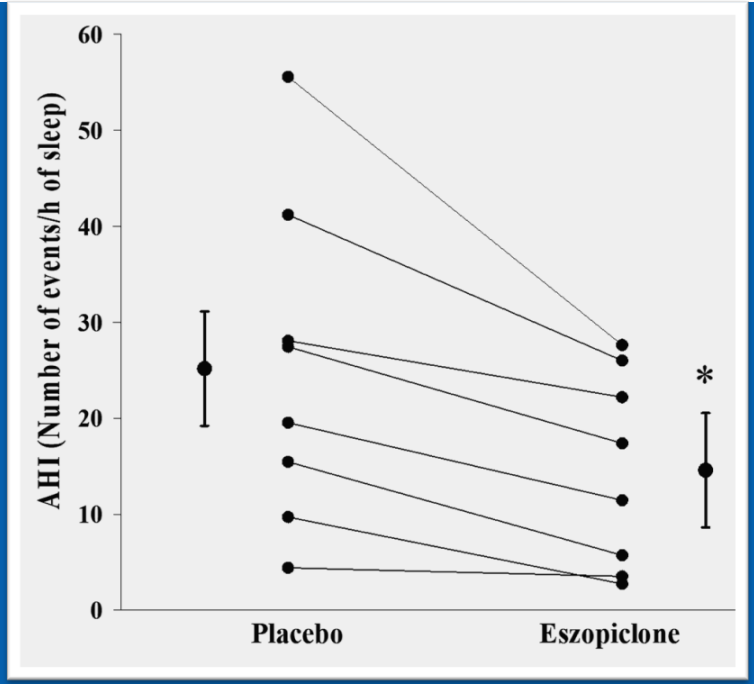
Clinical Science (2011) 120, 505–514 (Printed in Great Britain) doi:10.1042/CS20100588 505

ACCELERATED PUBLICATION

Eszopiclone increases the respiratory arousal threshold and lowers the apnoea/hypopnoea index in obstructive sleep apnoea patients with a low arousal threshold

Danny J. ECKERT, Robert L. OWENS, Geoffrey B. KEHLMANN, Andrew WELLMAN, Shilpa RAHANGDALE, Susie YIM-YEH, David P. WHITE and Atul MALHOTRA

Sleep Disorders Program, Division of Sleep Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, MA 02115, U.S.A.



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OSA Underlying Mechanisms (Endotypes) that guide Personalised Interventions

- Pharyngeal Anatomy
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- **High Loop gain**

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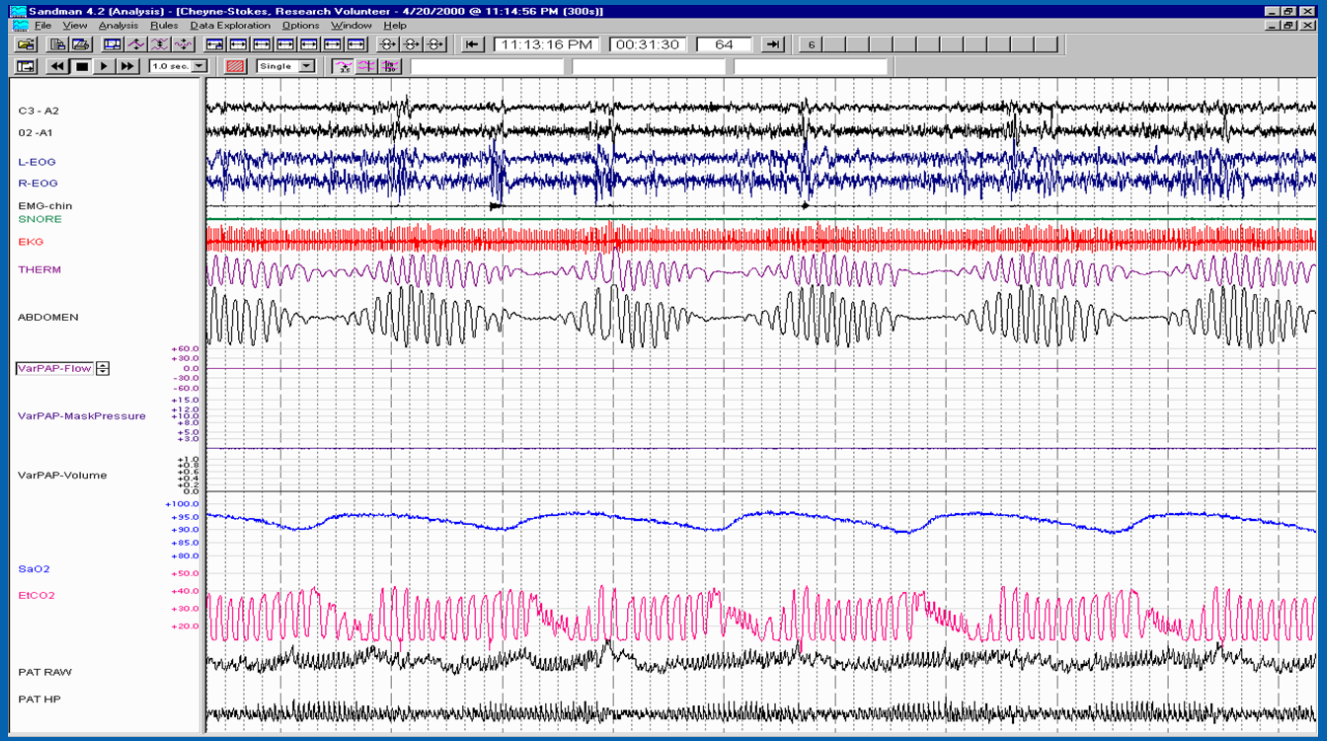
High Loop Gain (Cheyne Stokes Respiration)



Agents to reduce Loop Gain in an OSA subset – Acetazolamide; Oxygen

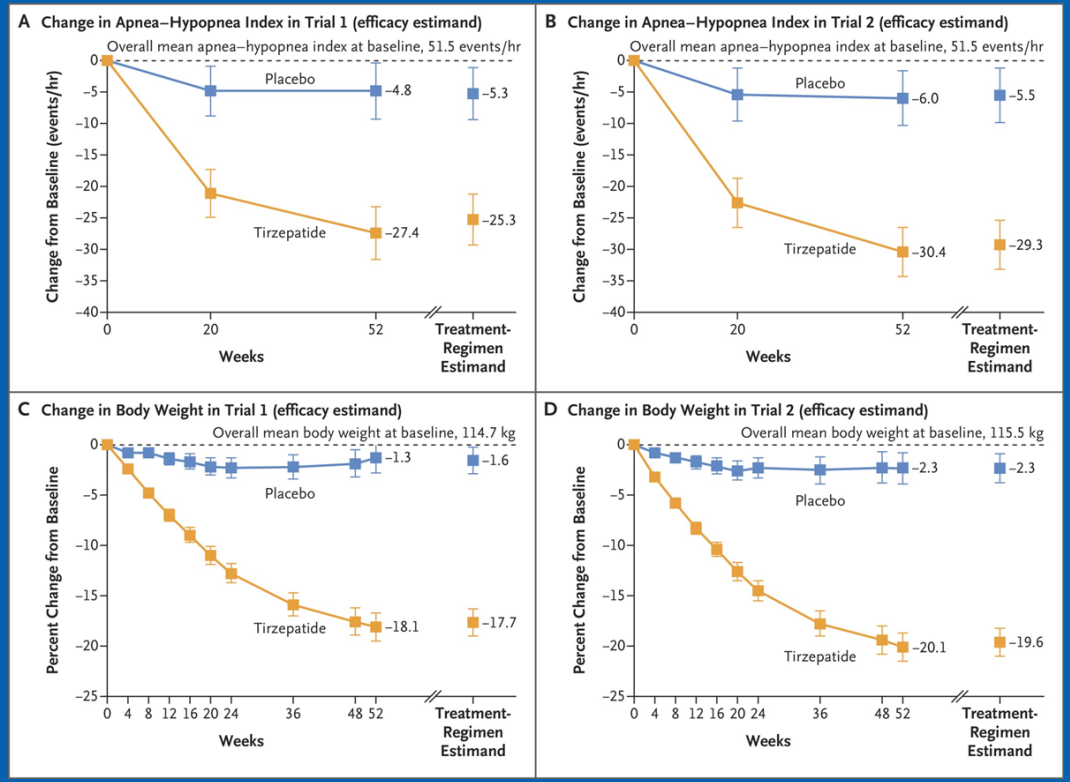
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity

Atul Malhotra, M.D., Ronald R. Grunstein, M.D., Ph.D., Ingo Fietze, M.D., Terri E. Weaver, Ph.D., Susan Redline, M.D., M.P.H., Ali Azarbarzin, Ph.D., Scott A. Sands, Ph.D., Richard J. Schwab, M.D., Julia P. Dunn, M.D., Sujatro Chakladar, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Josef Bednarik, M.D., for the SURMOUNT-OSA Investigators*

Change in AHI and Body Weight



Malhotra A et al. N Engl J Med 2024;391:1193-1205

CONCLUSION

- OSA is very common
- Personalised diagnostics - PSG vs home wearables
- Multiple mechanistic pathways in causation of OSA
- CPAP therapy vs Personalised therapies

Thank you

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