Obstructive Sleep Apnea

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Disclosure

I have no financial interests or relationships to disclose.

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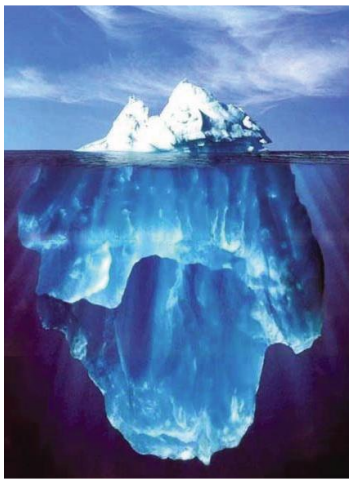
Obstructive Sleep Apnea:

The Iceberg Disease



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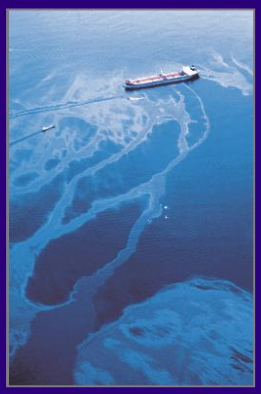
What do all three of these man made disasters have in common?



EXXON-VALDEZ
1989

THREE MILE ISLAND
1979

BHOPAL, INDIA
1984

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Introduction

OSA

-Epidemiology and Pathogenesis

-Diagnosis and Consequences

-CPAP Treatment

-non CPAP Treatment

-Cost

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OSA

-Relatively new diagnosis

-Credit has gone to Sidney Burwell

-*American Journal of Medicine* in 1956

-description of the first patient with OSA

-More careful review will find an article in *Lancet* by a London physician by the name of W. H. Broadbent:

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OSA

"When a person, especially advanced in years, is lying on his back in heavy sleep and snoring loudly, it very commonly happens that every now and then the inspiration fails to overcome the resistance in the pharynx of which stretor or snoring is the audible sign, and there will be perfect silence through two, three, or four respiratory periods, in which there are ineffectual chest movements; finally, air enters with a loud snort, after which there are several compensatory deep inspirations before the breathing settles down to its usual rhythm. In the case to which I allude there was something more than this. The snoring ceased at regular intervals, and the pause was so long as to excite attention, and indeed alarm."

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Epidemiology

-AHI (# of Apneas and Hypopneas in 1 hour)
- 0-4 is normal
- 5-14 is mild
- 15-29 is moderate
- 30+ is severe

-Prevalence of AHI 5+
- -Men = 24% (EDS = 4%)
- -Women = 9% (EDS = 2%)

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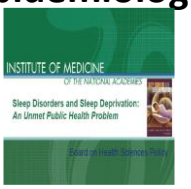
Epidemiology



Institute of Medicine of the National Academies
-Sleep Disorders and Sleep Deprivation: An Unmet Public Health Problem (2006)

"50-70 million suffer from a chronic disorder of sleep"
"Majority of these individuals are not appropriately treated"
"Awareness among health care professionals is low considering the size of the problem"

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Importance of Understanding Risk Factors for Sleep-Disordered Breathing

- Majority (70-80%) of patients with sleep-disordered breathing (SDB) not diagnosed and not treated[1,2]
- Understanding underlying risk factors, varying clinical presentations, and phenotypes is crucial to case identification
- Clinical epidemiologic studies: significant proportion of occult SDB would be missed if screening based solely on obesity or male sex[3]
- Genetic epidemiologic studies: majority of genetic variance in sleep-disordered breathing mediated by obesity independent pathways

1. Young, Sleep, 1997
2. Kapur, Sleep and Breathing, 2002
3. Young, Arch In Med, 2002
4. Patel, Int J of Obesity, 2008

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Risk Factors for Obstructive Sleep Apnea

- Male gender
- Post-menopausal state
- Excess body weight
- Increasing age
- Race
- Craniofacial anatomy
- Familial and genetic predisposition

* Not Hypothyroidism

Young; Am J Respir Crit Care Med 2002

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Epidemiology

Man versus Woman:
- -women less likely to endorse “classic symptoms”
- -women more likely to have
  - -daytime fatigue
  - -morning headaches
  - -mood disturbances

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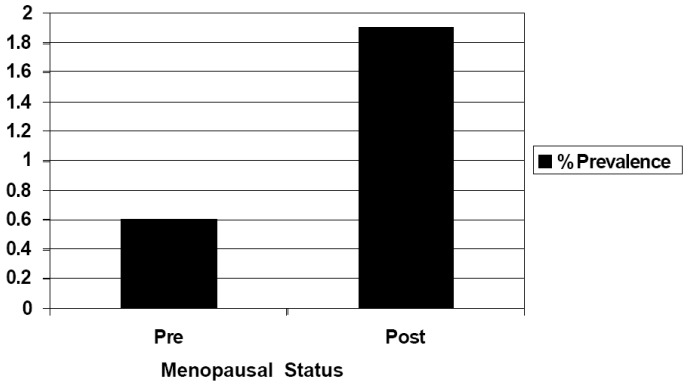
Prevalence of OSA in Women by Menopausal Status



Bixler; Am J Respir Crit Care Med 2001

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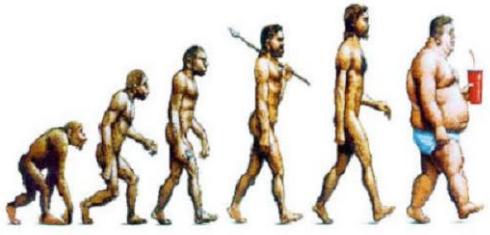
Weight: Size Matters



10% = 6X risk

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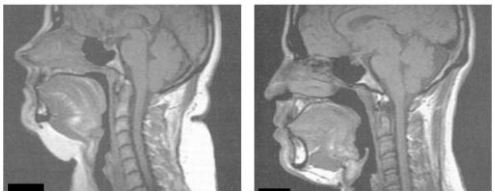
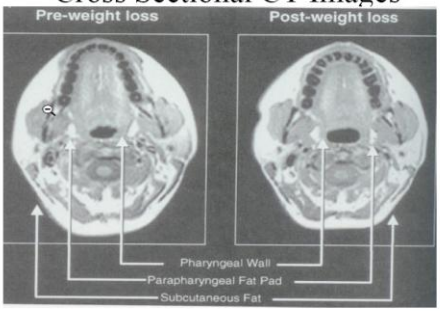
Weight:

Impact of Weight on the Upper Airway:
Sagittal MR Images



Impact of Weight on the Upper Airway:
Cross Sectional CT Images



Schwab; Clinics Chest Med 1996

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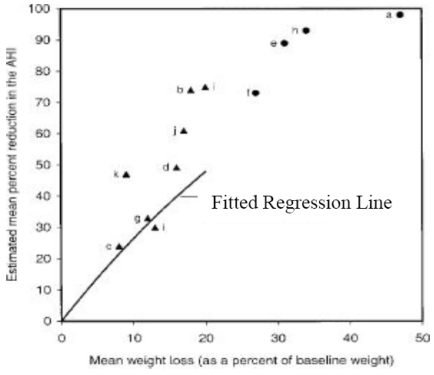
Weight Loss – Does it Help?

Impact of Weight Reduction on Sleep Apnea

% reduction in the AHI



% weight loss

Young; Am J Respir Crit Care Med 2002

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AGE:

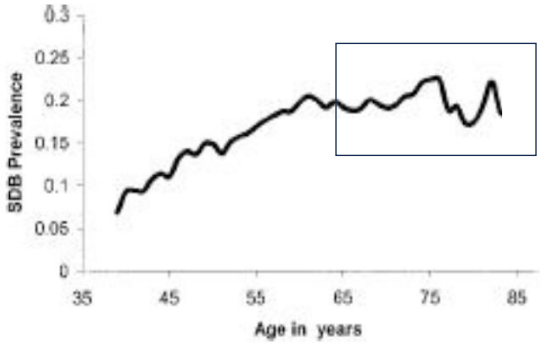
AHI > 20 versus Age:

20-44 = 2%

45-64 = 6%

65-100 = 5% (not higher)

Prevalence of OSA by Age



Young; Arch Intern Med 2002

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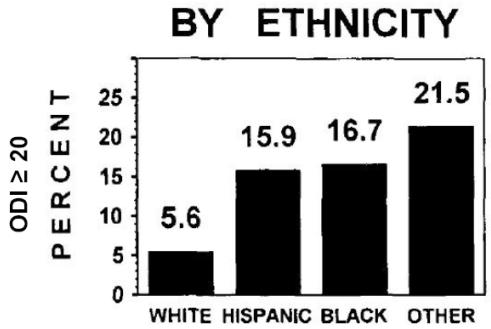
Prevalence of Sleep-disordered Breathing in **Ages 40-64**



Kripke, Sleep, 1997

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Craniofacial Anatomy among Asian and White patients with OSA

- OSA patients had:
  - ↑ Thyromental angle, ↑ Mallampati score
- After controlling for BMI and neck circumference Asians had:
  - Higher Mallampati score, smaller thyromental distance and larger thyromental angle
  - More severe OSA than whites

Lam; Thorax 2005

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Risk Factors:

-Craniofacial Abnormalities

-bone and soft tissue morphology

-Nasal Obstruction

-Allergic Rhinitis

-Genetic Factors

-1st degree relatives increase prev 22 → 86%

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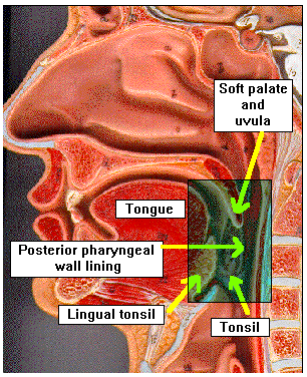
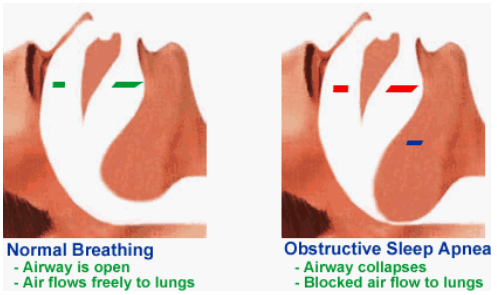
Pathogenesis:

-obstruction in the upper airway

-reduced neuromuscular dilatory compensation in PM

-ventilatory control instability





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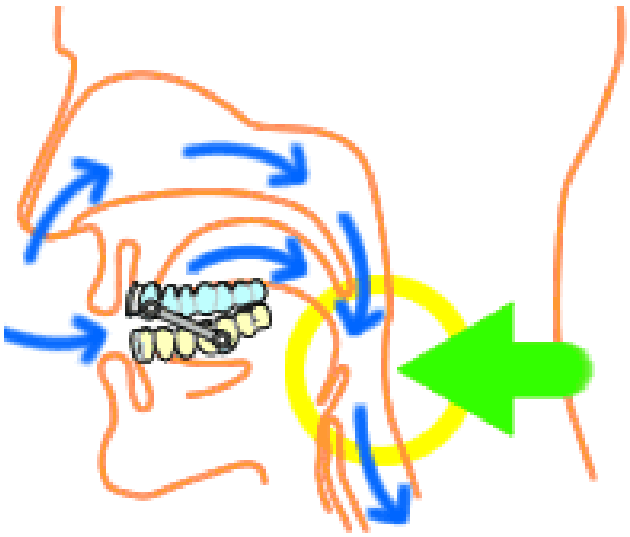

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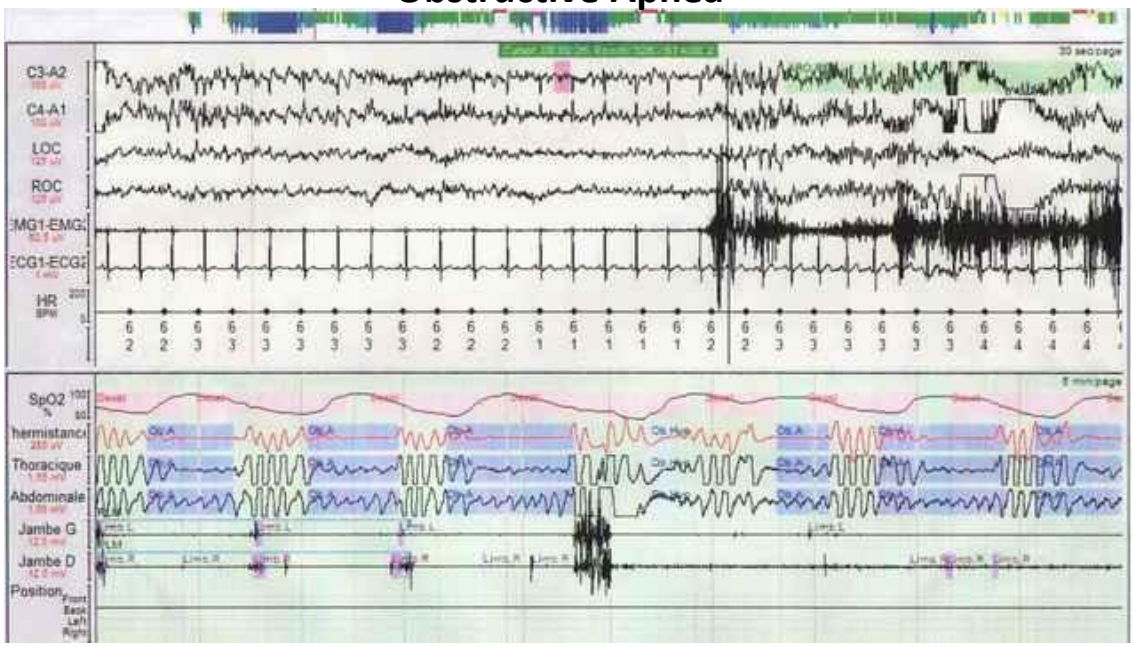
Obstructive Apnea



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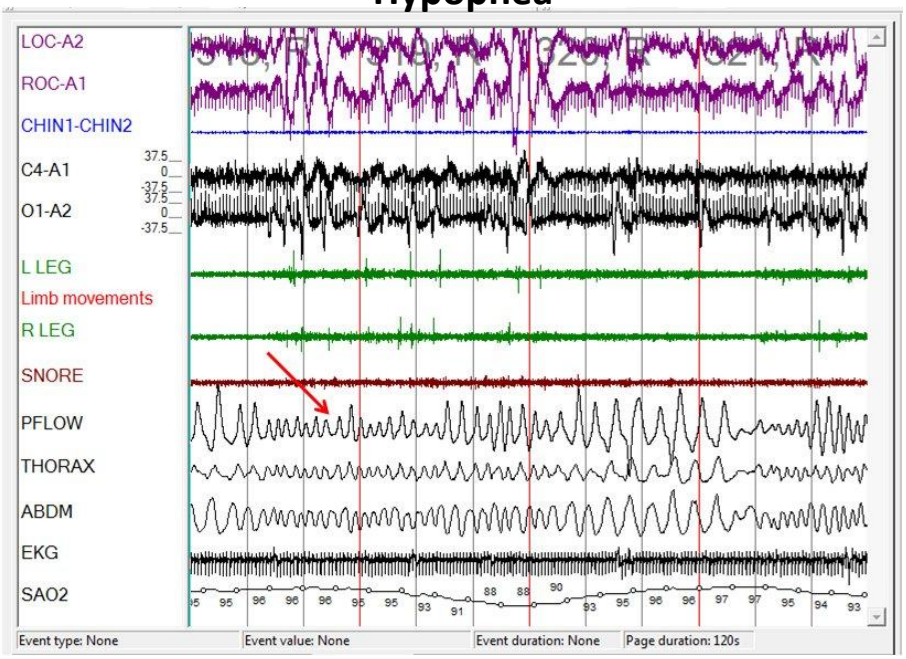
Hypopnea



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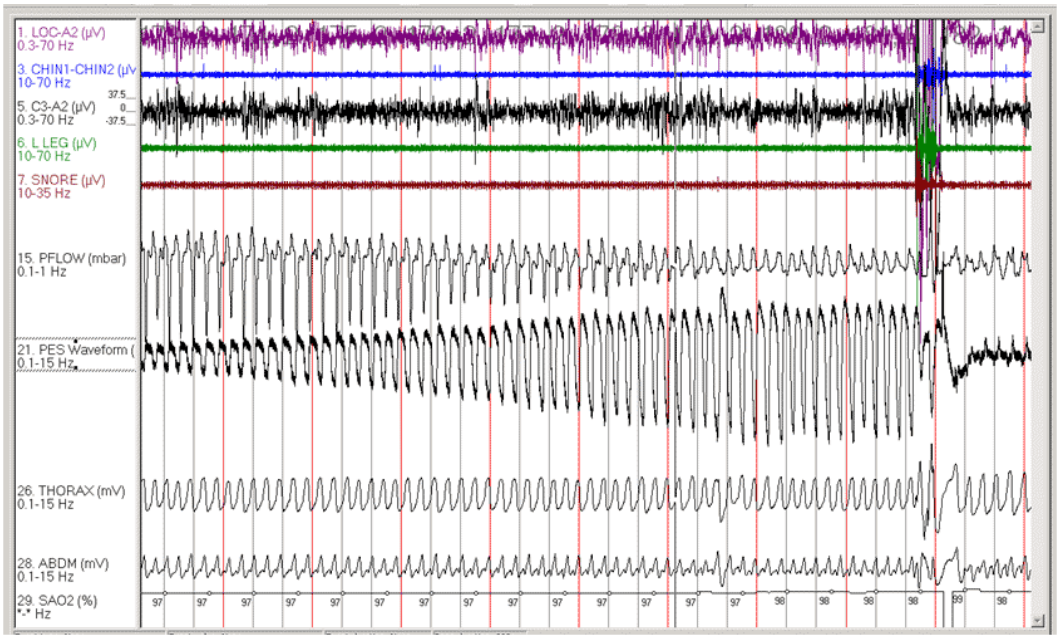
Respiratory Effort Related Arousal (RERA) - UARS



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Diagnosis:

CPAP will be covered for adults with SDB, if:

- AHI ≥15

[OR]

- AHI ≥5 with ("mild, symptomatic")
  - Hypertension
  - Stroke
  - Sleepiness
  - Ischemic heart disease
  - Insomnia
  - Mood disorders

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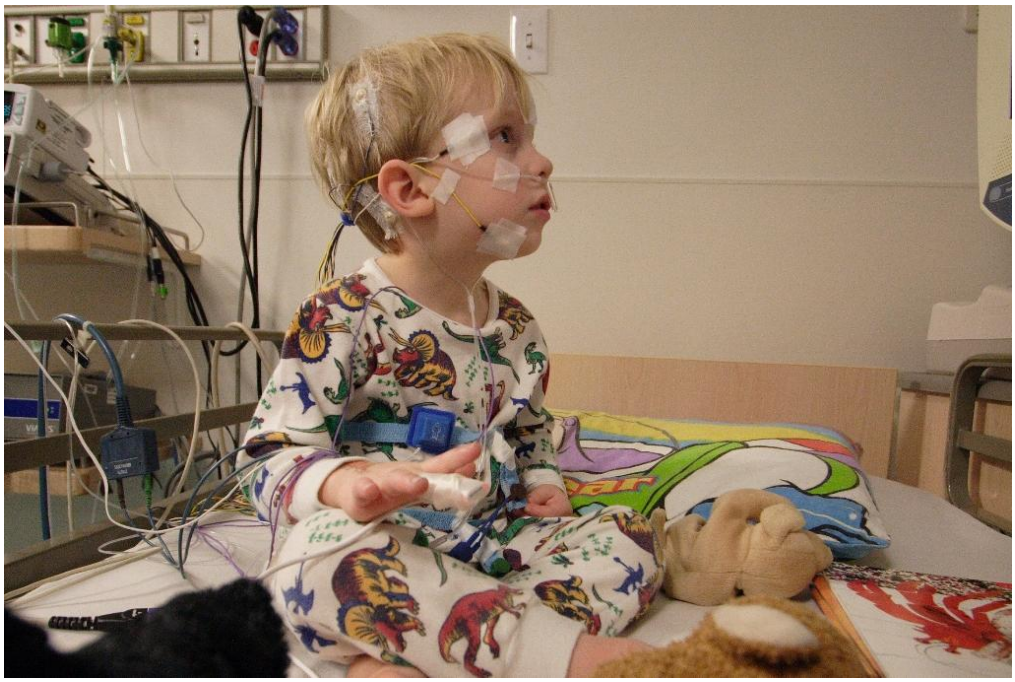

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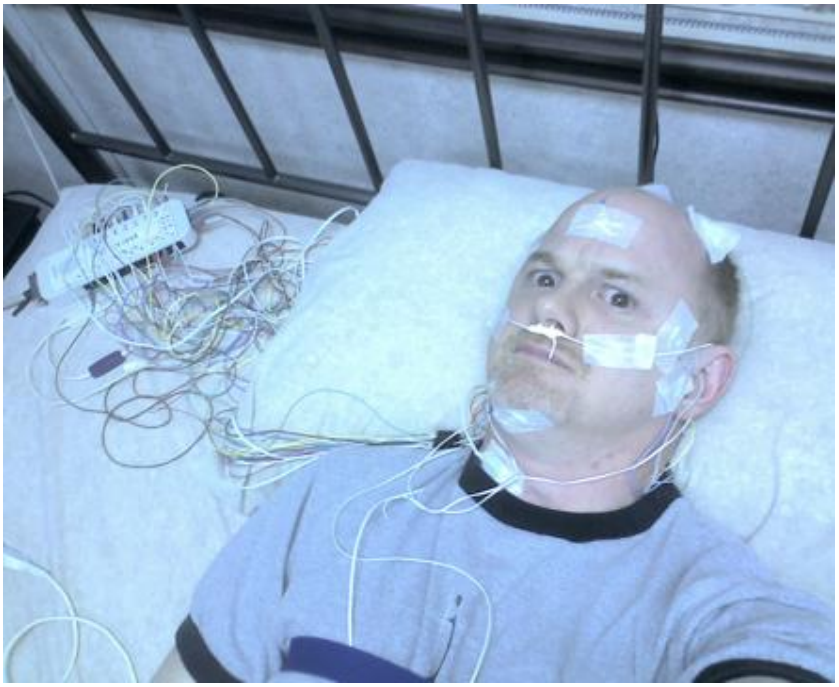

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Diagnosis:

-Overnight Pulse Oximetry can see it if desaturations but not a good screening tool

-outcome data predicts abnormal AHI

-look for desaturations of 2-4% and < 90%

-Polysomnogram is the **Gold Standard**

-now reserved for those suspected of central sleep apnea

-COPD on oxygen or CHF

-Home Sleep Test (HST)

-now **acceptable** for most payors

-**great if no other co-morbidities (CHF or COPD)**

-no tech needed – done at home (1-2 days)

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Consequences: (Association and Causation)

-Daytime sleepiness

-Neurocognitive/psychological functioning

-Mood Disorders (depression)

-Decreased Quality of Life (QOL)

-Hypertension (HTN)

-Diabetes (Glucose Intolerance)

-Stroke (CVA)

-Cardiovascular Disease

-Motor Vehicle Accidents

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Consequences: (Association and Causation)

"Patients with obstructive sleep apnea (OSA) have an increased prevalence of systemic and pulmonary hypertension, left ventricular (LV) hypertrophy, LV systolic and diastolic dysfunction, and congestive heart failure, increased platelet aggregability, and increased susceptibility to thrombotic and embolic cardiac and cerebrovascular events. Patients with OSA have an increased prevalence of coronary artery disease, myocardial infarction, nocturnal angina, and myocardial ischemia, arrhythmias, and sudden cardiac death. Patients with OSA also have an increased prevalence of stroke. Treatment of OSA with continuous positive airway pressure improves cardiac efficiency in patients with heart failure, causes a reduction in the frequency of nocturnal ischemic ST-segment depression, relieves nocturnal angina, and causes a reduction in the occurrence of new cardiovascular events and an increase in the time to such events."

Cardiovascular Manifestations Seen in Obstructive Sleep Apnea Comprehensive Therapy Volume 33, Number 2 / June, 2007 82-86

SAVE trial (secondary prevention) did **not** show a reduction in composite CV events overall, despite symptom/QOL improvements.

McEvoy RD, Antic NA, Heeley E, et al; SAVE Investigators and Coordinators. **CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea.** *N Engl J Med.* 2016;375(10):919-931. doi:10.1056/NEJMoa1606599. PMID:27571048.

"*Evidence for reduction in major CV events is mixed; adherence likely matters.*"

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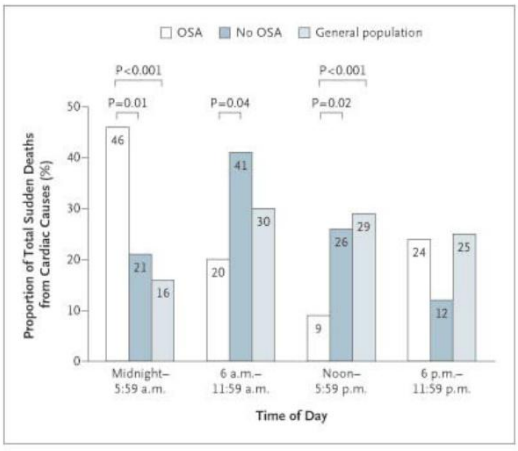
Day-night Pattern of Sudden Death in Obstructive Sleep Apnea



Gami; NEJM 2005

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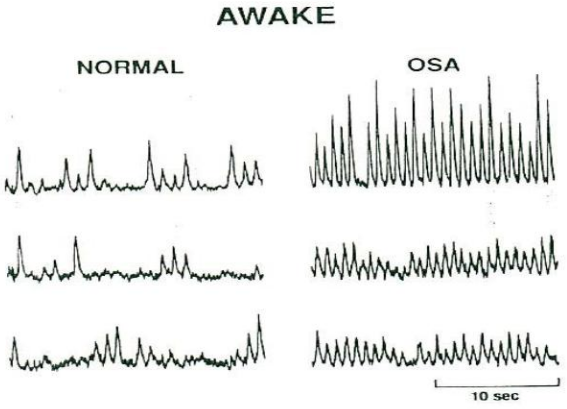
Increased Sympathetic Nerve Activity in OSA and Systemic Hypertension



Somers; J Clin Invest 1995

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Sleep Apnea and Diurnal Hypertension

Apnea Hyponea Index	Adjusted* Odds Ratio
0	Reference
> 0 - < 5	1.42
≥ 5- <15	2.03
≥15	2.89

*adjusted for baseline hypertension, age, gender, BMI, waist circumference, alcohol, and tobacco use

P for trend=0.002

Peppard; NEJM 2000

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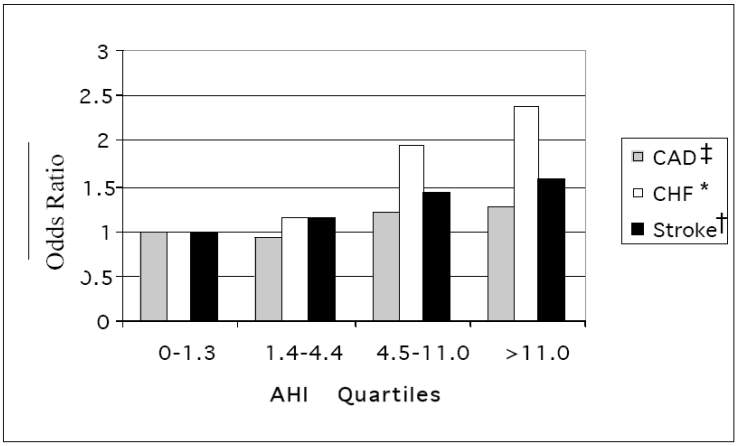
Adjusted Odds Ratios for Coronary Artery Disease (CAD), Congestive Heart Failure (CHF), and Stroke as a Function of Severity of Sleep Apnea



*P=0.004, † P=0.002, ‡ P=0.03 for linear trend across quartiles

Shahar; Am J Respir Crit Care Med 2001

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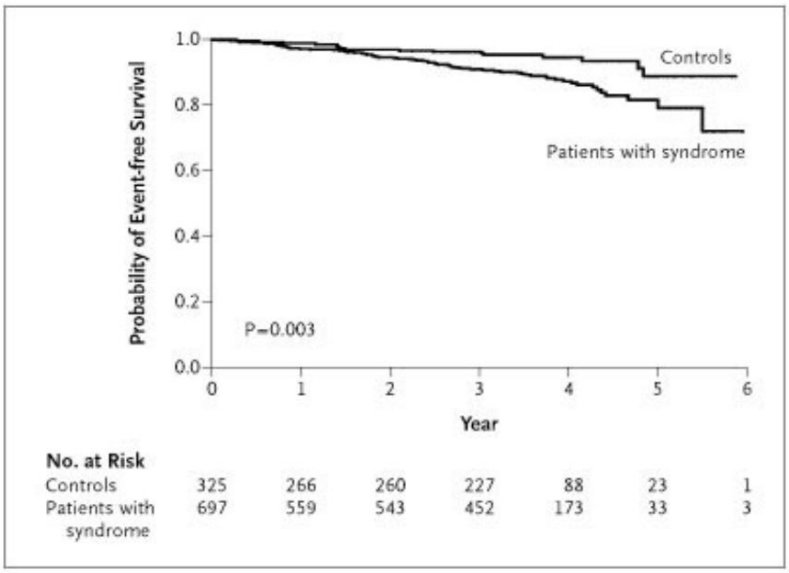
Event-free Survival (TIA, Stroke, Death)



Yaggi; NEJM 2005

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Dose-Response (Trend) Analysis

Severity of Syndrome	Stroke or Death No. of events	No. of patients	Follow-up yrs.	Hazard Ratio (95% C.I.)
AHI ≤ 3 (ref)	13	271	3.08	1.00
AHI 4-12	21	258	3.06	1.75 (0.88-3.49)
AHI 13-36	20	243	3.09	1.74 (0.87-3.51)
AHI >36	34	250	2.78	3.30 (1.74-6.26)

P=0.005 (Chi-square test for linear trend)

Yaggi; NEJM 2005

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Risk of Stroke or Death

Covariate	Unadjusted Hazard Ratio (95% C.I.)	Adjusted Hazard Ratio (95% C.I.)
Age (yrs)	1.09 (1.06-1.11)	1.08 (1.06-1.11)
Male sex	0.99 (0.62-1.60)	0.78 (0.48-1.28)
Body Mass Index	0.99 (0.97-1.02)	0.99 (0.96-1.02)
Current Smoker	1.21 (0.90-1.64)	1.46 (0.78-2.98)
Diabetes Mellitus	1.56 (1.02-2.59)	1.31 (0.76-1.26)
Hyperlipidemia	1.04 (0.64-1.68)	1.01 (0.61-1.66)
Hypertension	1.48 (0.95-2.28)	1.20 (0.75-1.90)
Atrial Fibrillation	1.56 (0.79-3.12)	0.91 (0.45-1.86)
Obstructive Sleep Apnea	2.24 (1.30-3.86)	1.97 (1.12-3.28)

Yaggi; NEJM 2005

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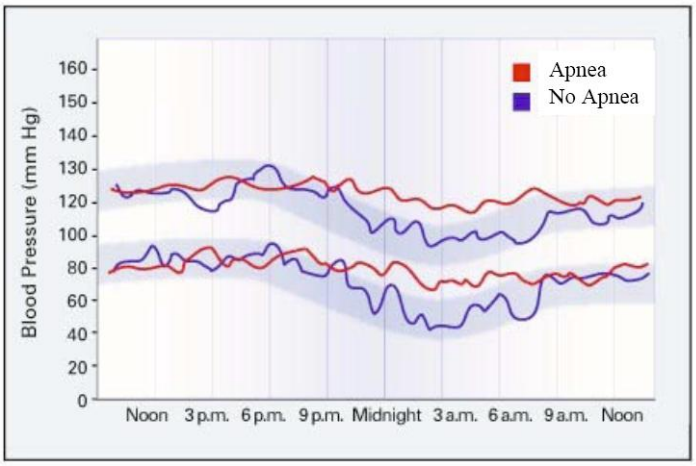
Circadian Blood Pressure and "Nondipping"



Somers; J Clin Invest 1995
Ancoli-Israel; Chest 2002
Hla, Sleep, 2008

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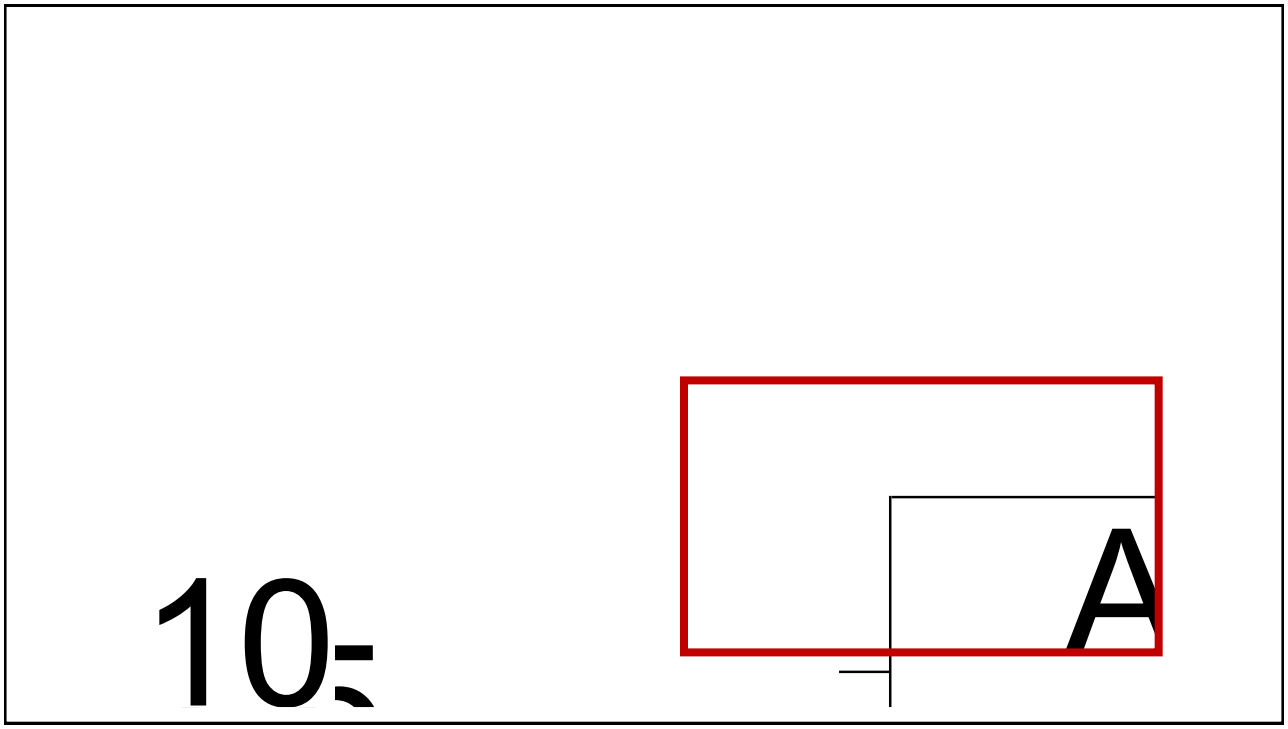

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Full Face Mask

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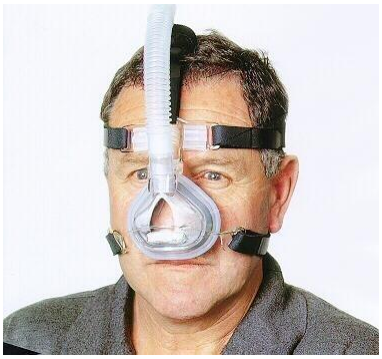

Nasal Mask

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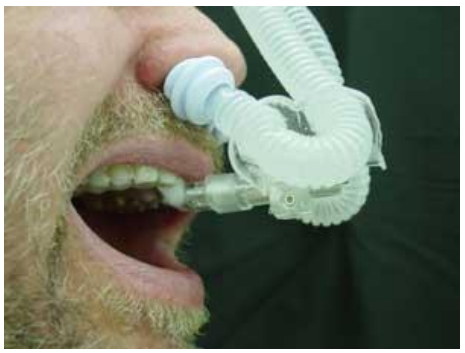


Nasal Pillows

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Chin Strap

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CPAP (Continuous Positive Airway Pressure) Machine

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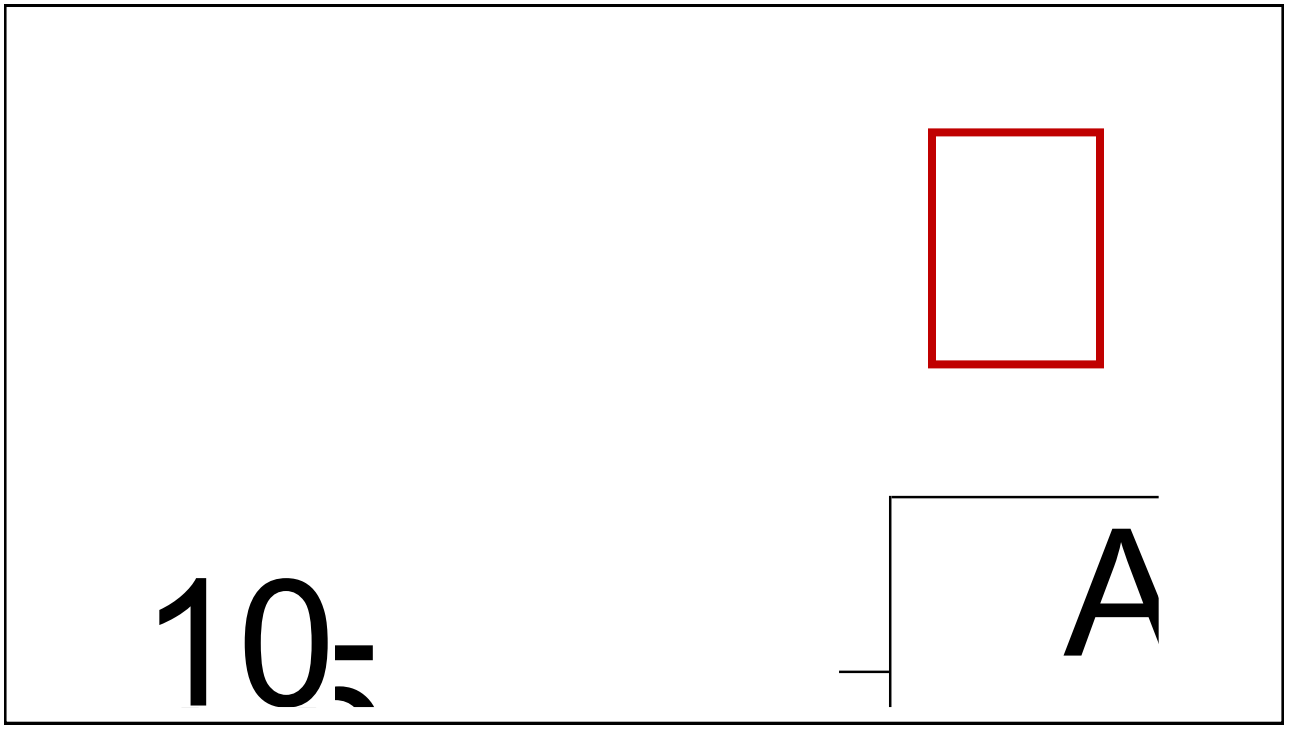

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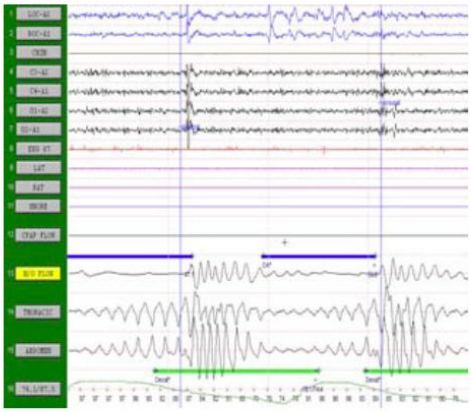
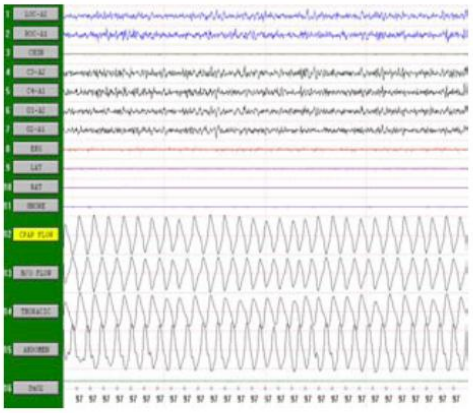
CPAP Therapy:

CPAP Eliminates Obstructive Sleep Apnea Cycle

Untreated sleep apnea



On CPAP



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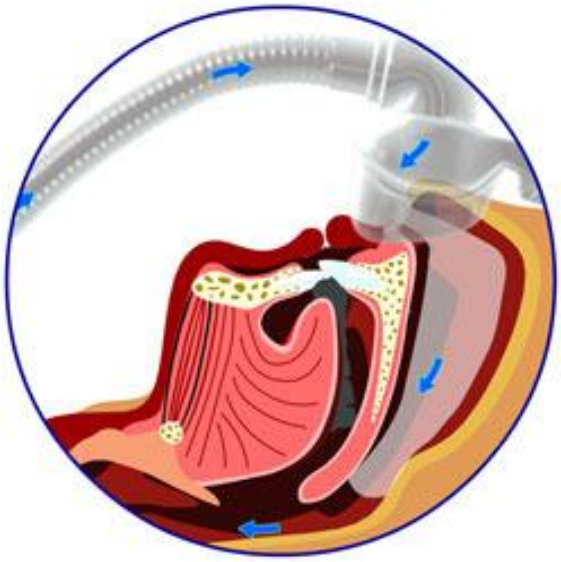

CPAP Therapy to Open the Obstruction

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CPAP Therapy:

-first line therapy for OSA for all severity

-improves or resolves daytime sleepiness

-reduces BP

-mixed results for neurocognitive/psychological

-3-12 months in memory and cognition

-improvement in depression was minimal if at all

-QOL improves with CPAP

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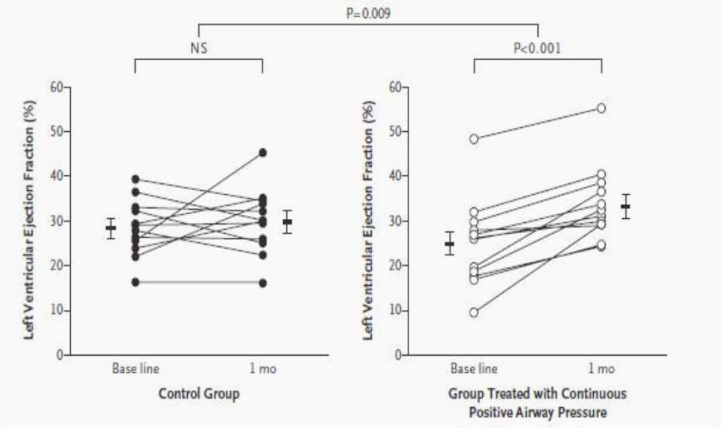
CPAP Therapy:

Effects of CPAP on LVEF in Patients with Heart Failure and OSA



Kaneko; NEJM 2003

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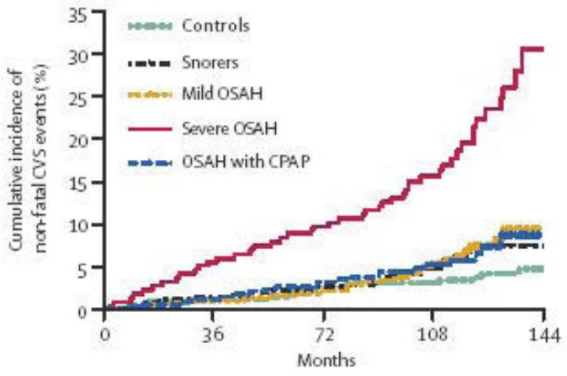
CPAP Therapy:

Cardiovascular outcomes in Obstructive Sleep Apnea With and Without Treatment



Marin; Lancet 2005

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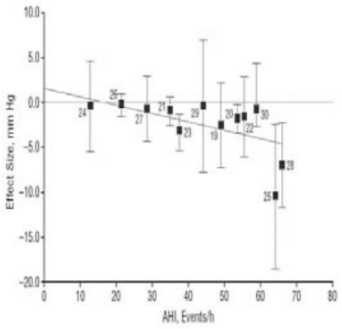
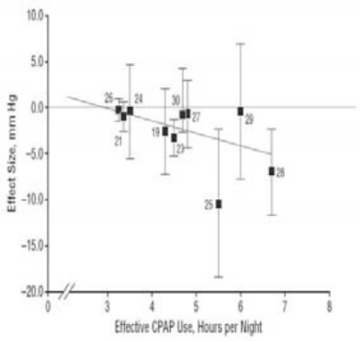
CPAP Therapy:
Impact of CPAP on Blood Pressure

Severity of Sleep Apnea



Effective CPAP Use



Haentjens; Arch Int Med 2007

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CPAP Therapy:
CPAP Treatment and Cardiovascular Risk

- ↓ Blood pressure[1]
- ↓ Sympathetic activity and catecholamines[2,5]
- ↓ Recurrent atrial fibrillation[3]
- ↑ Left ventricular function[4]
- ↓ Early Signs of Atherosclerosis[5]

1. Haentjens; Arch Int Med 2007
2. Faccenda; AJRCCM 2001
3. Kanagol; Circulation 2003
4. Kaneko; NEJM 2003
5. Drager; AJRCCM 2007

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CPAP Therapy:

-compliance

-defined as ≥4 h/night on ≥70% of nights in a consecutive 30-day period during the first 90 days

-CPAP pressure is not predictive

-experience the first night is predictive

-68% of patients use CPAP after 5 years

-claustrophobia, nasal congestion, fit

-ways to improve compliance

-humidification[1], education, follow-up

-work on the right fit

1. Respir Care. **2016** May 24. pii: respcare.04536. **Effect of Heated Humidification on CPAP Therapy Adherence in Subjects With Obstructive Sleep Apnea With Nasopharyngeal Symptoms.**
Soudorn C1, Muntham D2, Reutrakul S3, Chirakalwasan N4.

59

CPAP Therapy:

-other variations

-Auto CPAP

-C-flex (? may improve compliance)

-BiPAP

-can now do a few options

-LAB: CPAP titration → fixed CPAP

-Home: AutoCPAP titration → fixed CPAP

-just given them a AutoCPAP!

-Home sleep study -> AutoCPAP

-not for CHF or if needing supplemental oxygen

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Introduction

Snoring

OSA

-Epidemiology and Pathogenesis

-Diagnosis and Consequences

-CPAP Treatment

-non CPAP Treatment

-Cost

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Non CPAP Therapy:

-Weight Loss

-even 10% reduction

-history of weight gain

-Stop Smoking

-smokers have an increased risk

-ETOH reduction

-arousal threshold

-apneas are longer

-Positional Therapy

-tennis ball

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Non CPAP Therapy:

-Oral Appliances

-mild to moderate OSA (FDA)

-especially good for positional OSA

-don't need to fail CPAP generally

-NEED FOLLOWUP!

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Non CPAP Therapy:

-Oral Appliances

-2 types

-jaw advancers

-over a period of time

-tongue suckers

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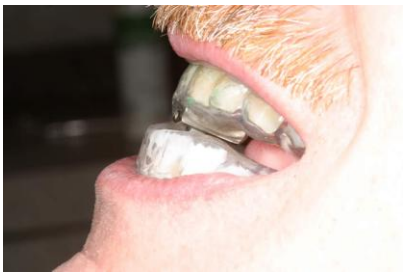
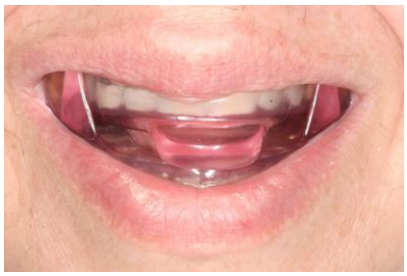
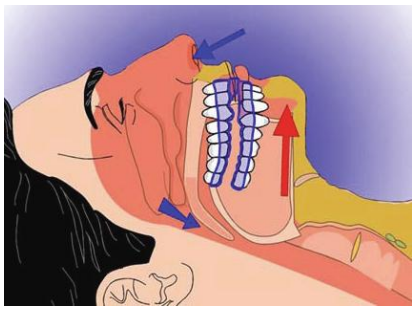
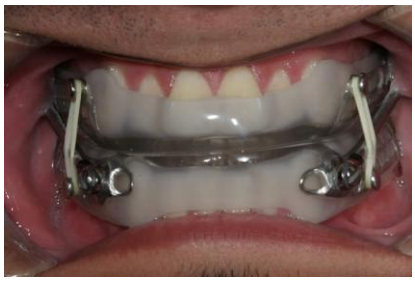

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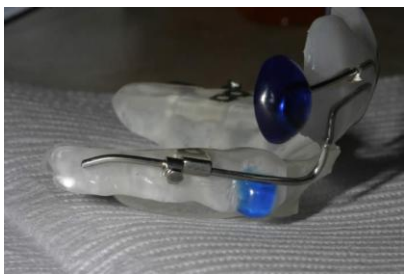
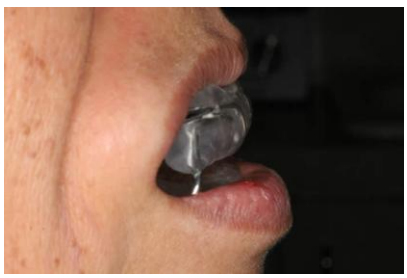

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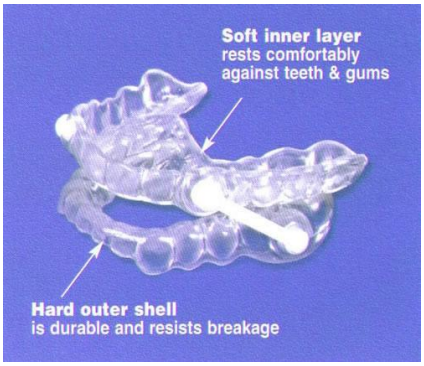
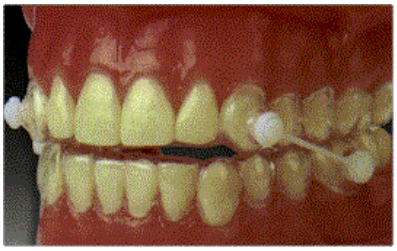

Soft inner layer
rests comfortably
against teeth & gums
Hard outer shell
is durable and resists breakage



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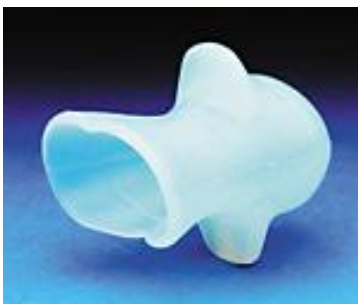

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Non CPAP Therapy:

-Oral Appliances

Consider oral appliance therapy **for adults with OSA who are intolerant of CPAP or prefer an alternative**, ideally **custom, titratable** with follow-up sleep testing.

-Evidence

-52% were able to get AHI < 10

-42% got AHI less than 5

-improved O_2 saturation, sleepiness, QOL,

-Compliance

-77% stay with it after the first year

-jaw discomfort and lack of efficacy

-periodontal disease is contraindication

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Non CPAP Therapy:

-Surgery

-Tracheostomy (gold standard)

-UPPP (**Uvulopalatopharyngoplasty**)

-disappointing

-RFVTR (Radiofrequency Volumetric Tissue Reduction) - -disappointing

-Oromaxillofacial Surgery

-good success (96%)

-high risk of surgery

-Palatal Implants – no good studies

-Bariatric Surgery (laparoscopic)?

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Non CPAP Therapy: Medications

-intranasal steroids[1]

-Medications orally (do not unobstruct)

Modafinil (Provigil; generics) — *Mechanism:* wake-promoting; binds dopamine transporter (DAT) and inhibits dopamine reuptake (overall mechanism "unknown").
Dose (OSA-EDS): **200 mg PO qAM**; doses up to 400 mg/day tolerated but no consistent added benefit beyond 200 mg/day.

Armodafinil (Nuvigil; generics) — Mechanism: wake-promoting; binds DAT and inhibits dopamine reuptake (overall mechanism "unknown"; described as indirect dopamine receptor agonist).
Dose (OSA-EDS): **150–250 mg PO qAM**; doses up to 250 mg/day tolerated but no consistent added benefit beyond 150 mg/day in OSA.

Solriamfetol (Sunosi) — *Mechanism:* dopamine + norepinephrine reuptake inhibitor (DNRI) (MOA "unclear," likely via DNRI activity).
Dose (OSA-EDS): start **37.5 mg PO once daily** upon awakening; may double q ≥3 days to **max 150 mg once daily**; **avoid dosing within 9 hours of bedtime.**

1) Am J Rhinol Allergy. **2016** May;30(3):215-21. doi: 10.2500/ajra.2016.30.4305. **Intranasal corticosteroid therapy in the treatment of obstructive sleep apnea: A meta-analysis of randomized controlled trials.**

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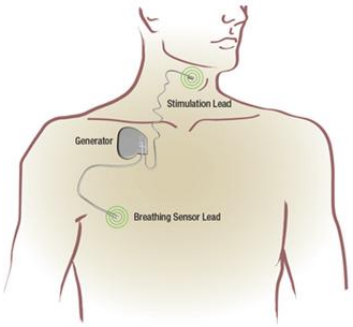
Take Comfort.

Help your body work the way it's supposed to.



Inspire therapy works *inside* your body, and with your natural breathing process, to treat sleep apnea. It continuously monitors your breathing patterns while you sleep. Based on your unique breathing patterns, the system delivers mild stimulation to key airway muscles, which keeps the airway open.

The Inspire system consists of three components: a small generator, a breathing sensor lead, and a stimulation lead —all controlled by the small handheld Inspire sleep remote. Simply turn the therapy on at night before bed, and off in the morning when you wake up.

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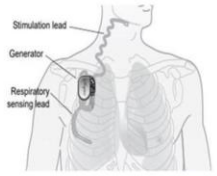
Inspire Upper Airway Stimulation – P130008/S090



This is a brief overview of information related to FDA's approval to market this product. See the links below to the Summary of Safety and Effectiveness Data (SSED) and product labeling for more complete information on this product, its indications for use, and the basis for FDA's approval.

When is it used?

The Inspire UAS system is used to treat people with moderate to severe obstructive sleep apnea (15≤ AHI ≤ 100) who are age 22 and older and who:

- Are not able to use or tolerate positive airway pressure (PAP) or bi-level positive airway pressure (BiPAP) treatments according to clinical criteria that define the inability to eliminate obstructive sleep apnea or an intolerance for PAP.
- Do not have complete blockage or concentric collapse of the back, muscular part of the roof of the mouth, called the soft palate.

BMI?

FDA ≤ 40 kg/m²

CMS < 35 kg/m²

Com: ≤32–35 kg/m²

73

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	

* Plus–minus values are means ±SD. Two participants did not complete follow-up at 12 months: one participant died unexpectedly 10 months after implantation owing to a cardiac event that was not thought to be related to the implant, and one requested explantation of the device because of personal choice. In the primary-outcome analysis, both participants were considered not to have had a response to therapy. Means, standard deviations, medians, and interquartile ranges are presented because some variables (e.g., the 12-month scores on the apnea–hypopnea index [AHI] and oxygen desaturation index [ODI]) show evidence of nonnormality.

† The AHI score indicates the number of apnea or hypopnea events per hour; a score of 15 or more events per hour indicates moderate-to-severe obstructive sleep apnea.

‡ The ODI score indicates the number of times per hour of sleep that the blood oxygen level drops by 4 percentage points or more from baseline.

§ Scores on the Functional Outcomes of Sleep Questionnaire (FOSQ) range from 5.0 to 20.0, with higher scores indicating better functioning. A score of more than 17.9 is considered to be the threshold for persons with normal sleep-related quality of life. A change of 2.0 or more points in the score is considered to indicate a clinically meaningful improvement of daily functioning.[28] Data at 12 months were missing for one participant in addition to the two who did not complete the 12-month follow-up.

¶ Scores on the Epworth Sleepiness Scale range from 0.0 to 24.0, with lower scores indicating less daytime sleepiness. Data at 12 months were missing for one participant in addition to the two who did not complete the 12-month follow-up.

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Table S1. Adverse Events

The following summary of adverse events (AEs) include all AE reported as of July 31, 2013 for an average of 628 days per subject of monitoring since implant for all participants.

Table S1. Summary of Adverse Events		
Adverse Events	**No. of events**	**Number of Participants with event (%)**
Serious adverse event	35	27 (21%)
Device-revision	2	2 (2%)
Death, unrelated¥	2	2 (2%)
Other unrelated*	31	23 (18%)
Procedure-related non-serious adverse event	169	72 (57%)
Post-op discomfort related to incisions	46	33 (26%)
Post-op discomfort not-related to incision	39	31 (25%)
Temporary tongue weakness	35	23 (18%)
Intubation effects	18	15 (12%)
Headache	8	8 (6%)
Other post-op symptoms	22	14 (11%)
Mild infection	1	1 (1%)
Device-related non-serious adverse event	190	85 (67%)
Discomfort due to electrical stimulation	80	50 (40%)
Tongue abrasion	33	26 (21%)
Dry mouth	13	13 (10%)
Mechanical pain associated with device presence	8	8 (6%)
Temporary internal device functionality compliant	14	12 (10%)
Temporary external device usability or functionality complaint	8	7 (6%)
Other acute symptoms	25	19 (15%)
Mild or moderate infection**	1	1 (1%)

* Other unrelated serious adverse events included cardiac conditions: coronary artery disease, arrhythmias, and chest pain (n = 8), accidents or injuries (n = 11), and other surgeries (n=12) **Skin cellulitis. ¥ One death from a cardiac event thought to be unrelated to the device, one death related to a homicide.

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ORIGINAL ARTICLE

Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity

This article has been corrected. VIEW THE CORRECTION

Authors: 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., +5 , for the SURMOUNT-OSA Investigators* Author Info & Affiliations

Published June 21, 2024 | N Engl J Med 2024;391:1193-1205 | DOI: 10.1056/NEJMoa2404881 | VOL. 391 NO. 13

SURMOUNT-OSA CME

https://www.nejm.org/doi/full/10.1056/NEJMoa2404881

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SURMOUNT-OSA 2

Population: Adults with moderate-to-severe OSA (apnea-hypopnea index [AHI] ≥ 15 events per hour) and obesity (body mass index [BMI] ≥ 30 kg/m²)

Intolerant of CPAP (N = 234)

Tirzepatide 2.5mg weekly inj -increased by 2.5mg q4wk until 10mg or 15mg X 52 weeks

Placebo

Tirzepatide group: Mean reduction in AHI of **25.3 events** per hour

Placebo group: Mean reduction in AHI of **5.3 events** per hour

Estimated treatment difference: **-20.0 events per hour** (95% CI: -25.8 to -14.2, P < 0.001)

Weight loss: Approximately **18-20% reduction in body weight** compared to minimal change in the placebo group.

Disease resolution: 43% of participants on the highest dose of tirzepatide met criteria for disease resolution (AHI < 5 events/hour or 5-14 events/hour with minimal sleepiness).

CPAP (N = 235)

Tirzepatide 2.5mg weekly inj -increased by 2.5mg q4wk until 10mg or 15mg X 52 weeks

Placebo

Tirzepatide group: Mean reduction in AHI of **29.3 events** per hour

Placebo group: Mean reduction in AHI of **5.5 events** per hour

Estimated treatment difference: **-23.8 events per hour**

Weight loss: Approximately **20% reduction in body weight** compared to minimal change in the placebo group.

Disease resolution: 51.5% of participants on the highest dose of tirzepatide met criteria for disease resolution (AHI < 5 events/hour or 5-14 events/hour with minimal sleepiness).

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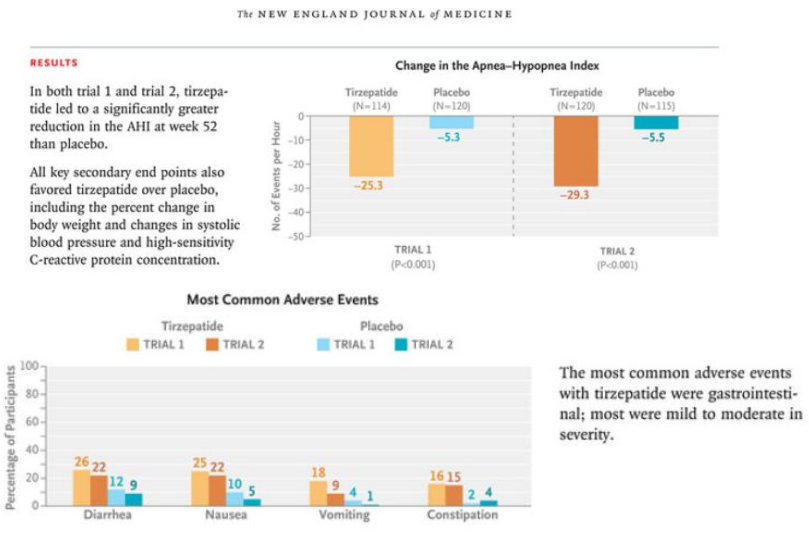

FDA approved **Zepbound (tirzepatide)** on **Dec 20, 2024** for **moderate-to-severe OSA in adults with obesity**
Works primarily through weight loss.

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Oropharyngeal Myofunctional Therapy (OMT)

▸ Sleep. 2015 May 1;38(5):669–675. doi: 10.5665/sleep.4652

Myofunctional Therapy to Treat Obstructive Sleep Apnea: A Systematic Review and Meta-analysis

Macario Camacho [1,✉], Victor Certal [2], Jose Abdullatif [3], Soroush Zaghi [4], Chad M Ruoff [1], Robson Capasso [5], Clete A Kushida [1]

▸ Author information ▸ Article notes ▸ Copyright and License information

PMCID: PMC4402674 PMID: 25348130

Conclusion:

Current literature demonstrates that myofunctional therapy decreases apnea-hypopnea index by approximately 50% in adults and 62% in children. Lowest oxygen saturations, snoring, and sleepiness outcomes improve in adults. Myofunctional therapy could serve as an adjunct to other obstructive sleep apnea treatments.

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Effect of sleep apnoea interventions on multiple health outcomes: an umbrella review of meta-analyses of randomised controlled trials

Camille Figard,[a,d] Raoua Ben Messaoud,[b,d] Sébastien Baillieul,[a,b] Marie Joyeux-Faure,[a,b] Marie Destors,[b] Renaud Tamisier,[a,b] Charles Khouri,[b,c,*,e] and Jean-Louis Pépin[a,b,*,e]

[a]EFCR Laboratory, Thorax and Vessels Division, Grenoble Alpes University Hospital, Grenoble, France
[b]HP2 Laboratory, Inserm U1300, University Grenoble Alpes, Grenoble, France
[c]Regional Pharmacovigilance Center & Clinical Pharmacology Unit, Grenoble Alpes University Hospital, University Grenoble Alpes, Grenoble, France

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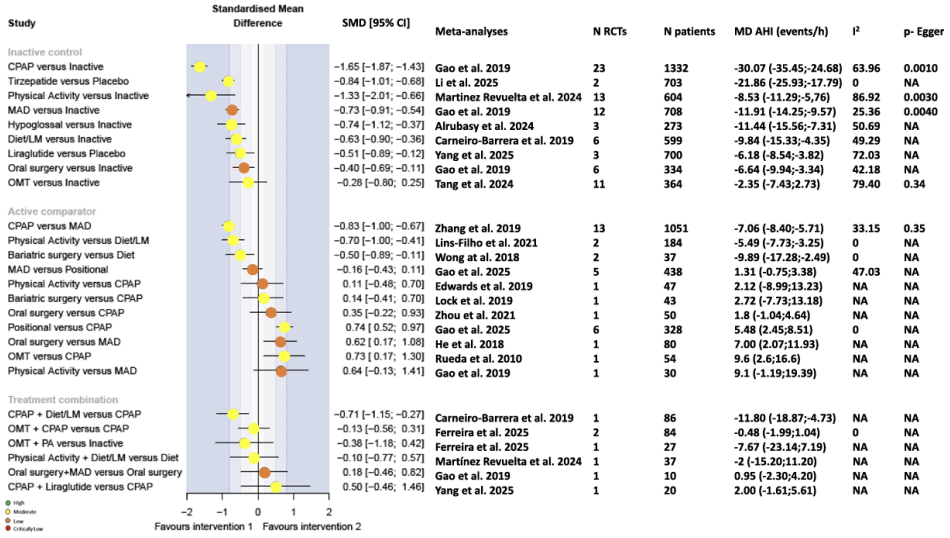
AHI



Study	SMD [95% CI]	Meta-analyses	N RCTs	N patients	MD AHI (events/h)	I^2	p- Egger
Inactive control							
CPAP versus Inactive	−1.65 [−1.87; −1.43]	Gao et al. 2019	23	1332	-30.07 (-35.45;-24.68)	63.96	0.0010
Tirzepatide versus Placebo	−0.84 [−1.01; −0.68]	Li et al. 2025	2	703	-21.86 (-25.93;-17.79)	0	NA
Physical Activity versus Inactive	−1.33 [−2.01; −0.66]	Martínez Revuelta et al. 2024	13	604	-8.53 (-11.29;-5,76)	86.92	0.0030
MAD versus Inactive	−0.73 [−0.91; −0.54]	Gao et al. 2019	12	708	-11.91 (-14.25;-9.57)	25.36	0.0040
Hypoglossal versus Inactive	−0.74 [−1.12; −0.37]	Alrubasy et al. 2024	3	273	-11.44 (-15.56;-7.31)	50.69	NA
Diet/LM versus Inactive	−0.63 [−0.90; −0.36]	Carneiro-Barrera et al. 2019	6	599	-9.84 (-15.33;-4.35)	49.29	NA
Liraglutide versus Placebo	−0.51 [−0.89; −0.12]	Yang et al. 2025	3	700	-6.18 (-8.54;-3.82)	72.03	NA
Oral surgery versus Inactive	−0.40 [−0.69; −0.11]	Gao et al. 2019	6	334	-6.64 (-9.94;-3.34)	42.18	NA
OMT versus Inactive	−0.28 [−0.80; 0.25]	Tang et al. 2024	11	364	-2.35 (-7.43;2.73)	79.40	0.34
Active comparator							
CPAP versus MAD	−0.83 [−1.00; −0.67]	Zhang et al. 2019	13	1051	-7.06 (-8.40;-5.71)	33.15	0.35
Physical Activity versus Diet/LM	−0.70 [−1.00; −0.41]	Lins-Filho et al. 2021	2	184	-5.49 (-7.73;-3.25)	0	NA
Bariatric surgery versus Diet	−0.50 [−0.89; −0.11]	Wong et al. 2018	2	37	-9.89 (-17.28;-2.49)	0	NA
MAD versus Positional	−0.16 [−0.43; 0.11]	Gao et al. 2025	5	438	1.31 (-0.75;3.38)	47.03	NA
Physical Activity versus CPAP	0.11 [−0.48; 0.70]	Edwards et al. 2019	1	47	2.12 (-8.99;13.23)	NA	NA
Bariatric surgery versus CPAP	0.14 [−0.41; 0.70]	Lock et al. 2019	1	43	2.72 (-7.73;13.18)	NA	NA
Oral surgery versus CPAP	0.35 [−0.22; 0.93]	Zhou et al. 2021	1	50	1.8 (-1.04;4.64)	NA	NA
Positional versus CPAP	0.74 [0.52; 0.97]	Gao et al. 2025	6	328	5.48 (2.45;8.51)	0	NA
Oral surgery versus MAD	0.62 [0.17; 1.08]	He et al. 2018	1	80	7.00 (2.07;11.93)	NA	NA
OMT versus CPAP	0.73 [0.17; 1.30]	Rueda et al. 2010	1	54	9.6 (2.6;16.6)	NA	NA
Physical Activity versus MAD	0.64 [−0.13; 1.41]	Gao et al. 2019	1	30	9.1 (-1.19;19.39)	NA	NA
Treatment combination							
CPAP + Diet/LM versus CPAP	−0.71 [−1.15; −0.27]	Carneiro-Barrera et al. 2019	1	86	-11.80 (-18.87;-4.73)	NA	NA
OMT + CPAP versus CPAP	−0.13 [−0.56; 0.31]	Ferreira et al. 2025	2	84	-0.48 (-1.99;1.04)	0	NA
OMT + PA versus Inactive	−0.38 [−1.18; 0.42]	Ferreira et al. 2025	1	27	-7.67 (-23.14;7.19)	NA	NA
Physical Activity + Diet/LM versus Diet	−0.10 [−0.77; 0.57]	Martínez Revuelta et al. 2024	1	37	-2 (-15.20;11.20)	NA	NA
Oral surgery+MAD versus Oral surgery	0.18 [−0.46; 0.82]	Gao et al. 2019	1	10	0.95 (-2.30;4.20)	NA	NA
CPAP + Liraglutide versus CPAP	0.50 [−0.46; 1.46]	Yang et al. 2025	1	20	2.00 (-1.61;5.61)	NA	NA

Fig. 2: Forest plots for the apnoea–hypopnoea index endpoint. CI, confidence interval; CPAP, continuous positive airway pressure; e, exponential; I^2, evaluation of heterogeneity; LM, lifestyle measures; MAD, mandibular advancement device; MD, mean difference; NA, not applicable; SMD, standardised mean difference.

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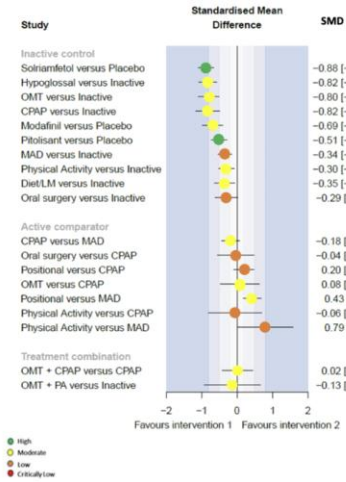
Epworth Sleepiness Score



Study	SMD [95% CI]	Meta-analyses	N RCTs	N patients	MD ESS	I^2	p- Egger
Inactive control							
Solriamfetol versus Placebo	−0.88 [−1.09; −0.66]	Pépin et al. 2024	3	352	-4.47 (-5.53;-3.40)	0	NA
Hypoglossal versus Inactive	−0.82 [−1.08; −0.57]	Alrubasy et al. 2024	3	270	-3.66 (-4.76;-2.55)	0	NA
OMT versus Inactive	−0.80 [−1.09; −0.50]	Tang et al. 2024	9	286	-3.44 (-4.5;-2.38)	40.86	NA
CPAP versus Inactive	−0.82 [−1.16; −0.48]	Li et al. 2022	41	8149	-2.50 (-1.82;0.2)	93.05	0.14
Modafinil versus Placebo	−0.69 [−0.98; −0.39]	Pépin et al. 2024	12	1910	-2.66 (-3.13;-2.19)	83.45	0.13
Pitolisant versus Placebo	−0.51 [−0.73; −0.29]	Pépin et al. 2024	2	436	-2.75 (-3.92;-1.57)	0	NA
MAD versus Inactive	−0.34 [−0.53; −0.14]	Gao et al. 2019	8	538	-2.06 (-2.92;-1.19)	17.52	NA
Physical Activity versus Inactive	−0.30 [−0.52; −0.09]	Tang et al. 2024	6	335	-1.23(-2.29;-0.18)	0	NA
Diet/LM versus Inactive	−0.35 [−0.64; −0.06]	Carneiro-Barrera et al. 2019	3	281	-1.60 (-2.87;-0.32)	31,18	NA
Oral surgery versus Inactive	−0.29 [−0.61; 0.03]	Gao et al. 2019	6	337	-1.18 (-1.93;-0.44)	51.18	NA
Active comparator							
CPAP versus MAD	−0.18 [−0.43; 0.07]	Gao et al. 2019	10	905	-0.81 (-1.82;-0.29)	63.36	0.44
Oral surgery versus CPAP	−0.04 [−0.56; 0.48]	Gao et al. 2019	1	60	-0.20 (-2.73; 2.33)	NA	NA
Positional versus CPAP	0.20 [−0.09; 0.49]	Gao et al. 2025	3	185	0.92 (-0.43; 2.28)	0	NA
OMT versus CPAP	0.08 [−0.46; 0.63]	Rueda et al. 2020	1	54	0.3 (-1.65;2.25)	NA	NA
Positional versus MAD	0.43 [0.17; 0.69]	Mohamed et al. 2024	3	228	2.06 (0.84;3.28)	0	NA
Physical Activity versus CPAP	−0.06 [−0.80; 0.69]	Gao et al. 2019	1	30	-1.2 (-16.44;14.04)	NA	NA
Physical Activity versus MAD	0.79 [0.01; 1.57]	Gao et al. 2019	1	30	4.57 (0.38;8.76)	NA	NA
Treatment combination							
OMT + CPAP versus CPAP	0.02 [−0.41; 0.45]	Ferreira et al. 2025	2	84	0.1 (-1.85;2.05)	0	NA
OMT + PA versus Inactive	−0.13 [−0.93; 0.66]	Ferreira et al. 2025	1	27	-0.57 (-3.83;2.7)	NA	NA

Fig. 3: Forest plots for the Epworth Sleepiness Scale score endpoint. CI, confidence interval; CPAP, continuous positive airway pressure; e, exponential; I^2, evaluation of heterogeneity; MAD, mandibular advancement device; MD, mean difference; NA, not applicable; SMD, standardised mean difference.

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Quality of Life

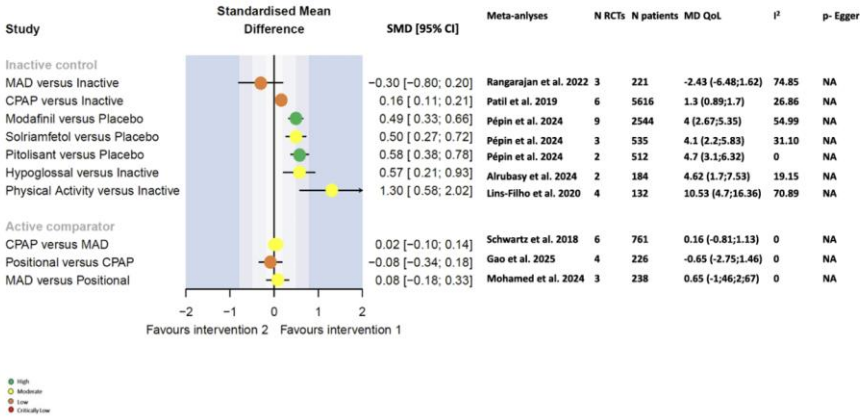

Fig. 4: Forest plots for quality-of-life measure endpoints (including the Functional Outcomes of Sleep Questionnaire, Sleep Apnoea Quality of Life Index, Short Form-36, Clinical Global Impression scale, and Patient Global Impression scale). CI, confidence interval; CPAP, continuous positive airway pressure; e, exponential; I^2, evaluation of heterogeneity; MAD, mandibular advancement device; MD, mean difference; NA, not applicable; SMD, standardised mean difference.

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Summary:

-OSA is a danger lurking in each primary care office

-diagnosis rests on **PSG or HSAT** (in appropriate patients); treatment initiation via **PAP titration** (lab) or **auto-PAP** (home) depending on patient factors

-CPAP is the first line choice

-behavioral change, the use of oral appliances, surgery in carefully selected (and well informed) patients, and perhaps judicious use of medications, may benefit some patients.

-oral appliances have emerged as an effective and safe second-line treatment for OSA

Education is key!

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Who Do I Suspect OSA in:

-Overweight male patients

-patients on more than 2 blood pressure medications

-Patients with history of

-CHF –SDB (49%) –CSA (37%) –OSA (12%)

-HTN (38%)

-resistant HTN (3+ medications) (83%)

-stroke (72%)

-Atrial Fibrillation (49%)

-Patients seeing a Cardiologist (32%)

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Who Do I Suspect OSA in:

-snoring at night

-witnessed apneas

-morning headaches

-falling asleep while watching TV or reading a book

-decreased energy

-can’t concentrate

-poor memory

-fibromyalgia

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Introduction

Snoring

OSA

-Epidemiology and Pathogenesis

-Diagnosis and Consequences

-CPAP Treatment

-non CPAP Treatment

-Cost

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Sleep. 1999 Sep 15;22(6):749-55.

The Medical Cost of Undiagnosed Sleep Apnea.

Kapur V, Blough DK, Sandblom RE, Hert R, de Maine JB, Sullivan SD, Psaty BM.
Department of Medicine, University of Washington, Seattle 98195, USA.

-consecutive 238 cases of OSA
-looked at cost and utilization with the past 12 months
-$2,720 versus $1,348 matched controls in age and gender ($p < 0.01$)
-~ $3.4 billion
-Cost increased with AHI ($p < 0.05$)

Crash risk soars among truck drivers who fail to adhere to sleep apnea treatment

Transportation safety is threatened when obstructive sleep apnea remains untreated

Date: March 21, 2016

Source: American Academy of Sleep Medicine

Summary: The largest study of obstructive sleep apnea and crash risk among CMV drivers involved 1,613 truck drivers with sleep apnea and an equal number of controls. The rate of preventable crashes was 5 times higher among truck drivers with sleep apnea who failed to adhere to PAP therapy, compared with matched controls. In contrast, the crash rate of drivers with sleep apnea who were fully or partially adherent with treatment was statistically similar to controls.

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Sleep. 2006 Oct 1;29(10):1307-11.

Healthcare Utilization in Women with Obstructive Sleep Apnea Syndrome 2 Years After Diagnosis and Treatment.

Banno K, Manfreda J, Walld R, Delaive K, Kryger MH.

Sleep Disorders Center, St. Boniface General Hospital, Section of Respiratory Diseases, Winnipeg, Manitoba, Canada.

-414 Women with OSA
-1404 Women without OSA (controls)

	Cost		Clinic Visits	
	Prior 2 years	Post 2 years	Prior 2 years	Post 2 years
OSA	+$123.43 +/-$25.01	-$37.96 +/-$21.35	+2.32 +/-0.43	-1.48 +/-0.42

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Generally, What Is the Circumstance That Most Predisposes for Obstructive Sleep Apnea?

A. Non-REM sleep, lateral position
B. REM sleep, lateral position
C. REM sleep, supine
D. Non-REM sleep, supine
E. Non-REM sleep, prone

CONTINUING EDUCATION COMPANY

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Which of the Following Is NOT a Risk Factor for OSA?

A. Hypothyroidism
B. Race
C. Age
D. Gender
E. Weight

What Is the Most Ideal Patient for a MAD (Mandibular Advancement Device)?

A. A patient with mild OSA, worse in the supine position
B. A patient with severe OSA, worse in REM sleep
C. A patient with moderate OSA, non positional
D. A patient with severe OSA, non positional
E. A patient with moderate OSA, worse in REM sleep

Which of the Following Does NOT Require a Full PSG to Diagnosis OSA?

A. 50-year-old overweight male that snores and has excessive daytime sleepiness.
B. 65-year-old male with COPD and requires 3L/min oxygen with excessive daytime sleepiness
C. 40-year-old female with excessive daytimes sleepiness but a HST negative for OSA
D. 75-year-old male with CHF (EF = 35%) and episodes of witnessed apneas at night.

Which of the Following Interventions Reduces the AHI the Most on Average?

A. CPAP
B. MAD
C. Tirzepatide
D. Hypoglossal Nerve Stimulator