State of Art Review in Sleep Medicine

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Disclosures

I have no disclosures, conflicts of interest related to this subject or talk

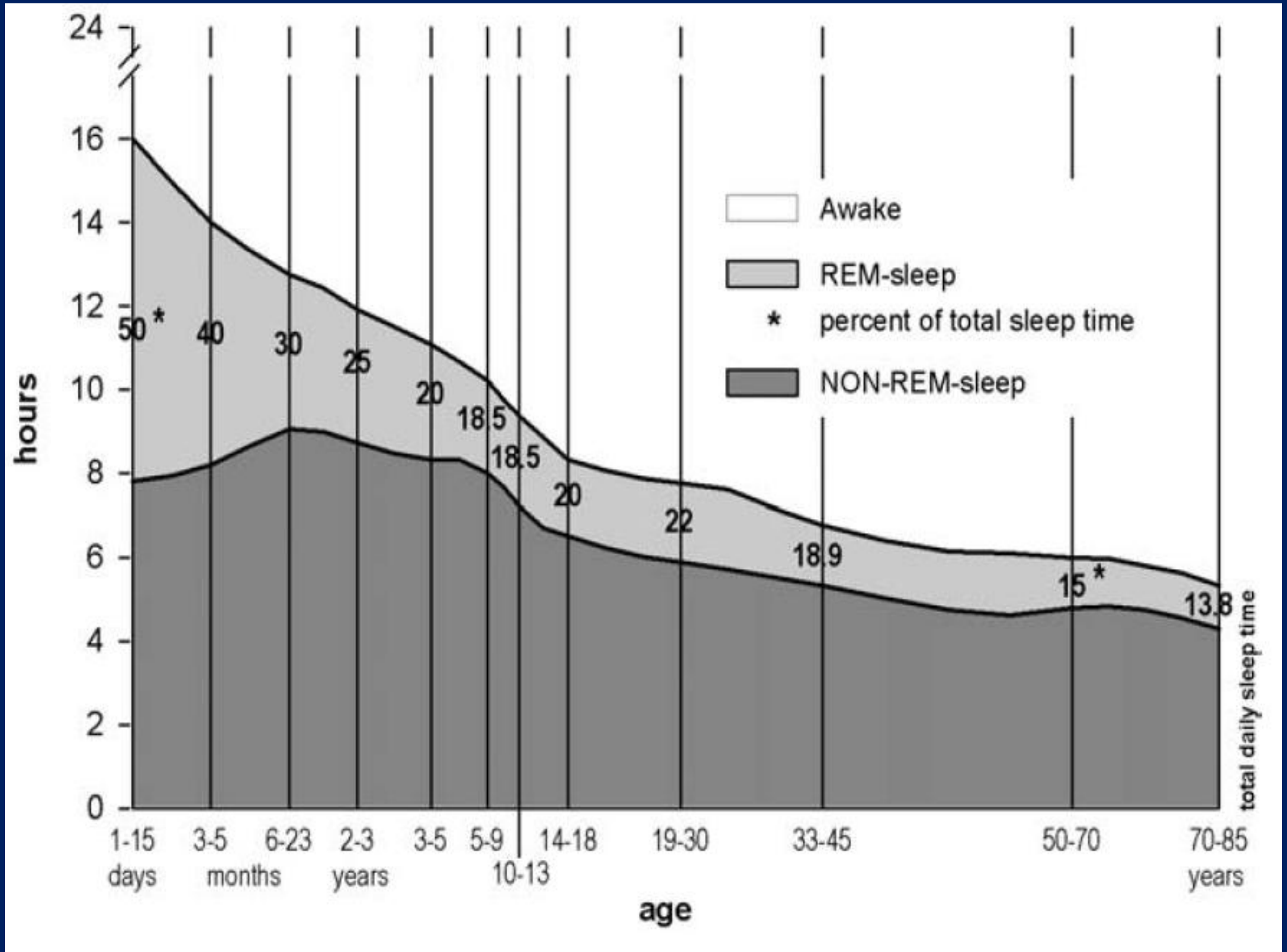
Learning Objectives

- Describe the normal & physiologic changes that occur during sleep
- Define the risk, diagnosis and consequences of sleep related diseases
- Define the risks, diagnosis and consequences of sleep apnea (OSA)
  - Link the impact of co-morbid sleep disordered breathing
- Review potential treatment options for sleep related disorders

Sleep deprivation effects

Physiologic Changes in Sleep

- **Body clock shifts earlier with age.**



Sources: Hobson. Sleep and Dreaming. In: Fundamental Neuroscience. 1999; Roffwarg et al. Science, 1996; 152:604

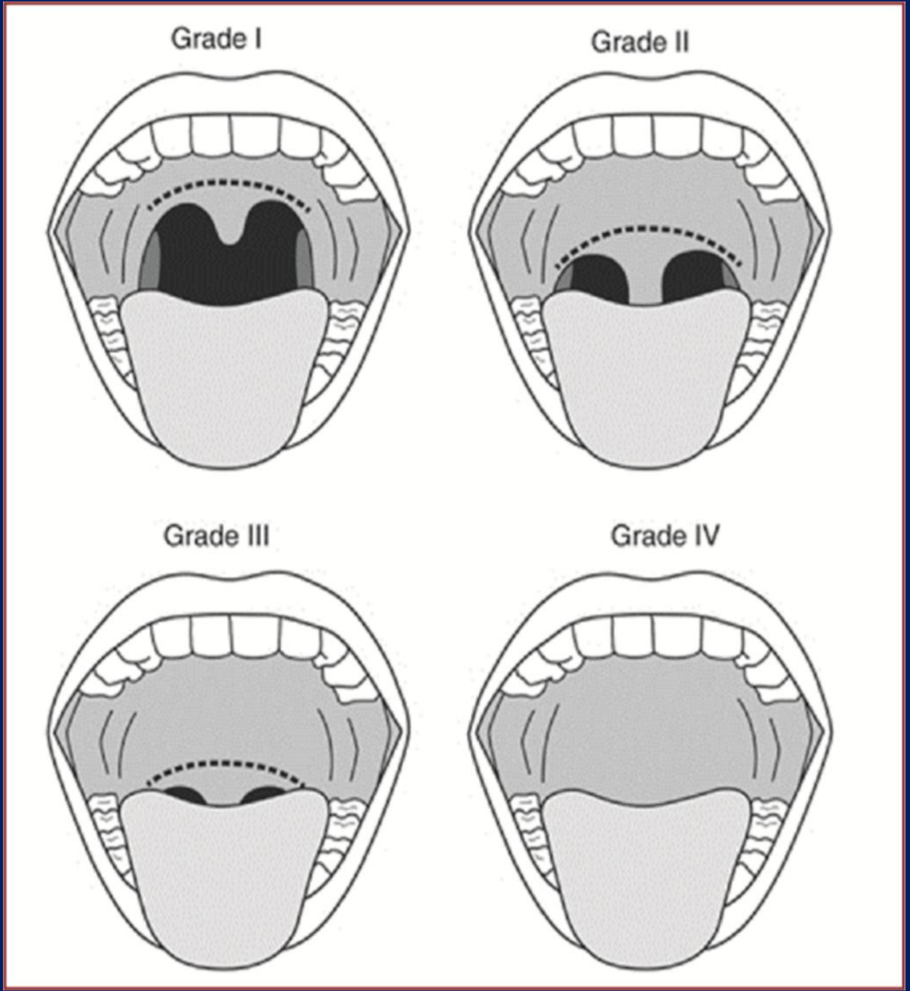
Obstructive Sleep Apnea Risk Factors

- Age (≥ with age = 50% at 65 years old)
- Gender (♂ 2 - 3x ≥ ♀)
- Post menopausal state (3x risk)
- Family History of sleep apnea
- Overweight & Obesity (neck size, >BMI)
- Upper airway anatomic changes
  - (micrognathia, retrognathia, TMJ, macroglossia)
- Medical Conditions
  - Atrial Fibrillation
  - Heart Failure (Diastolic & Systolic)
  - Down's syndrome, Thyroid, Polycystic Ovarian)

Strohl KP, et al; An official American Thoracic Society Clinical Practice Guideline: sleep apnea, sleepiness, and driving risk in noncommercial drivers. Am J Respir Crit Care Med. 2013;187:1259-66. [PMID: 23725615]

Risk Factors for Obstructive Sleep Apnea

- Airway anatomic changes:
  - Micrognathia,
  - Retrognathia,
  - TMJ,
  - Macroglossia,
  - Neck circumference;
    - ♀ > 17 inches
    - ♂ > 16 inches



Modified Mallampati Classification

The mouth is evaluated with the patient in a sitting position with higher risk for OSA. Grade I = soft palate, uvula, tonsillar fauces, and pillars visible; grade II = soft palate, uvular, and tonsillar fauces visible; grade III = only soft palate and base of uvula visible; grade IV = only hard palate visible.

Obstructive Sleep Apnea: Physical Examination

Structural Abnormalities

Guilleminault C et al. Sleep Apnea Syndromes. New York: Alan R. Liss, 1978.

Sleep Apnea Consequences

Daytime Sleepiness

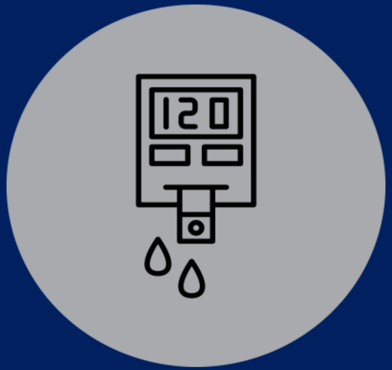
Snoring

Fatigue

Daytime Alertness

Cognitive Decline

Obesity



Diabetes

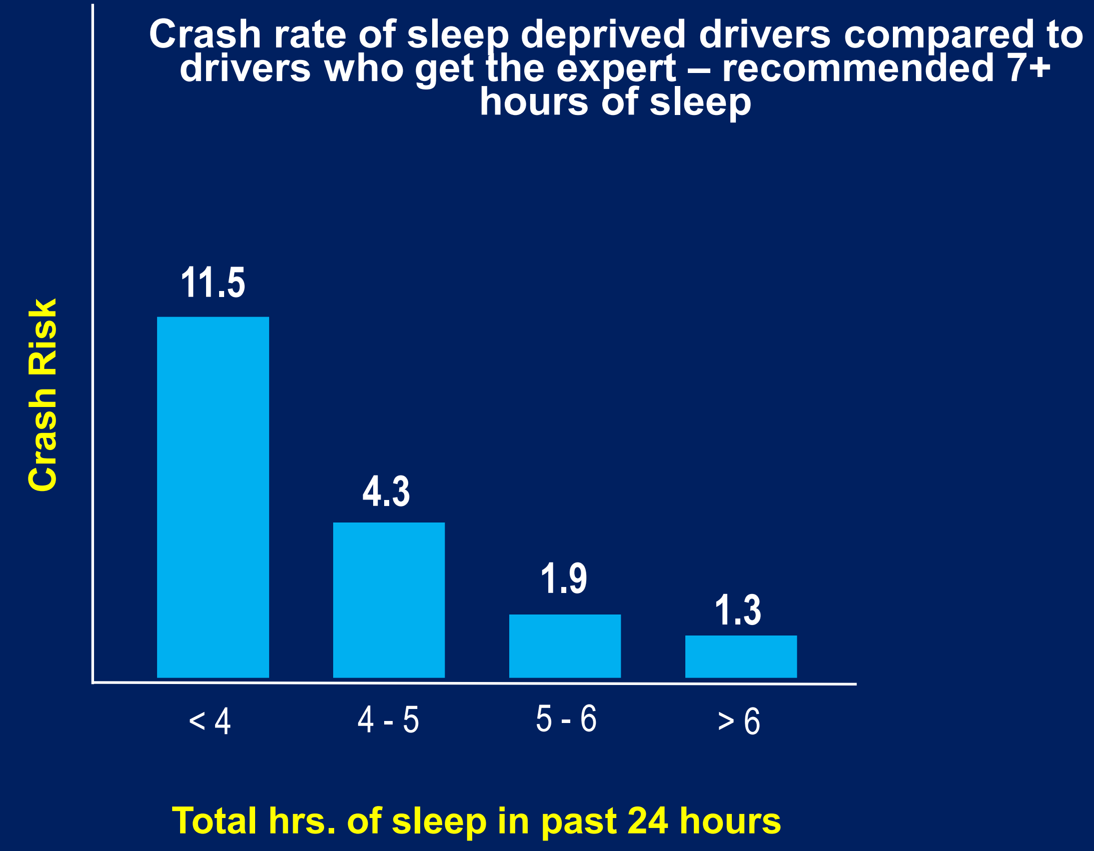
Hypertension Heart Disease

Gleeson M, McNicholas WT et al. Eur Respir Rev. 2022;31 (164):210256

There is a strong association between sleep apnea, as measured by the apnea-hypopnea index, and the risk of traffic accidents

Fatal Crashes Involve a Sleepy Driver

1in5

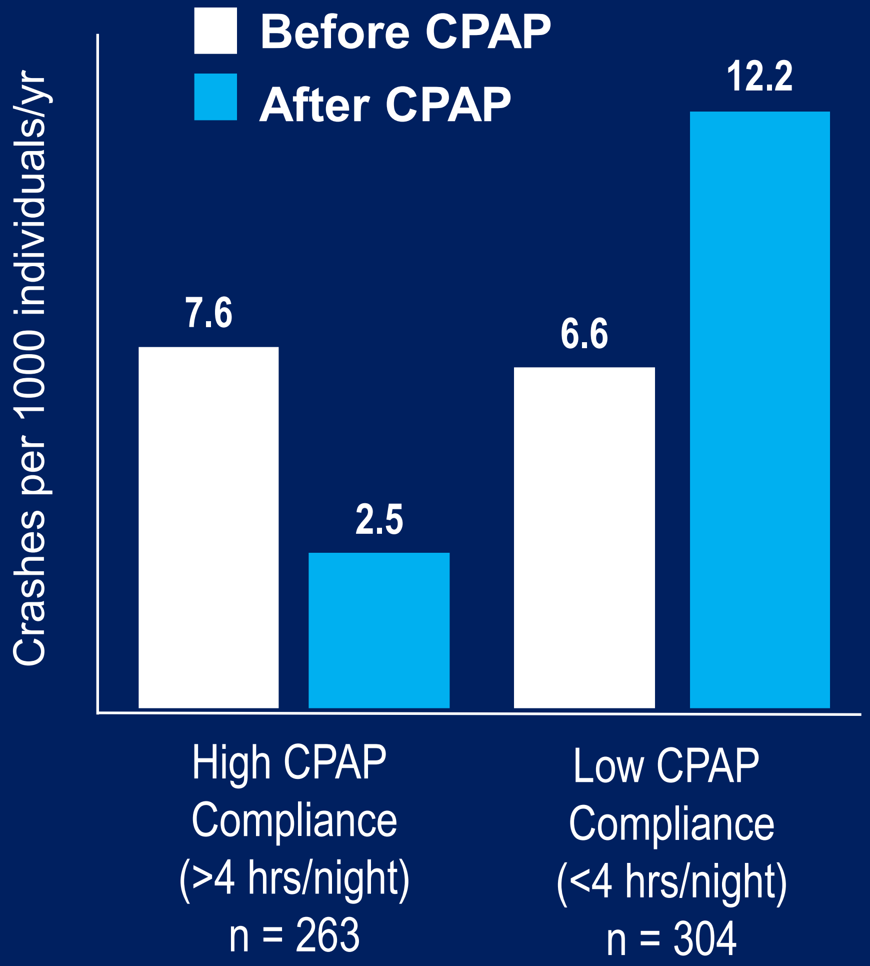


AAA Foundation for Traffic Safety, 2016

Strohl K, Brown D, Collop N., et al. American Thoracic Society Clinical Practice Guideline: Sleep Apnea, Sleepiness, and Driving Risk. An Update. Am J Respir Crit Care Med 2013; 187 (11): 1259–1266

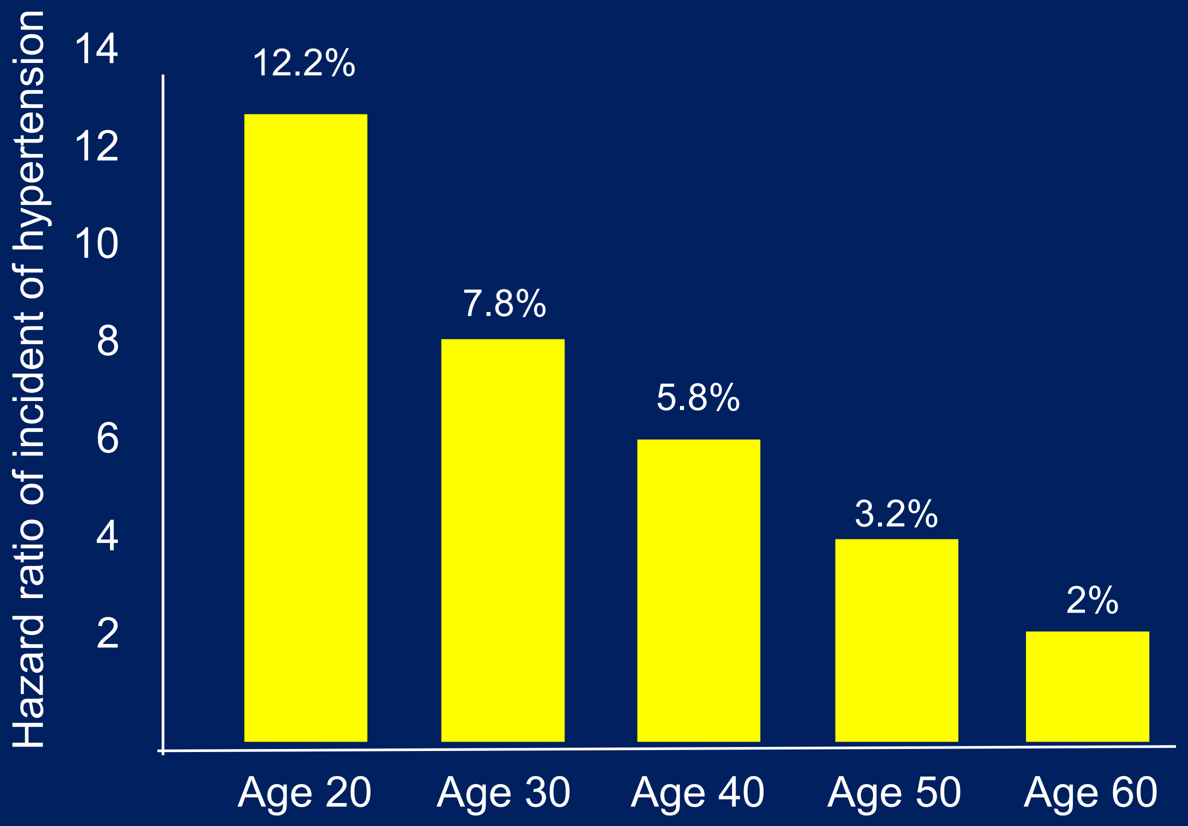
MVA rate in patients referred for OSA was compared to the rate in the general population (Swedish Traffic Accident Registry (STRADA), The risk factors for MVAs, using demographic and polygraphy data, and MVA rate before and after CPAP

- **Setting:**
  - **Clinical sleep laboratory and population based control (n = 635,786).**
- **Patients: There were 1,478 patients, male sex 70.4%, mean age 53.6 (12.8) yr.**
- **Interventions: CPAP**



Mahssa Karimi. Sleep Apnea Related Risk of Motor Vehicle Accidents is Reduced by Continuous Positive Airway Pressure: Swedish Traffic Accident Registry Data, *Sleep*, Volume 38, Issue 3, 1 March 2015, Pages 341–349.

The relationship with hypertension, age and sleep apnea

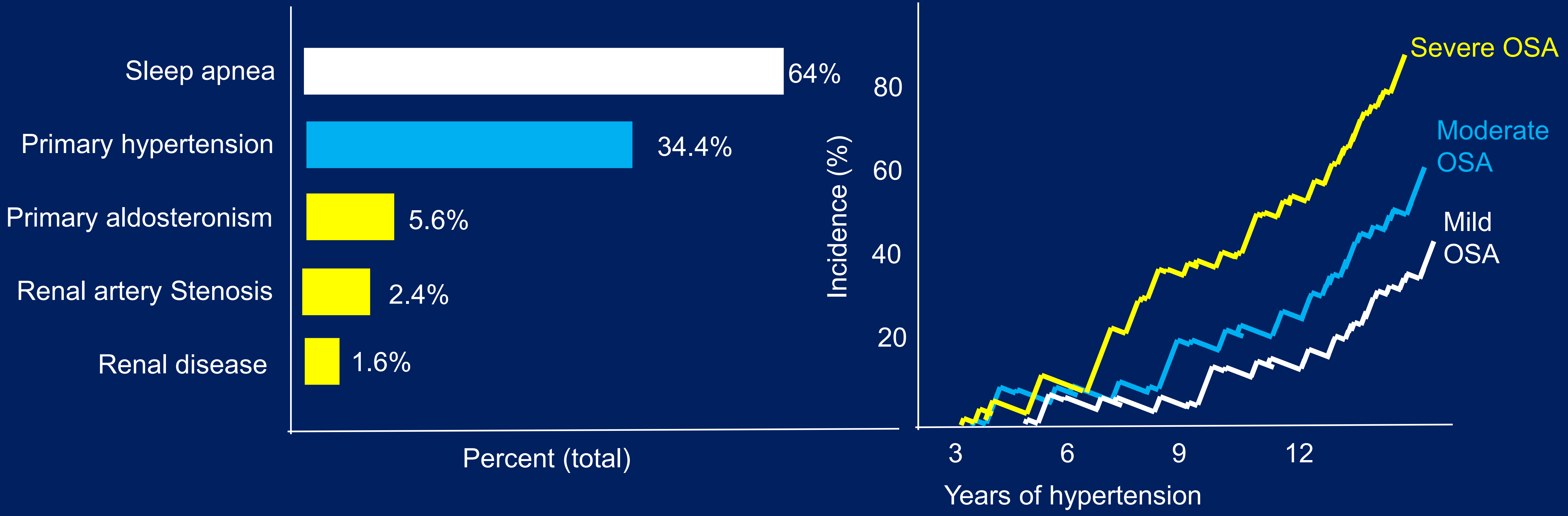


The estimated hazard ratio of incident hypertension across ages. The figure depicts the estimated hazard ratio of incident hypertension associated with mild-to-moderate OSA across ages with identical demographic (e.g. sex, race, and BMI) and clinical (e.g. prevalence of smoking, diabetes and treatment for OSA) characteristics. *$p < 0.05$.

- **Mortality Follow up**
- **Death certificate for deceased individuals from the US CDC**
- **N = 1741 patients**
  - **664 deaths**
- **Duration of follow was 20.1 years**

Vgontzas, Alexandros N., et al. "Mild-to-moderate sleep apnea is associated with incident hypertension: age effect." *Sleep* 42.4 (2019)

Obstructive Sleep Apnea and Hypertension

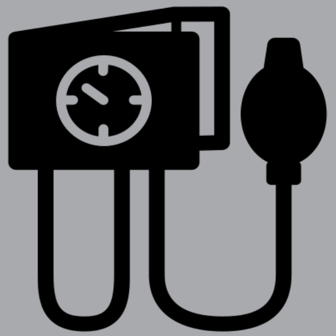


Pedrose RP et al. Hypertension 2011 58(5): 811 – 817
Marin JM et al. JAMA 2012; 307: 2169 - 2176

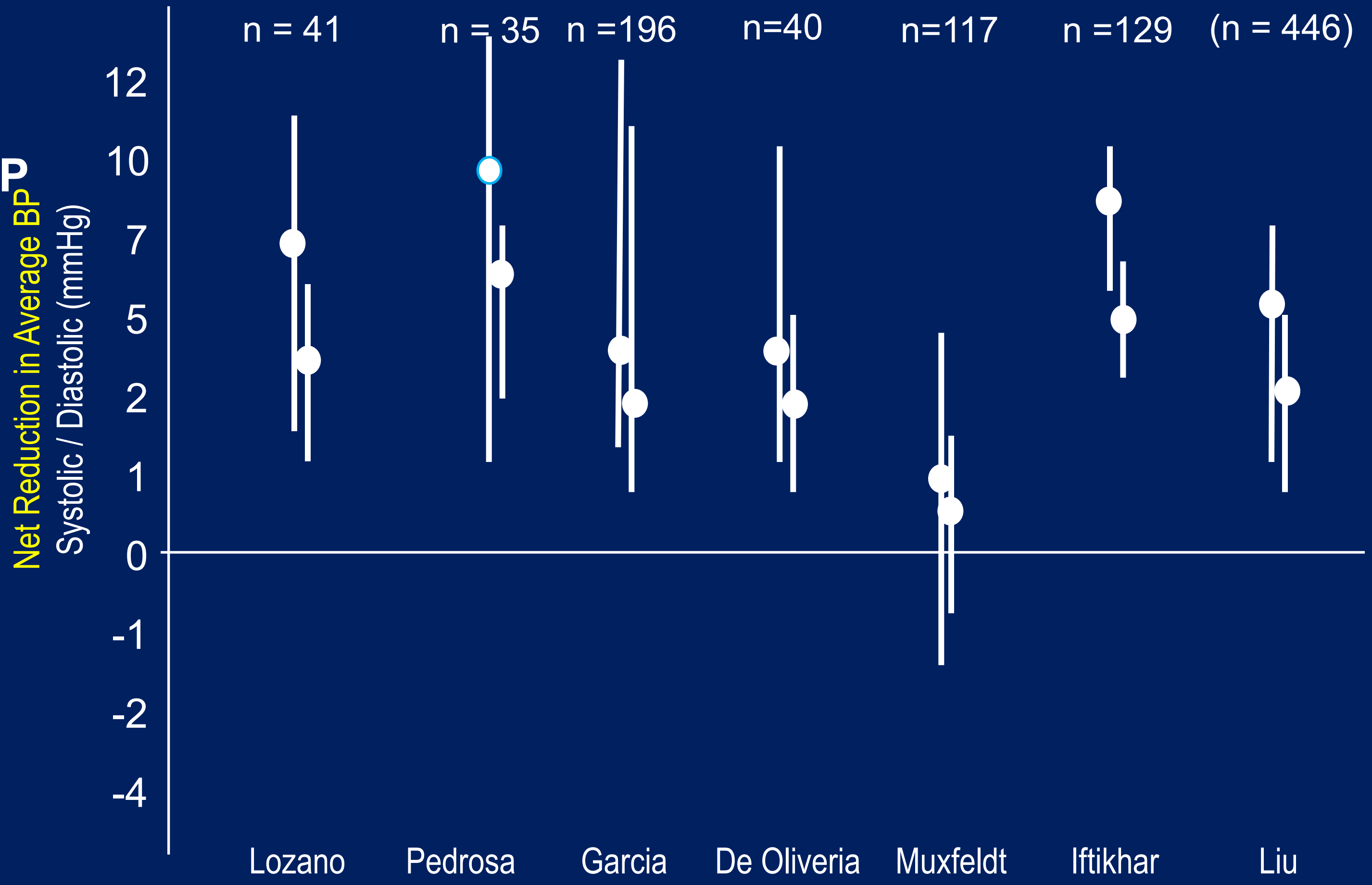
Effect of CPAP Therapy on BP in Patients With <u>Resistant</u> Hypertension

- **Summary of different studies with 2 additional meta-analyses of RCTs**
- **Positive figures mean improvement in BP level with CPAP (net changes)**

Average change in

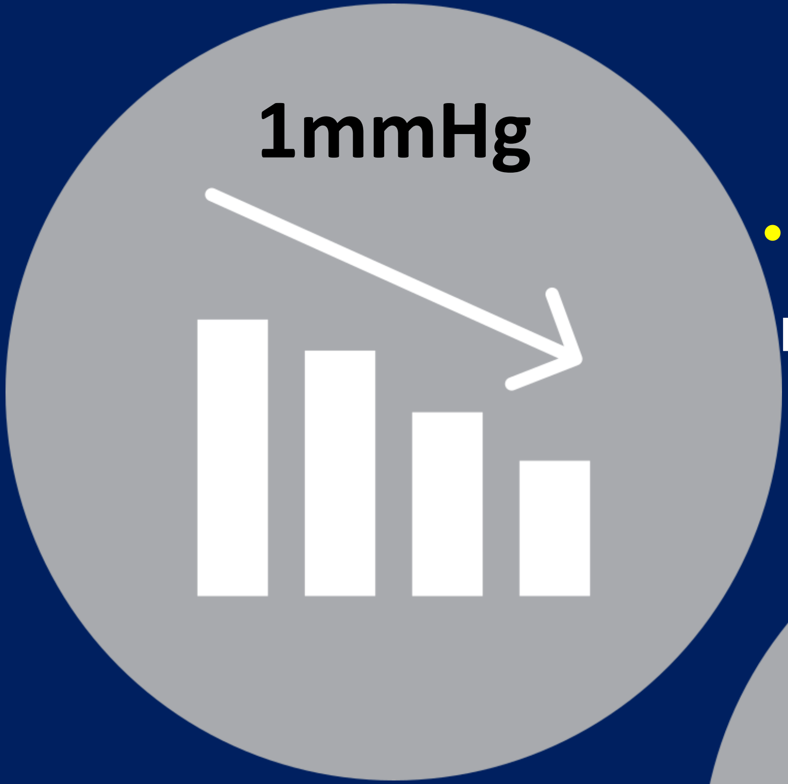


blood pressure = 7mmHg

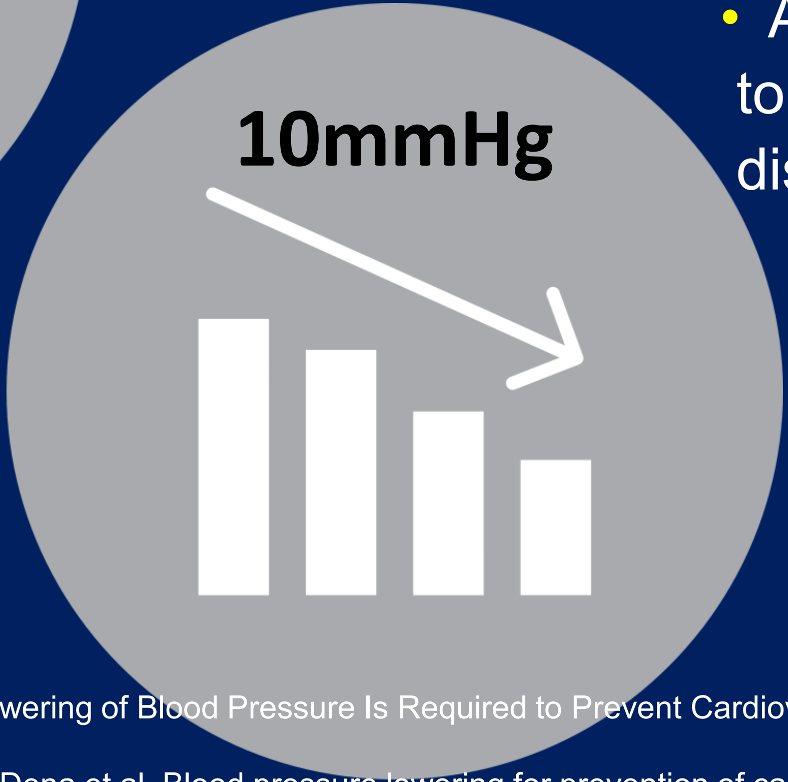


The figure shows 5 randomized controlled trials and 2 meta-analyses. The differences between the 2 meta-analyses depend on the most updated references included in the 2015 meta-analysis. Positive figures mean improvement in BP level with CPAP (net changes) *Number of studies included (number of patients included). Daytime BP values.

Shahrokh Javaheri et al. *J Am Coll Cardiol* 2017; 69:841-858.



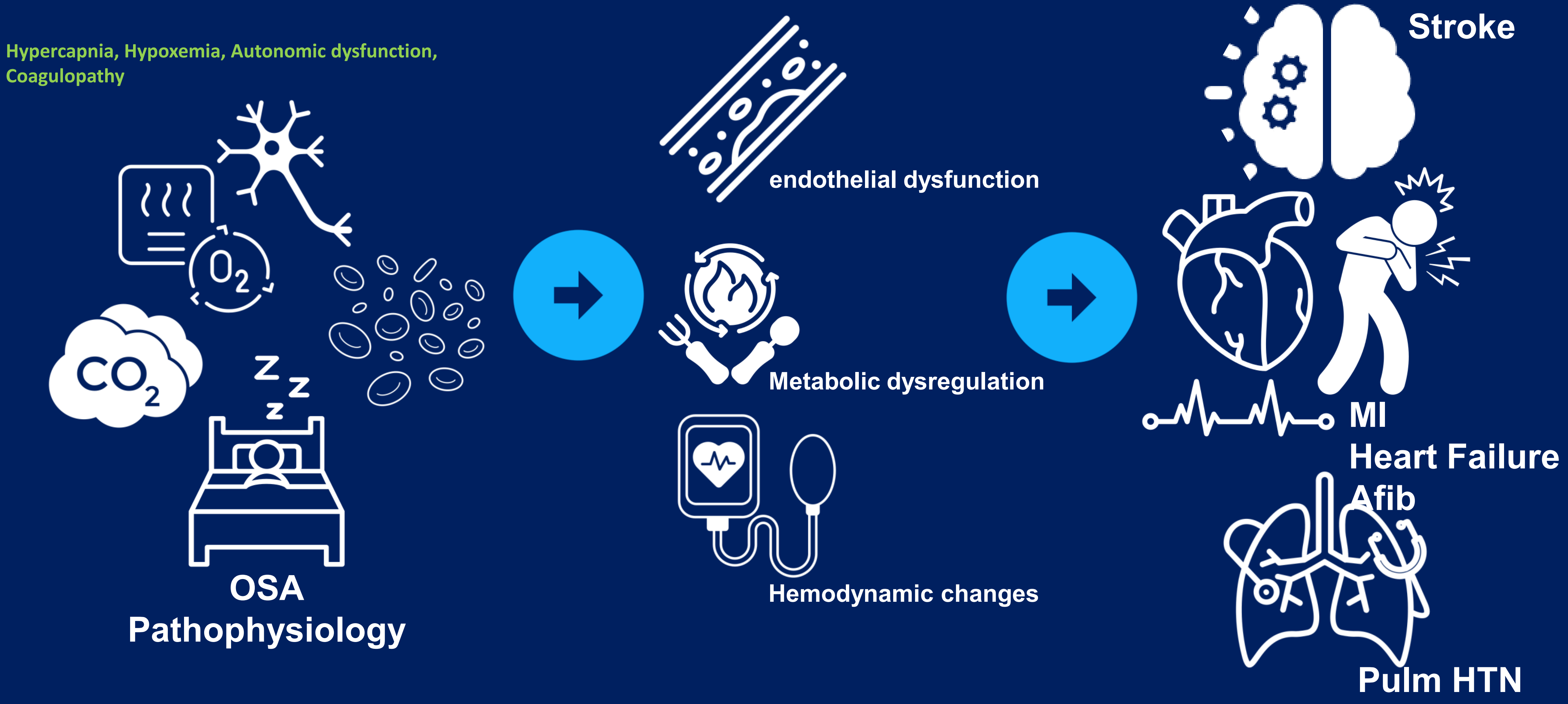
- With every 1 mmHg decrease in SBP, the risk of stroke is reduced by about 5%



- A 10mmHg reduction has been linked to a 10% reduction in coronary heart disease and a 27% reduction in stroke

Canoy D, Nazarzadeh M. How Much Lowering of Blood Pressure Is Required to Prevent Cardiovascular Disease in Patients With and Without Previous Cardiovascular Disease? Curr Cardiol Rep. 2022 Jul;24(7):851-860
Ettehad, Dena et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis The Lancet, Volume 387, Issue 10022, 957 - 967

Cardiovascular Implication of Sleep Apnea



Relationship to sleep disorder breathing and strokes

- Estimated 60% of all stroke patient have sleep disordered breathing (AHI>10)
- Similar frequency and severity of sleep apnea have been found among various stroke types and locations
- Prevalence of sleep disordered breathing appears to be similar in TIA and ischemic stroke syndromes

Parra O, Arboix A,. Time course of sleep-related breathing disorders in first-ever stroke or transient ischemic attack. Am J Respir Crit Care Med. 2000 Feb;161(2 Pt 1):375-80. doi: 10.1164/ajrccm.161.2.9903139. PMID: 10673174.

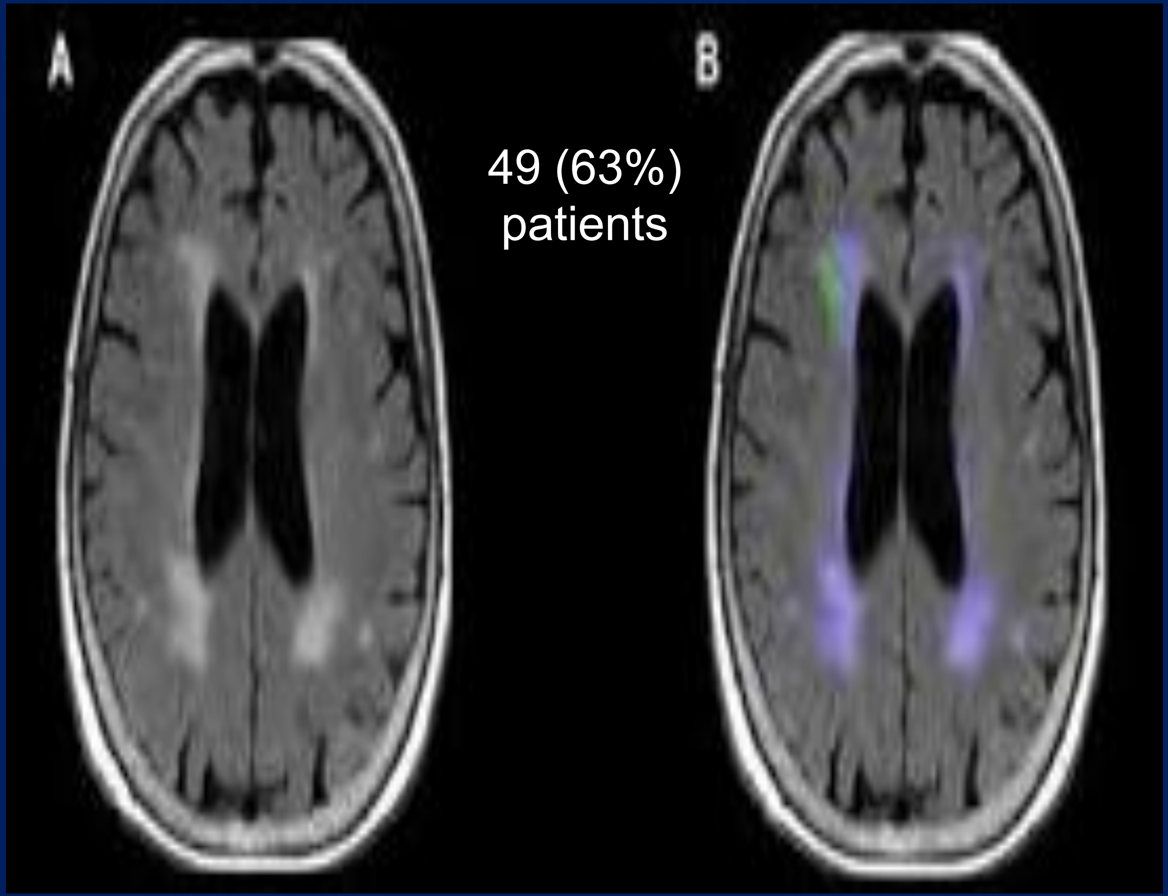
Asymptomatic brain scan in patients with sleep apnea

Prestroke cerebrovascular disease was present in 49 (63%) patients and was associated with worse SDB (mean AHI 35 vs 23, $p < 0.01$)

Stroke

PSG

n = 78
(mean age 73 years)
♂ 40; ♀ n = 38



Brain MRI shows silent brain infarct in 25% of patients with moderate to severe OSA

Presence and severity of white-matter disease on CT is associated with higher AHI

Harbison J, Gibson GJ, Birchall D, Zammit-Maempel I, Ford GA. White matter disease and sleep-disordered breathing after acute stroke. Neurology. 2003 Oct 14;61(7):959-63. PMID: 14557568.

Obstructive Sleep Apnea as a Risk Factor for Stroke and Death

n =1022

Study mean AHI = 35

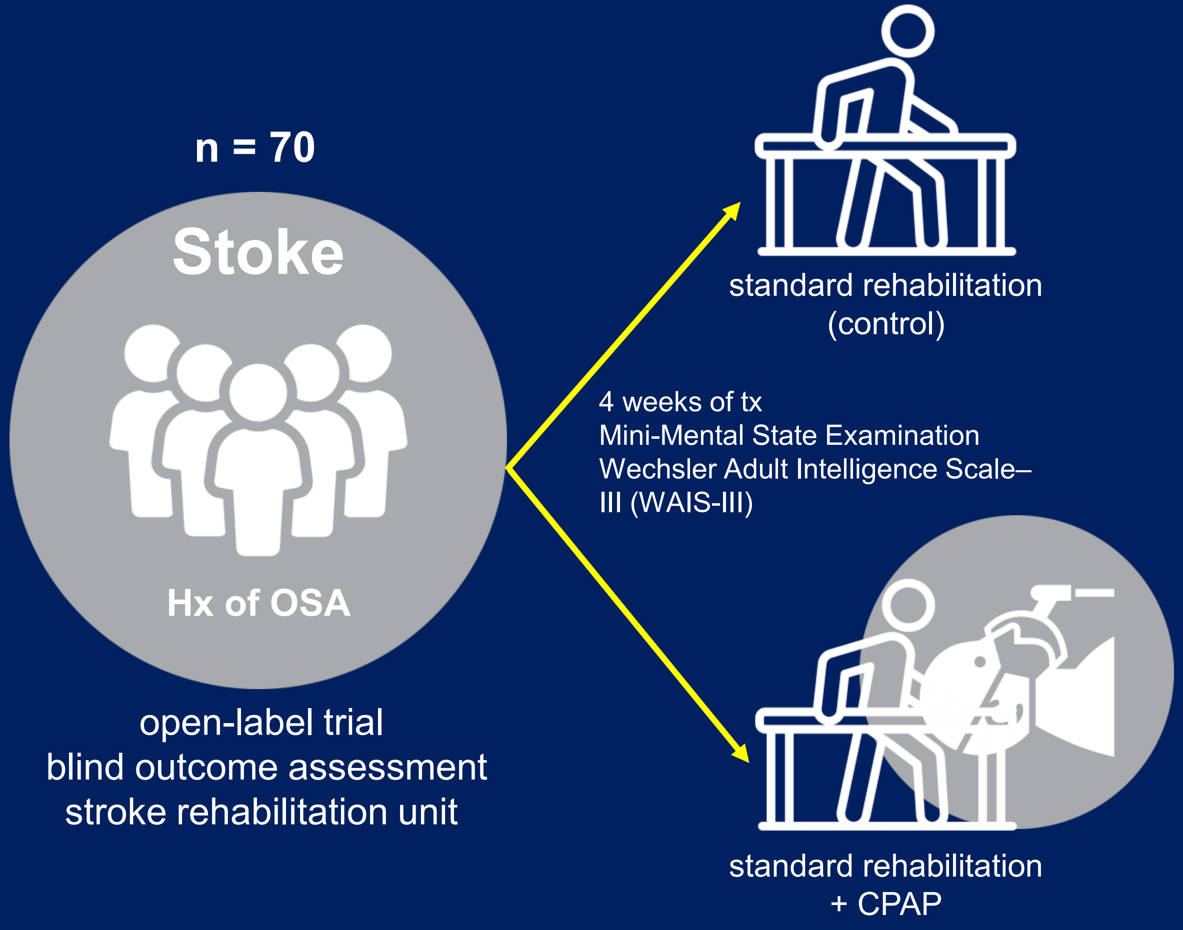
Control AHI = 2

Severity of OSA	Stroke /Death No. events	No. pts	Average Follow-up	Hazard Ratio (95% CI)
AHI < 3 (reference)	13	271	3.08 years	1.00
AHI 4 - 12	21	258	3.06 years	1.75 (0.88 – 3.49)
AHI 13 - 36	20	243	3.09 years	1.74 (0.87 – 3.51)
AHI > 36	34	250	2.78 years	3.30 (1.74 – 6.26)

P=0.005 by chi-square test for linear tread. AHI denotes AHI index, and CI confidence interval

H. Klar Yaggi, M et al. N Engl J Med 2005; 353:2034-2041

The effect of obstructive sleep apnea and treatment with continuous positive airway pressure on stroke rehabilitation: rationale, design and methods of the TOROS study



Outcomes: The primary outcome measures included functional and motor recovery, as well as neurocognitive outcomes.

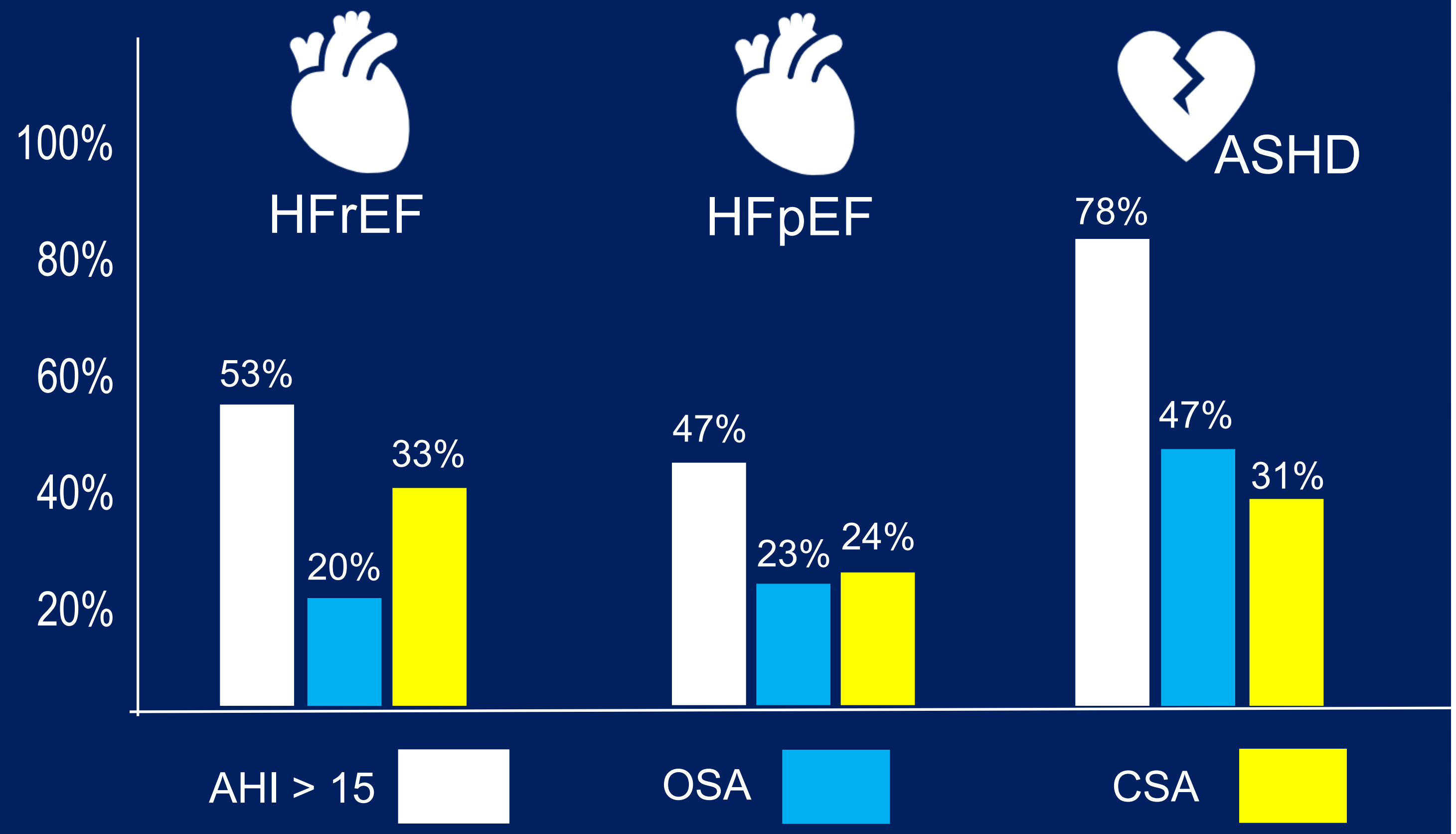
•**Cognitive benefits**: Patients who received CPAP showed a significantly greater improvement in the cognitive domains of attention and executive function compared to the control group. Greater compliance with CPAP was also linked to greater cognitive improvement.

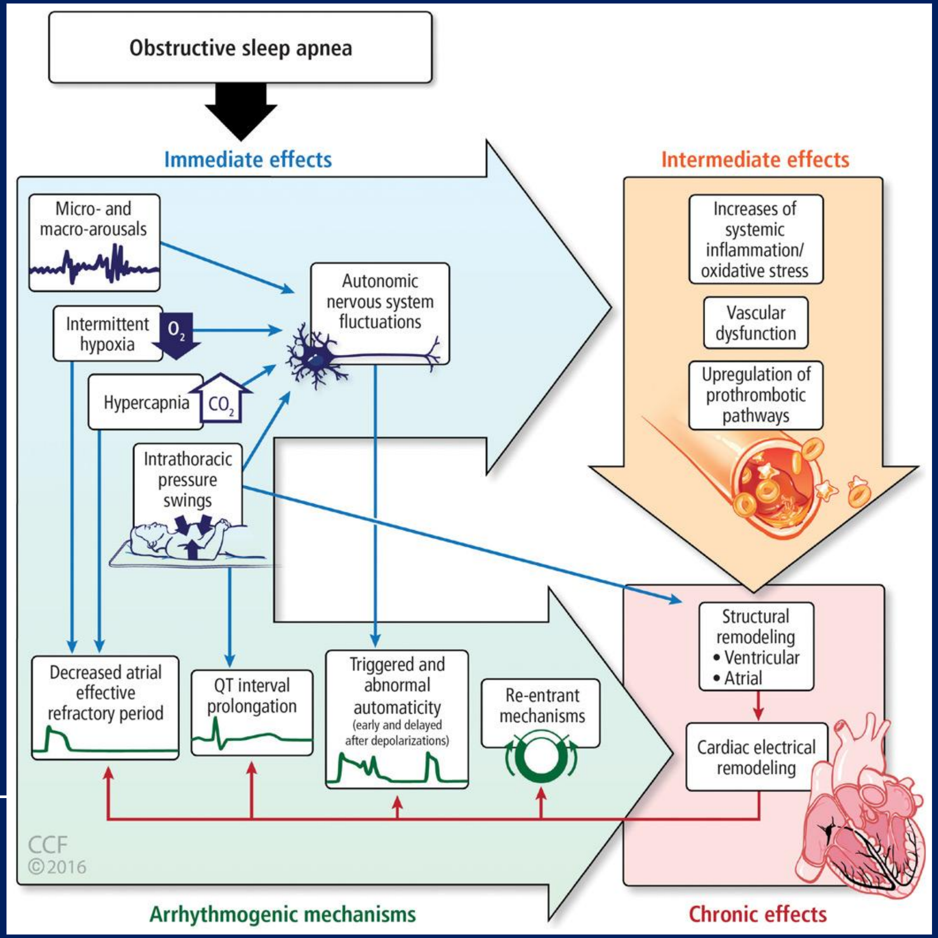
•**No functional improvement**: CPAP treatment did not lead to measurable improvements in neurological status, activities of daily living, or any of the study's secondary measures.

•**Compliance issues**: The study experienced low average CPAP compliance, with patients using the device for only 2.5 hours per night on average.

Aaronson, J.A., *et al.* The effect of obstructive sleep apnea and treatment with continuous positive airway pressure on stroke rehabilitation: rationale, design and methods of the TOROS study. *BMC Neurol* **14**, 36 (2014). https://doi.org/10.1186/1471-2377-14-36

The breakdown when it comes to heart disease





Javaheri S, Javaheri S. Obstructive Sleep Apnea in Heart Failure: Current Knowledge and Future Directions. J Clin Med. 2022 Jun 16;11(12):3458

Impact of Obstructive Sleep Apnea in Patients with Acute Heart Failure: A Nationwide Cohort Study

Acute Heart Failure 65,649	With OSA *n* (%)	Without OSA *n* (%)	*p* Value
HFrEF 39,345	2754	36,591	
Total Inpatient mortality	82 (3)	1463 (4)	0.29
AKI	991 (36)	10,611 (29)	<0.001
ACS	20 (0.7)	219 (0.6)	0.86
Atrial Fibrillation	1239 (45)	13,172 (36)	<0.001
CVA	25 (0.9)	183 (0.5)	0.27
LOS in days	6.45 ± 1	5.79 ± 1	0.02
Hospitalization cost	84,088 ± 14,000	79,722 ± 14,000	0.01

Two tailed *t*-test compared continuous variables, while chi-square tests assessed categorical variables. *p* value less than 0.05 indicates significance

Alharbi A, et al. Impact of Obstructive Sleep Apnea in Patients with Acute Heart Failure: A Nationwide Cohort Study. *Hearts*. 2024; 5(4):547-556. https://doi.org/10.3390/hearts5040040

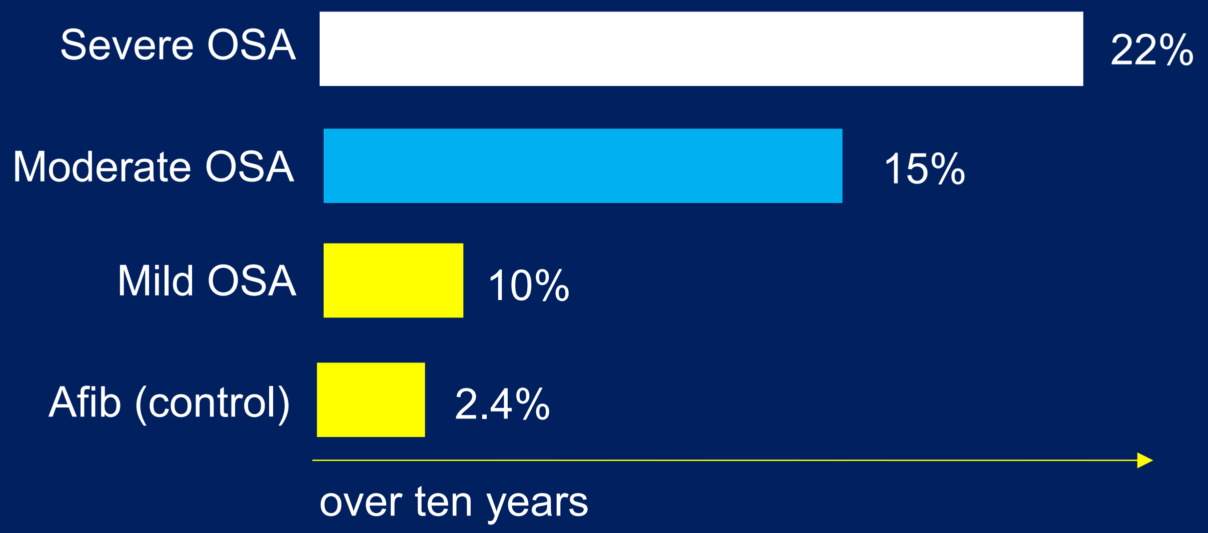
Impact of Obstructive Sleep Apnea in Patients with Acute Heart Failure: A Nationwide Cohort Study

Acute Heart Failure 65,649	With OSA *n* (%)	Without OSA *n* (%)	*p* Value
HFpEF 26,300	1841	24,459	
Total Inpatient mortality	37 (2)	978 (4)	0.002
AKI	423 (23)	5626 (23)	0.80
ACS	11 (0.6)	171 (0.7)	0.21
Atrial Fibrillation	920 (50)	11,251 (46)	0.04
CVA	15 (0.8)	146 (0.6)	0.16
LOS in days	5.33 ± 0.3	5.30 ± 0.1	0.43
Hospitalization cost	47,220 ± 3000	50,210 ± 3000	0.14

Two tailed *t*-test compared continuous variables, while chi-square tests assessed categorical variables. *p* value less than 0.05 indicates significance

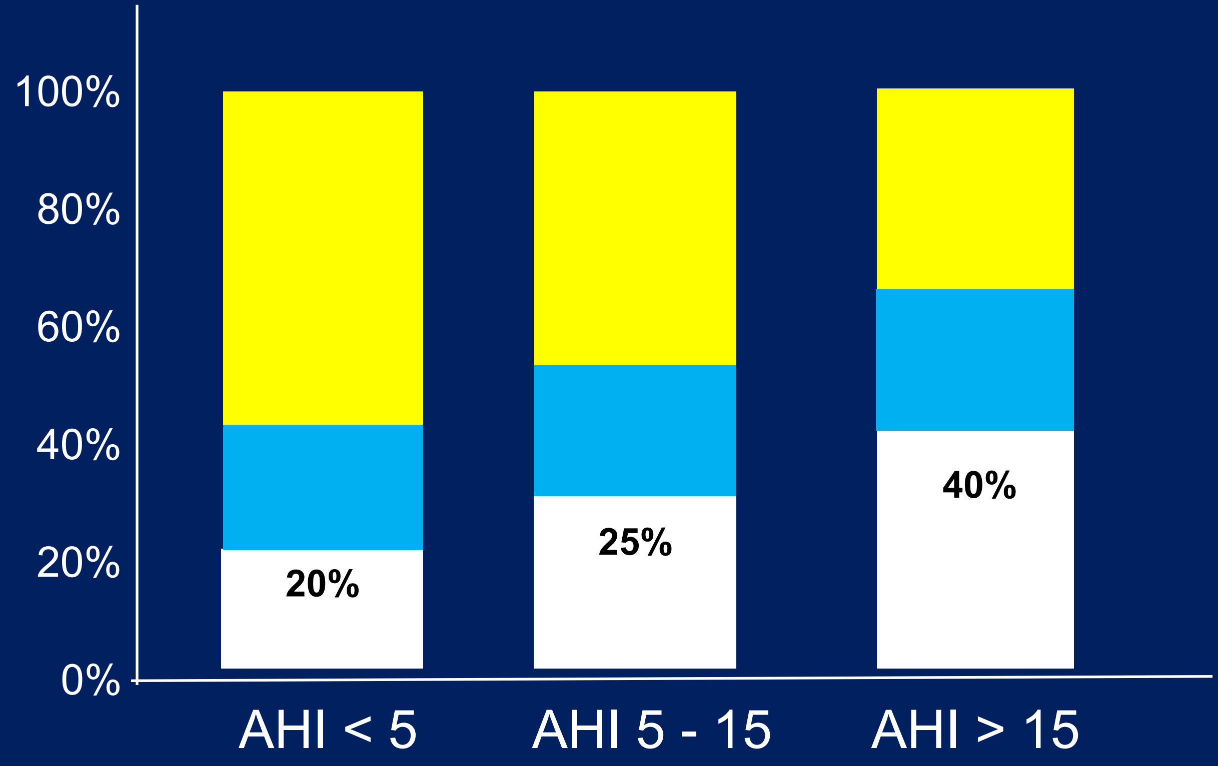
Alharbi A, et al. Impact of Obstructive Sleep Apnea in Patients with Acute Heart Failure: A Nationwide Cohort Study. *Hearts*. 2024; 5(4):547-556. https://doi.org/10.3390/hearts5040040

Incidence of atrial fibrillation by OSA severity

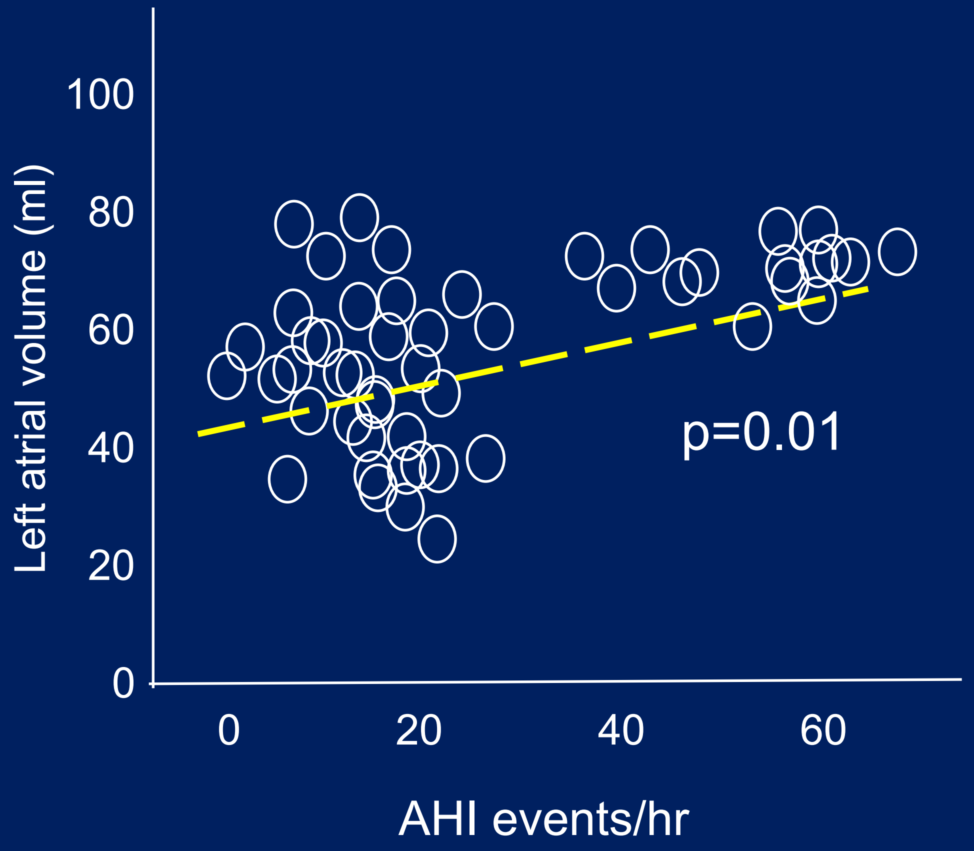


Gami, A, Hodge, D, Herges, R. et al. Obstructive Sleep Apnea, Obesity, and the Risk of Incident Atrial Fibrillation. J Am Coll Cardiol. 2007 Feb, 49 (5) 565–571.

Impact of Obstructive Sleep Apnea in Patients on diastolic function



Prevalence of diastolic dysfunction increased with the severity of sleep apnea from 44.8% to 56.8% (mild) to 69.7% (moderate to severe (p=0.002)



Lachter R et al. European Respiratory Journal 2013 41: 376 -383

Obstructive Sleep Apnea Testing/Diagnosis

- Sleep partners history
- Snoring & Witness Apnea (PPV 64%)

Obstructive Sleep Apnea Testing/Diagnosis

http://epworthsleepinessscale.com

- Dissatisfied with sleep then…
- Screening Tests

  (All have low quality of evidence)

  - Epworth Sleepiness Scale 54%
  - Berlin Questionnaire (PCP) 84%

    Netzer et al., Ann Intern Med
  - STOP-BANG (Pre-Op) 93%
  - Sleep Quality Index 63%

    Buysse et al. in 1989 (Psychiatry Research)

Screening tool for OSA: STOP-Bang

S	Does the patient snore loudly (louder than talking or loud enough to be heard through closed doors)?	Y/N
T	Does the patient often feel tired, fatigued, or sleepy during the day?	Y/N
O	Has anyone observed the patient stop breathing during their sleep?	Y/N
P	Does the patient have, or is the patient being treated for, high blood pressure?	Y/N
B	Does the patient have a BMI of more than 35?	Y/N
a	Age. Is the patient older than 50?	Y/N
n	Is the patient's neck circumference greater than 40cm?	Y/N
g	Gender. Is the patient male?	Y/N

Scoring: $Y \geq 3$ = high risk of OSA
$Y < 3$ = low risk of OSA

Abrishami A, A systematic review of screening questionnaires.
Can J Anaesth. 2010;57:423-38. & Anesthesiology 2008; 108: 812 – 21
Qaseem A. Clinical Guidelines of OSA. Ann Intern Med 2014; 161: 210 -220

Sleep Apnea Syndrome
Diagnostic Testing

- Polysomnography / Overnight Sleep Study
  - Considered the gold standard
  - > 5 events / hour with symptoms
  - > 15 events / hour with or without symptoms

- Home testing
  - Becoming more common (economics)
  - Indicated for high clinical suspicion <u>without</u> associate comorbidities (HF, Hypoventilation, COPD, Stroke)
  - Not for patients with insomnia, RLS, Narcolepsy, BMI >40

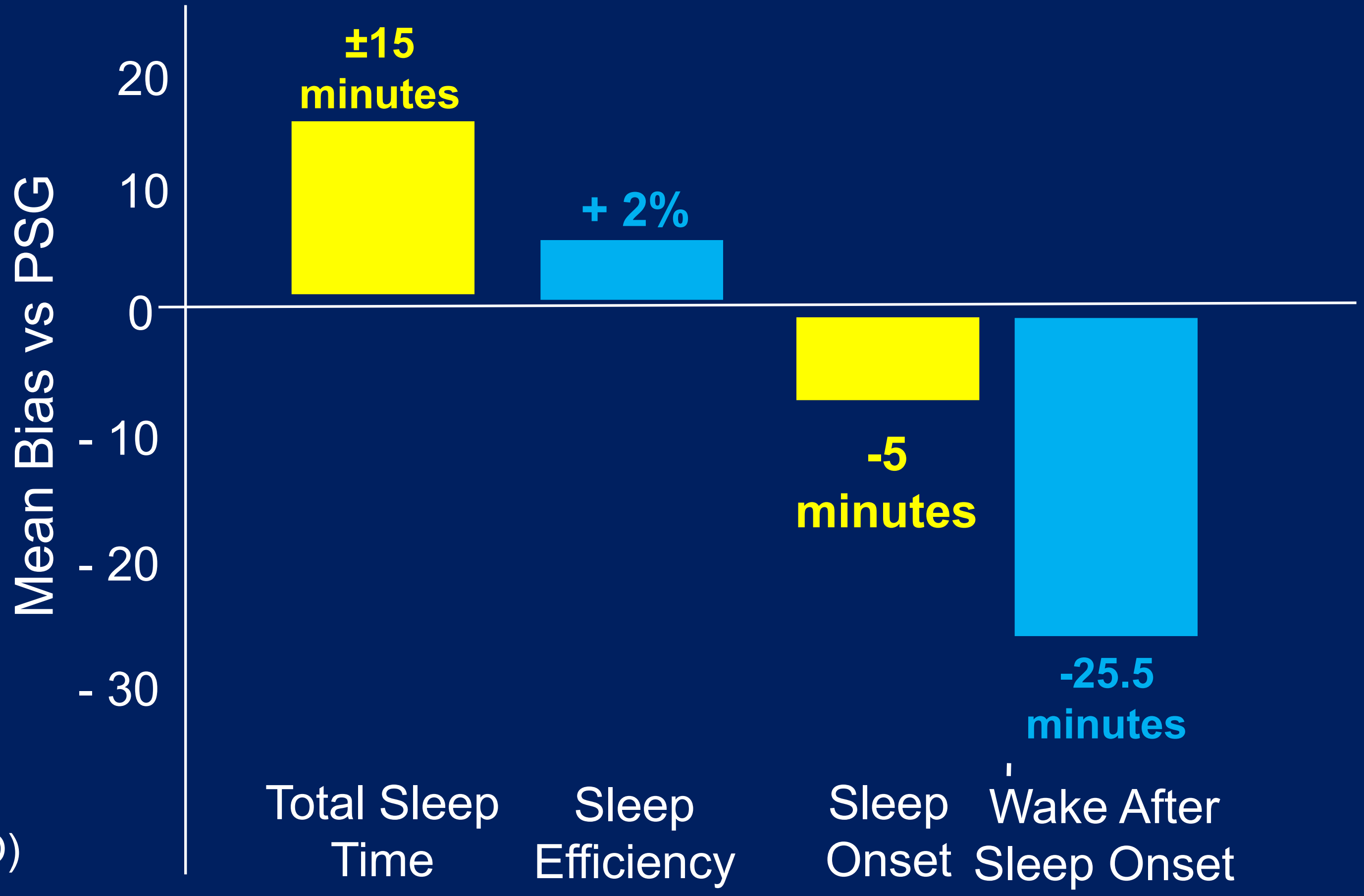
Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. J Clin Sleep Med. 2017;13:479-504. PMID: 28162150 doi:10.5664/jcsm.6506

Performance of consumer wrist-worn sleep tracking devices compared to polysomnography: a meta-analysis

24 studies

798 patients

Fitbit, Jawbone, myCadian watch, WHOOP strap, Garmin, Basis B1, Zulu Watch, Huami Arc, E4 wristband, Fatigue Science Readiband, Apple Watch, or Xiaomi Mi Band 5



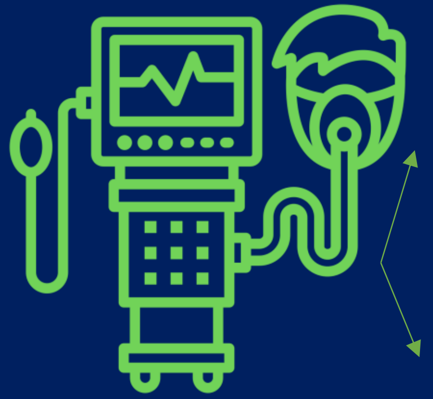
Key Clinical Implications:

- Reasonably accurate for Total Sleep Time (TST)
- Overestimates Sleep Efficiency (SE)
- Underestimates Sleep Onset Latency (SOL)
- Poor detection of Wake After Sleep Onset (WASO)
- Useful for trends, not for diagnosis

Lee YJ. Performance of consumer wrist-worn sleep tracking devices compared to polysomnography: a meta-analysis. J Clin Sleep Med. 2025;21(3):573–582.

Feature	Polysomnography (PSG)	Actigraphy (Professional)	Smartwatches (Consumer)
Accuracy	Gold standard for diagnosis. Measures brain waves, eye movement, and muscle tone for precise sleep staging.	Accurate for long-term sleep-wake patterns and detecting insufficient sleep.	Offers helpful insights, but accuracy for sleep stages and disorder detection is limited.
Data type	Comprehensive physiological data, including brain waves, breathing, heart rhythm, and blood oxygen levels.	Movement-based data, and sometimes light exposure, collected over multiple nights.	Tracks metrics like movement, heart rate, heart rate variability, and blood oxygen.
Monitoring	Single-night, in-lab, or home study with prescribed clinical-grade equipment.	Multi-night, at-home wear of a professional-grade device, usually worn on the wrist.	Continuous, long-term monitoring at home while the user wears the device.
Use case	Diagnosis of sleep disorders like sleep apnea, narcolepsy, and REM sleep behavior disorder.	Assessing circadian rhythm disorders or chronic insomnia, or as a preliminary screening tool.	Raising awareness of potential sleep issues or monitoring progress for informational purposes.

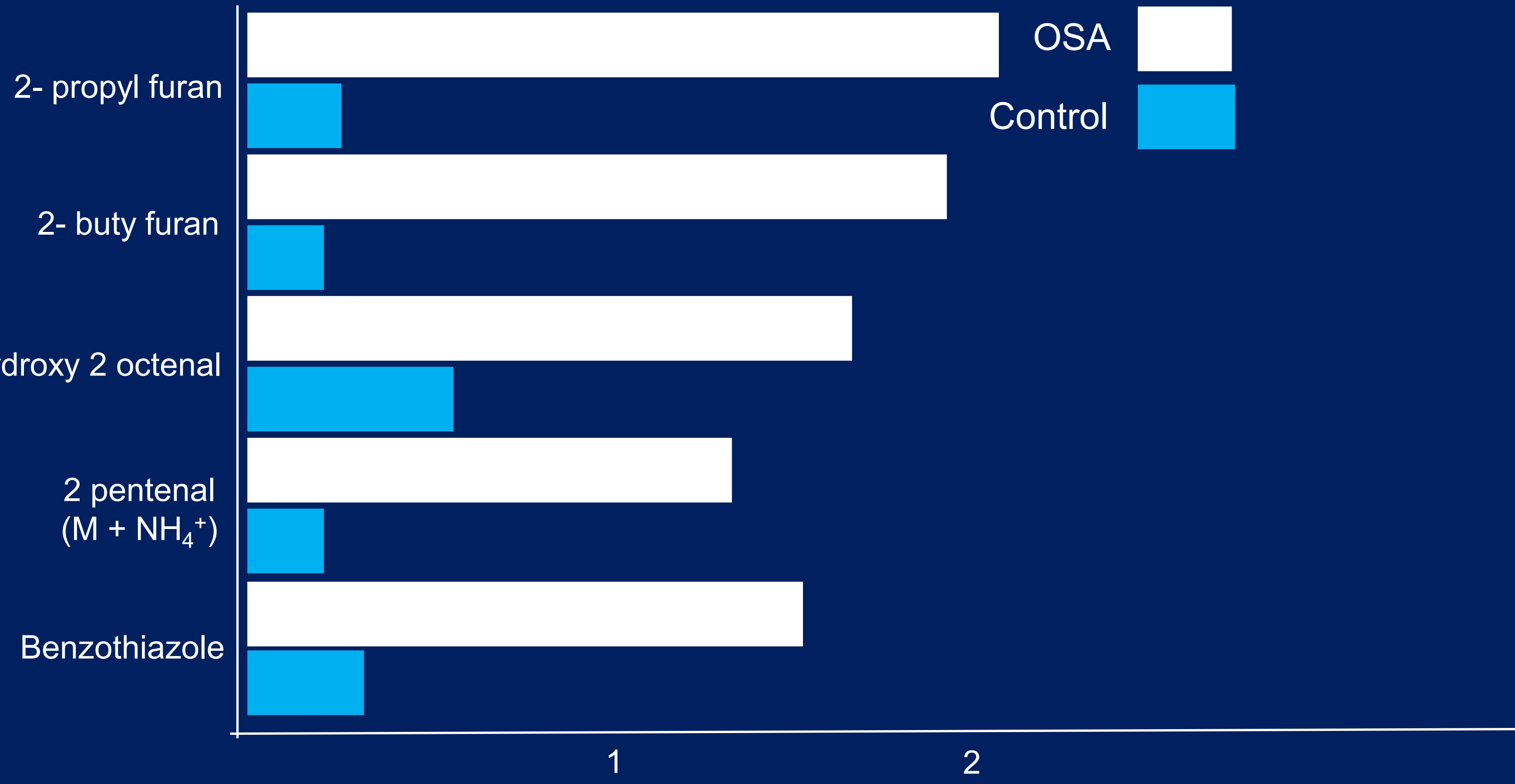
Breath biomarkers for obstructive sleep apnea



Breath
Analysis

OSA
n =149

Control
n =149



Levels detected - log(p) by electrospray ionization high-resolution mass spectrometry (SESI-HRMS)l

Sleep Apnea
Treatment Options

- Avoidance of alcohol, sedatives & narcotics
- Position therapy
  - Works only in combination
- Weight loss
- Continuous Positive Airway Pressure (CPAP)
- Oral Appliance
  - PAP more effective
  - Best for (obstructive) & mild disease
- Surgery (UPPP, Maxillary Advancement)
- Hypoglossal nerve stimulator

Morgenthaler TI, et al; Standards of Practice Committee. Practice parameters for the medical therapy of obstructive sleep apnea. Sleep. 2006;29:1031-5.

Sommer JU, Kraus M, Birk R, Schultz JD, Hörmann K, Stuck BA. Functional short- and long-term effects of nasal CPAP with and without humidification on the ciliary function of the nasal respiratory epithelium. Sleep Breath. 2014;18:85-93.

The current role of Auto-CPAP treatment for OSA

- Algorithms to detect and respond to changes in upper airway (flow, pressure and resistance)
- Avoid in-laboratory treatment
- Decrease the cost to OSA management
- Best in uncomplicated moderate to severe OSA
- Tolerance is very good.

What are the issues related to treatment options with sleep apnea

Delay in referral to testing

Delay from testing completion to therapy

Adequate follow up and reassessment

Patient compliance

Who does it better? Primary Care vs Specialist Sleep Center Management of Obstructive Sleep Apnea and Daytime Sleepiness and Quality of Life

Severe OSA Randomized, controlled, noninferiority study involving 155 patients

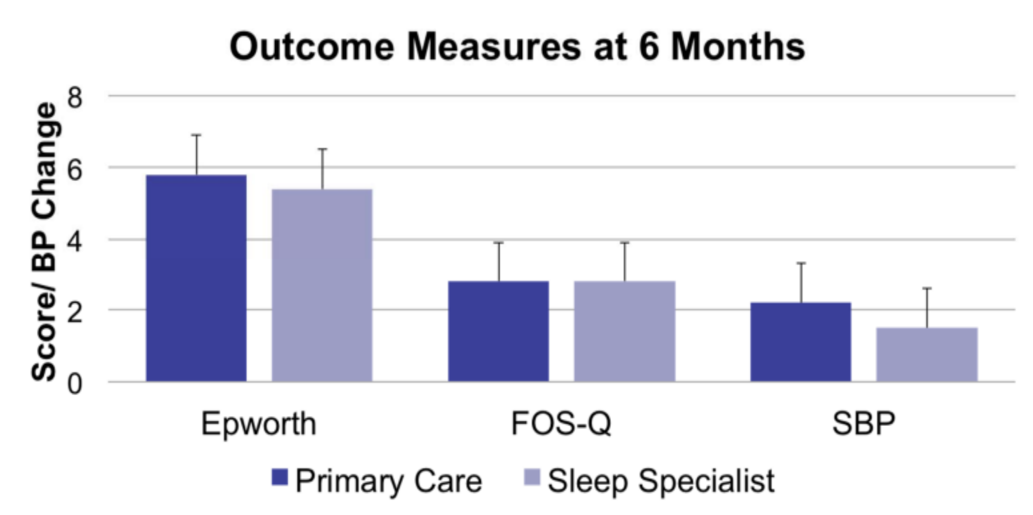
Primary Care
n= 81

85% ♂
BMI 33± 5
ESS 12.8 ± 4
ODI/AHI 32 ± 18

vs.

Sleep Specialist
n= 74

77% ♂
BMI 33± 5
ESS 12.5 ± 4
ODI/AHI 35 ± 17



- Sleep specialists prescribe alternative non-CPAP therapy (28% vs. 3%)
- < withdrawal from study with sleep specialist (8% vs. 21%)
- < CPAP discontinuation with sleep specialist

Chai-Coetzer CL, Antic NA, Rowland LS, et al. Primary Care vs Specialist Sleep Center Management of Obstructive Sleep Apnea and Daytime Sleepiness and Quality of Life: A Randomized Trial. *JAMA.* 2013;309(10):997–1004. doi:10.1001/jama.2013.1823

CPAP for the Prevention of Cardiovascular Events in OSA

Known CAD
ESS < 15 (not sleepy)
3,246 patients
89 Institutions, 7 countries

2,717 patients randomized

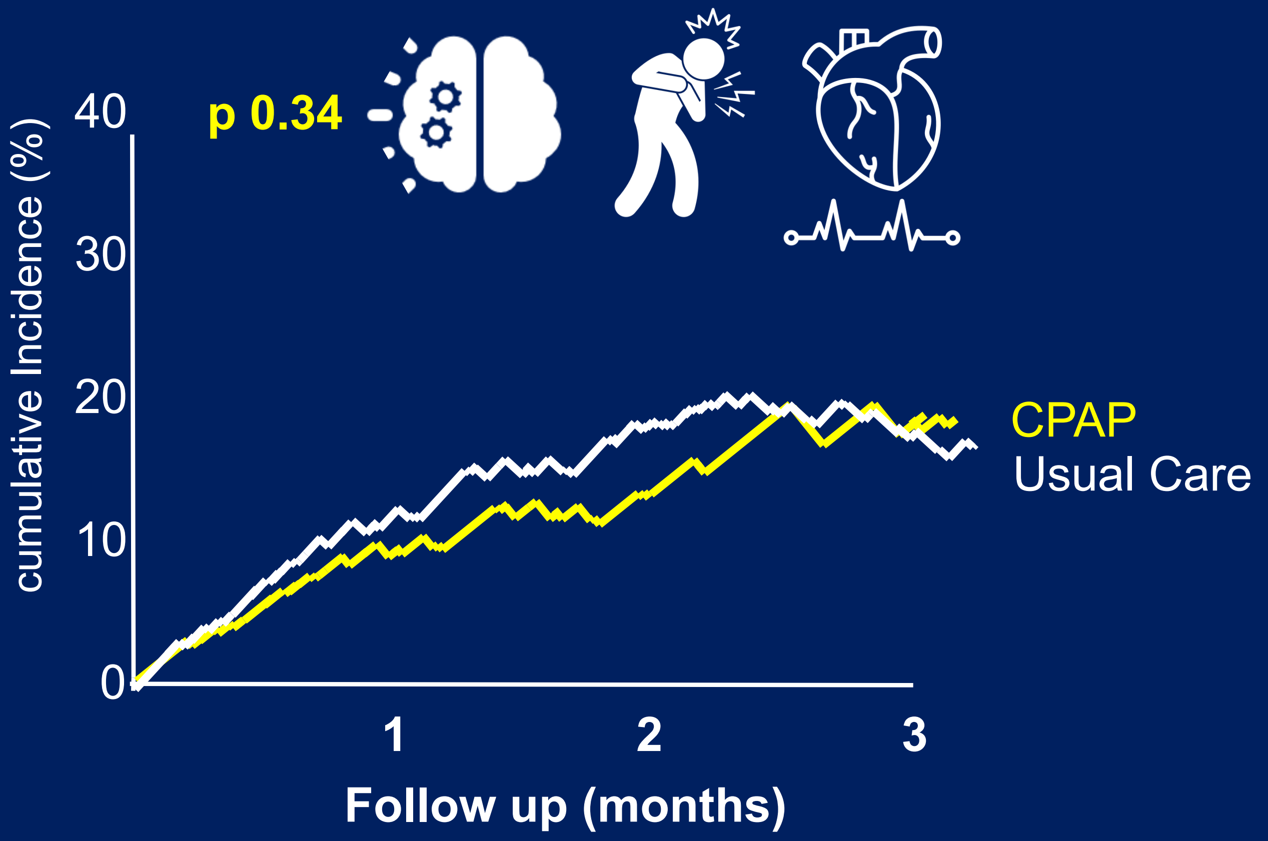
CV Deaths
MI/CAD
Stroke/TIA
Heart Failure

CPAP
1,359

Usual Care
1,358

mean f/u
3.7 years

Excluded ESS > 15, SpO2 10% TRT, resting hypoxemia, severe COPD

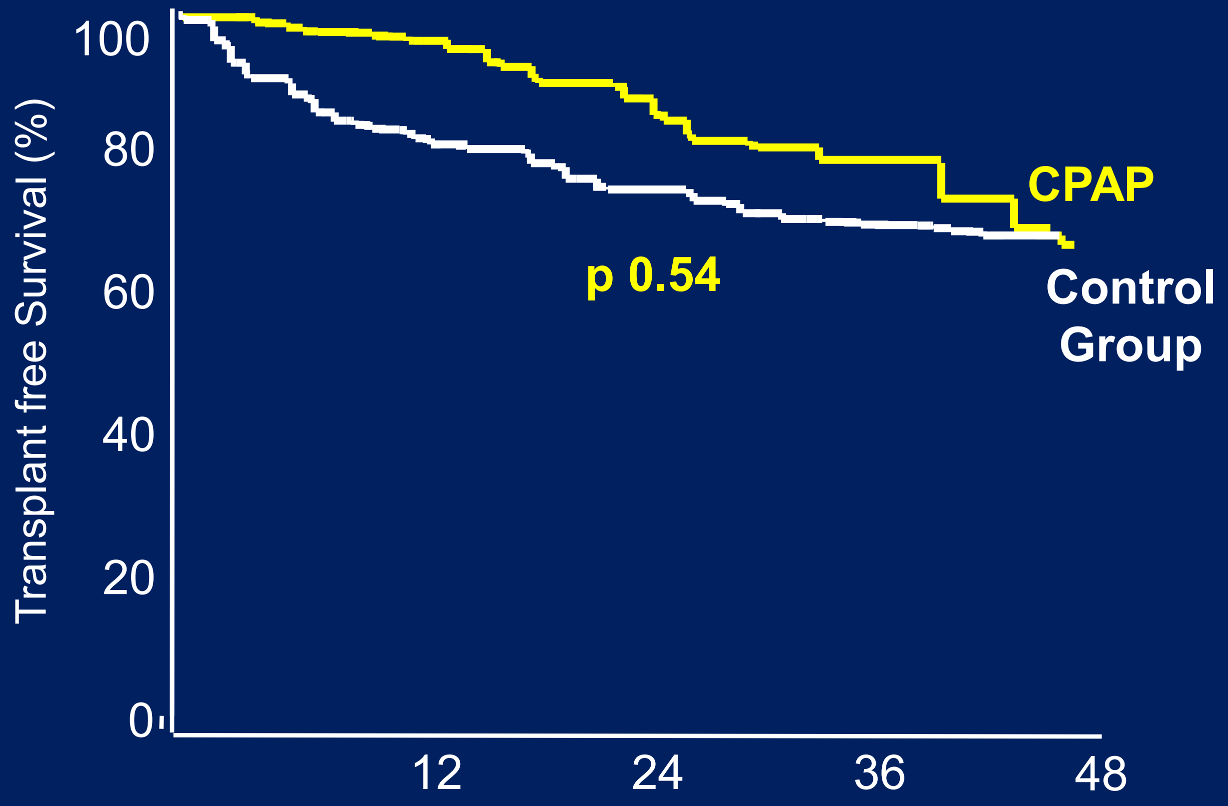


Adherence	1 Week	1 month	12 months	Thereafter
Hours	5.2±1.4	4.4±2.2	3.5±2.4	3.3±2.3

McEvoy, RD, Antic, NA, Heeley, E, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. *N Engl J Med* 2016;375:919-931

Effect of CPAP on the AHI, Nocturnal Oxygen Saturation, and Left Ventricular Ejection Fraction
CANPAP Investigators

- **In the Canadian Continuous Positive Airway Pressure trial, continuous positive airway pressure (CPAP) therapy administered to patients with heart failure was found to reduce the severity of central sleep apnea and increase the left ventricular ejection fraction, but did not improve survival**

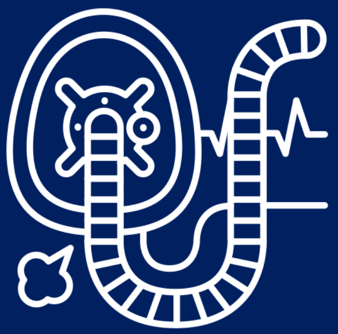


Bradley TD, Logan AG, Kimoff RJ, et al. CANPAP Investigators. Continuous positive airway pressure for central sleep apnea and heart failure. N Engl J Med. 2005 Nov 10;353(19):2025-33. doi: 10.1056/NEJMoa051001

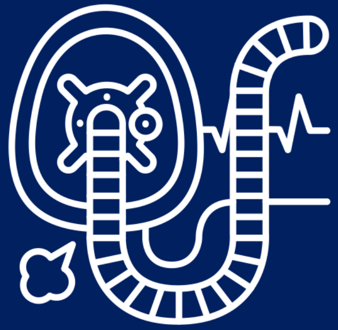
Does Adaptive Servo Ventilation (ASV) improve survival in CSA and heart failure

Multicenter RCT
Secondary prevention of CV

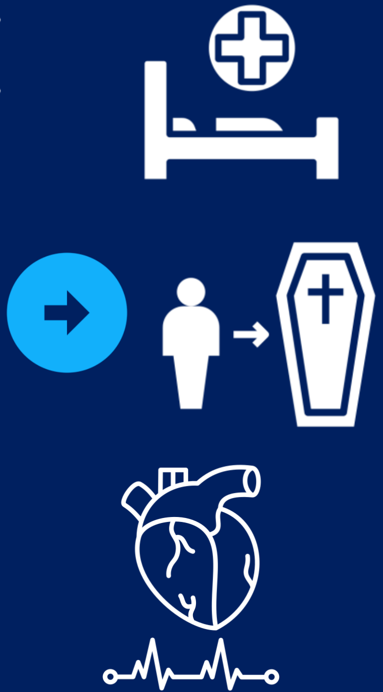
HF < 45%
NYHCA Class > II
moderate-severe
Central Sleep Apnea
(AHI >15/hr)
n=1325

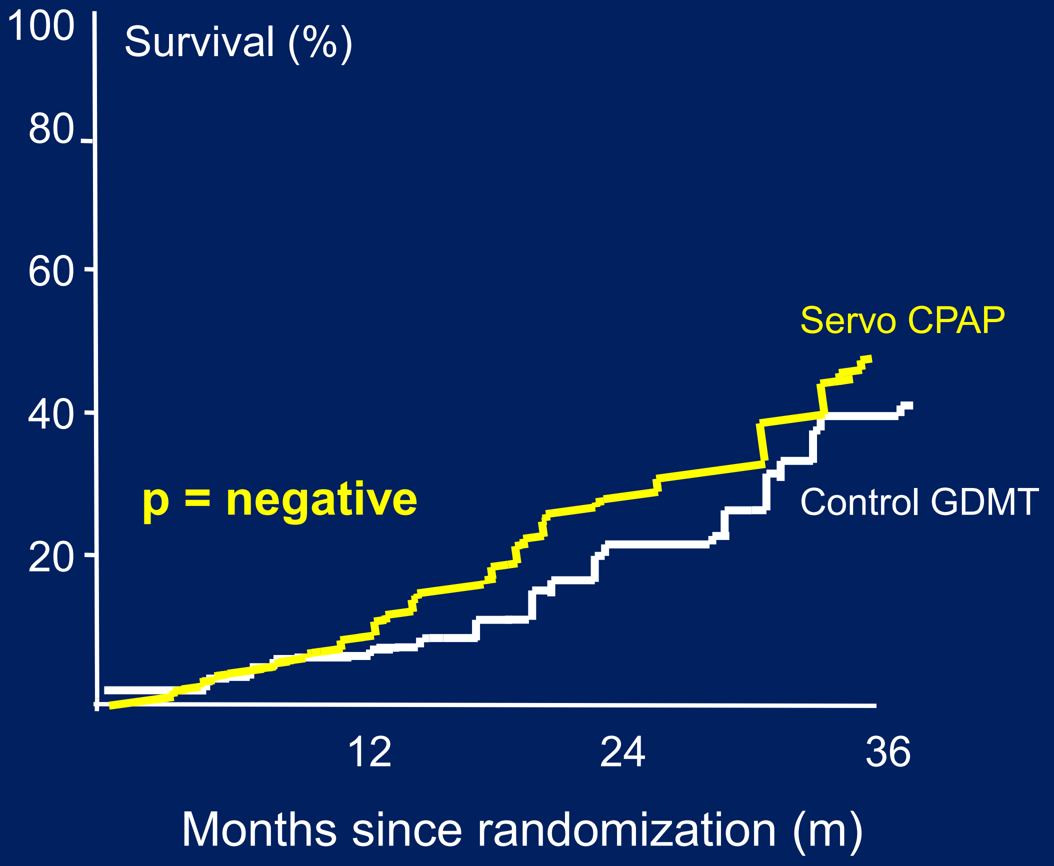


n= 666
+ASV



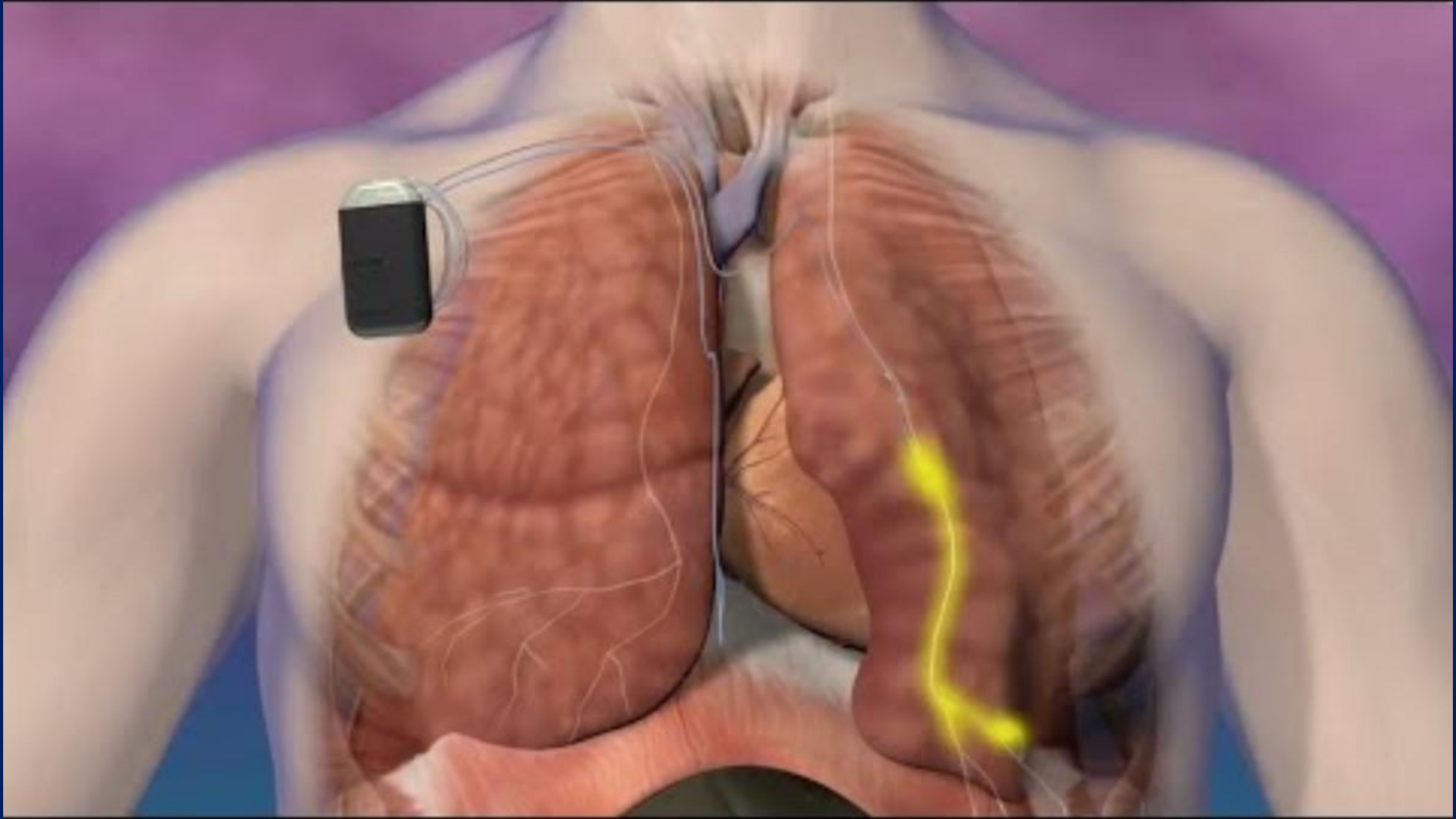
n =659
No ASV



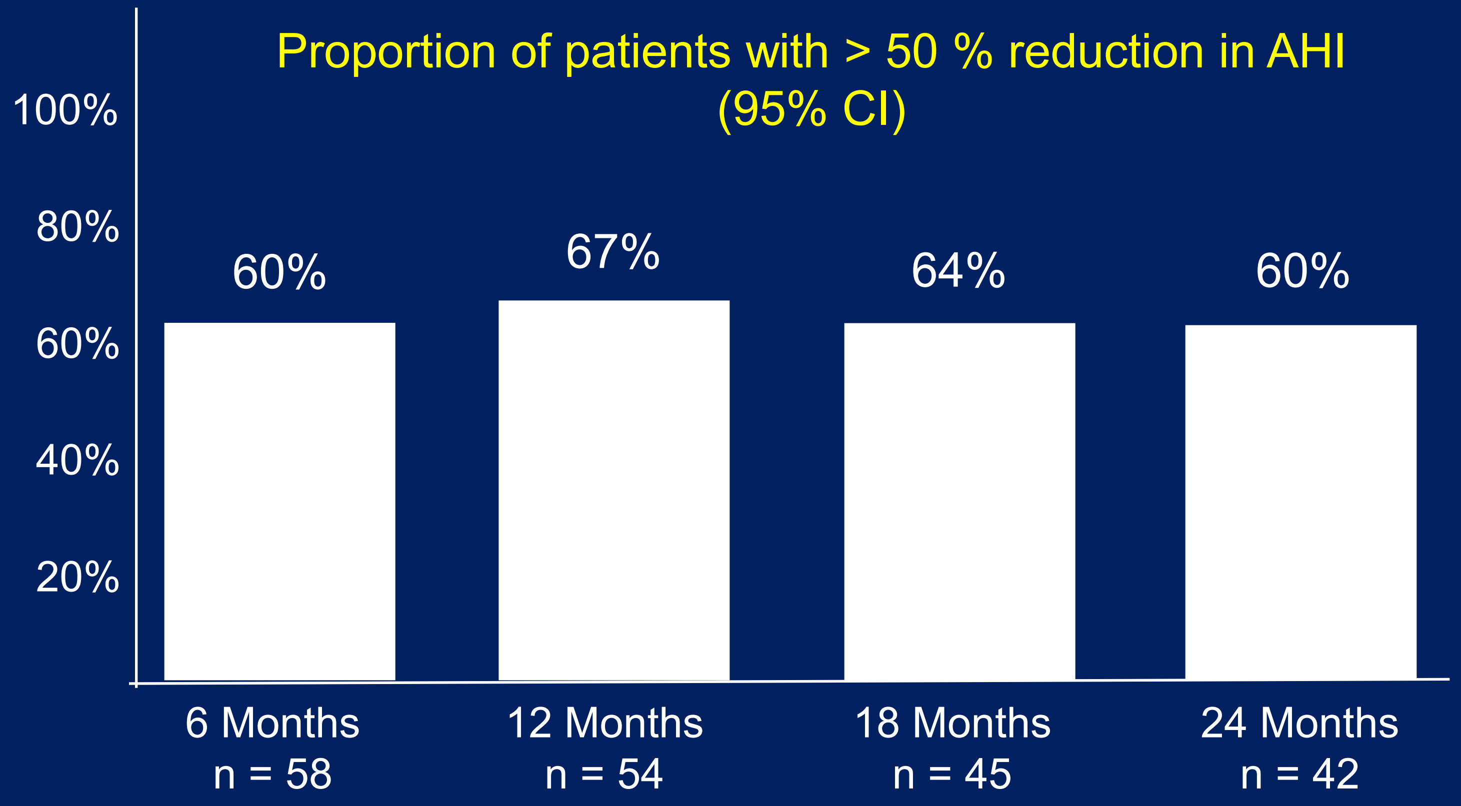


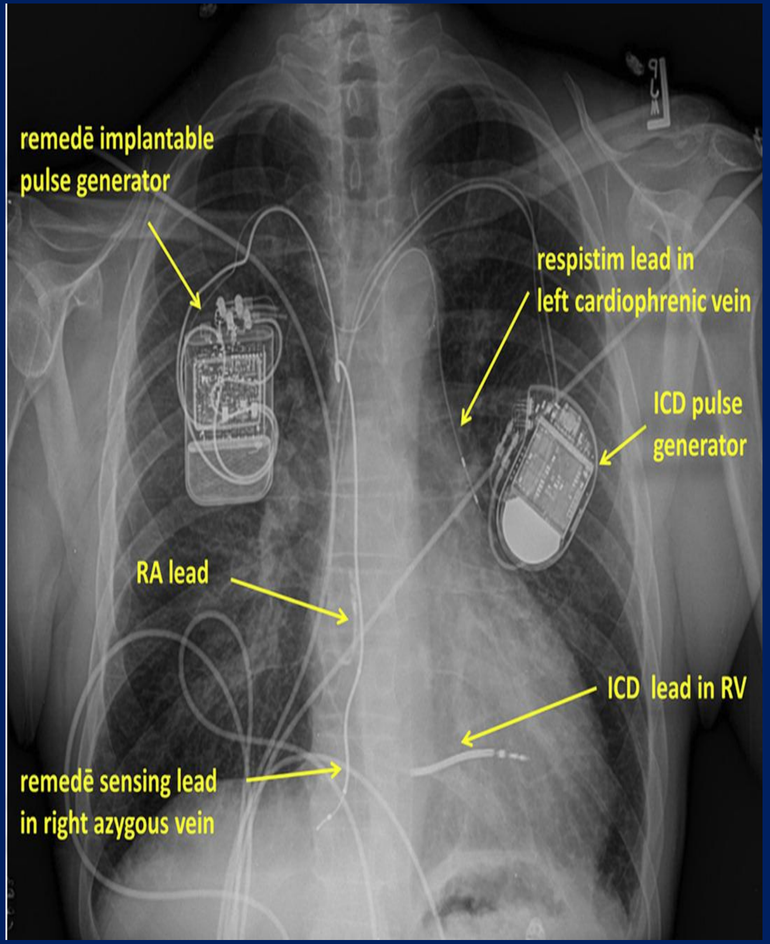
90% were male, Mean Age 68 years old.

Cowie MR et al. Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure. N Engl J Med 2015;373:1095-1105



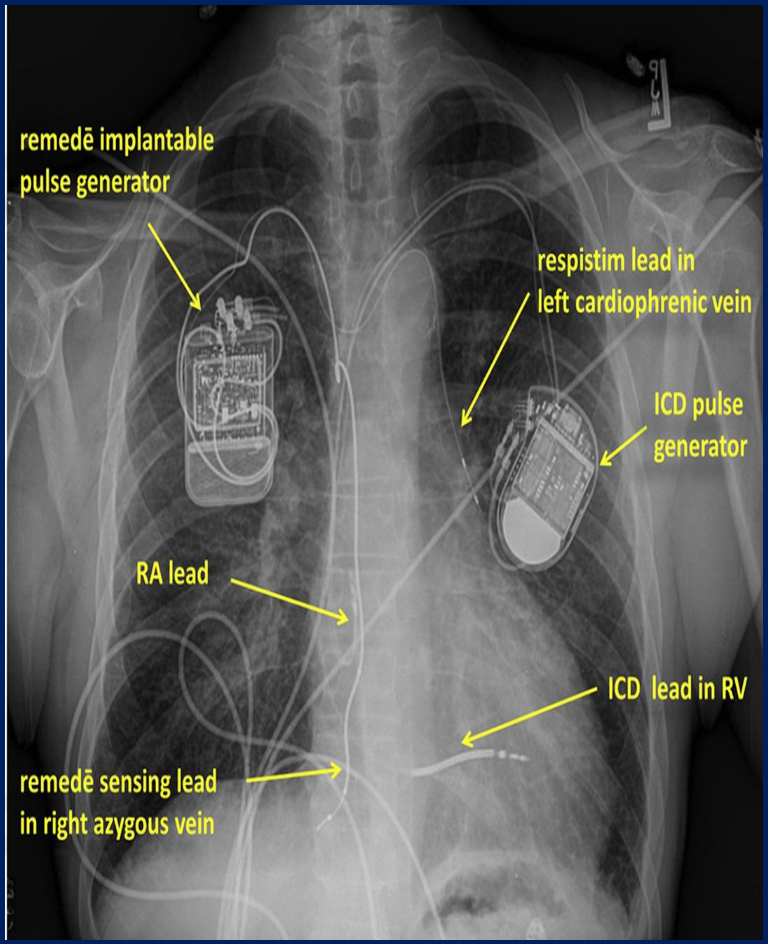
Long term efficacy and safety of phrenic nerve stimulation for the treatment of CSA

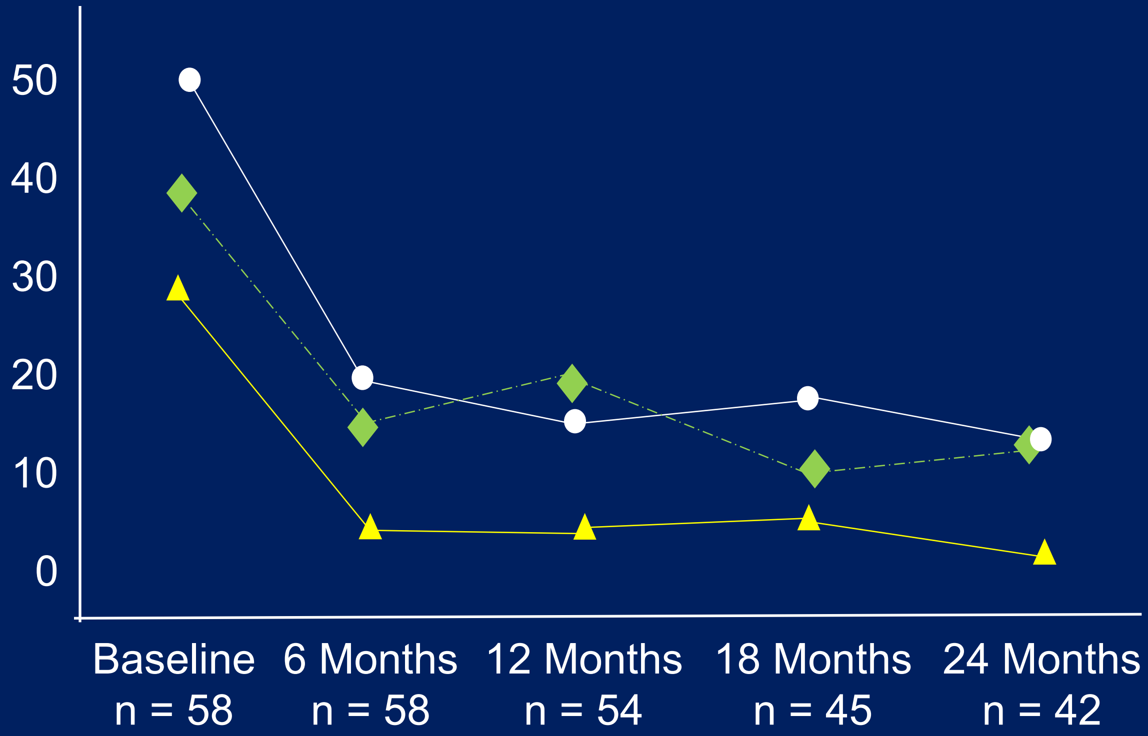




Nayak, Hemal M. et al. Transvenous phrenic nerve stimulation for central sleep apnea is safe and effective in patients with concomitant cardiac devices. Heart Rhythm, Volume 17, Issue 12, 2029 - 2036

Long term efficacy and safety of phrenic nerve stimulation for the treatment of CSA





OD14 = Oxygen desaturations

AHI = apnea hypopnea index

CAI = Central apnea index

Nayak, Hemal M. et al. Transvenous phrenic nerve stimulation for central sleep apnea is safe and effective in patients with concomitant cardiac devices. Heart Rhythm, Volume 17, Issue 12, 2029 - 2036

In two trials, researchers assessed the efficacy and safety of tirzepatide for the treatment of adults with obstructive sleep apnea and obesity

Trial 1 enrolled participants who were <u>not</u> receiving positive airway pressure (PAP) therapy.

TRIAL

1

n = 234
mean age 48 years
♂ 67%; ♀ 28%

AHI > 15 (x 50)
BMI 30 (x approx 39)
No DM 1 or 2

10 mg or 15 mg

Tirzepatide
n = 114

Placebo
n = 120

hsC-reactive protein

% change in body weight

18%

changes in BP

Atul Malhotra. SURMOUNT-OSA Investigators. 2024
N Engl J Med 2024;391 (13): 1193-1205. DOI: 10.1056/NEJMoa2404881

In two trials, researchers assessed the efficacy and safety of tirzepatide for the treatment of adults with obstructive sleep apnea and obesity

TRIAL

2

Trial 2 enrolled participants who <u>were receiving</u> positive airway pressure (PAP) therapy.

n = 234
mean age 48 years
♂ 67%; ♀ 28%

AHI > 15 (x approx 50)
BMI 30 (x approx 39)
No DM 1 or 2

10 mg or 15 mg

Tirzepatide
n = 120

Placebo
n = 115

hsC-reactive protein

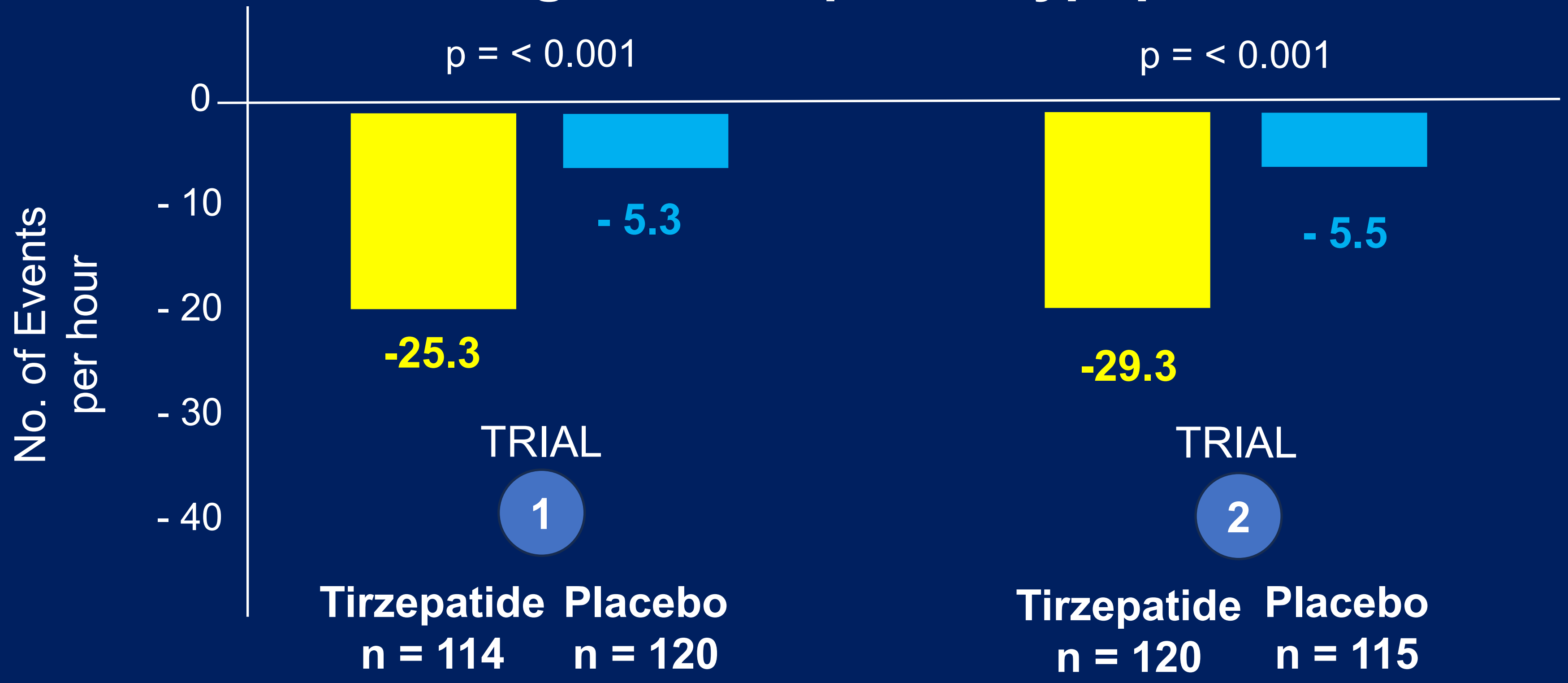
% change in body weight

changes in BP

Atul Malhotra. SURMOUNT-OSA Investigators. 2024
N Engl J Med 2024;391 (13): 1193-1205. DOI: 10.1056/NEJMoa2404881

In two trials, researchers assessed the efficacy and safety of tirzepatide for the treatment of adults with obstructive sleep apnea and obesity

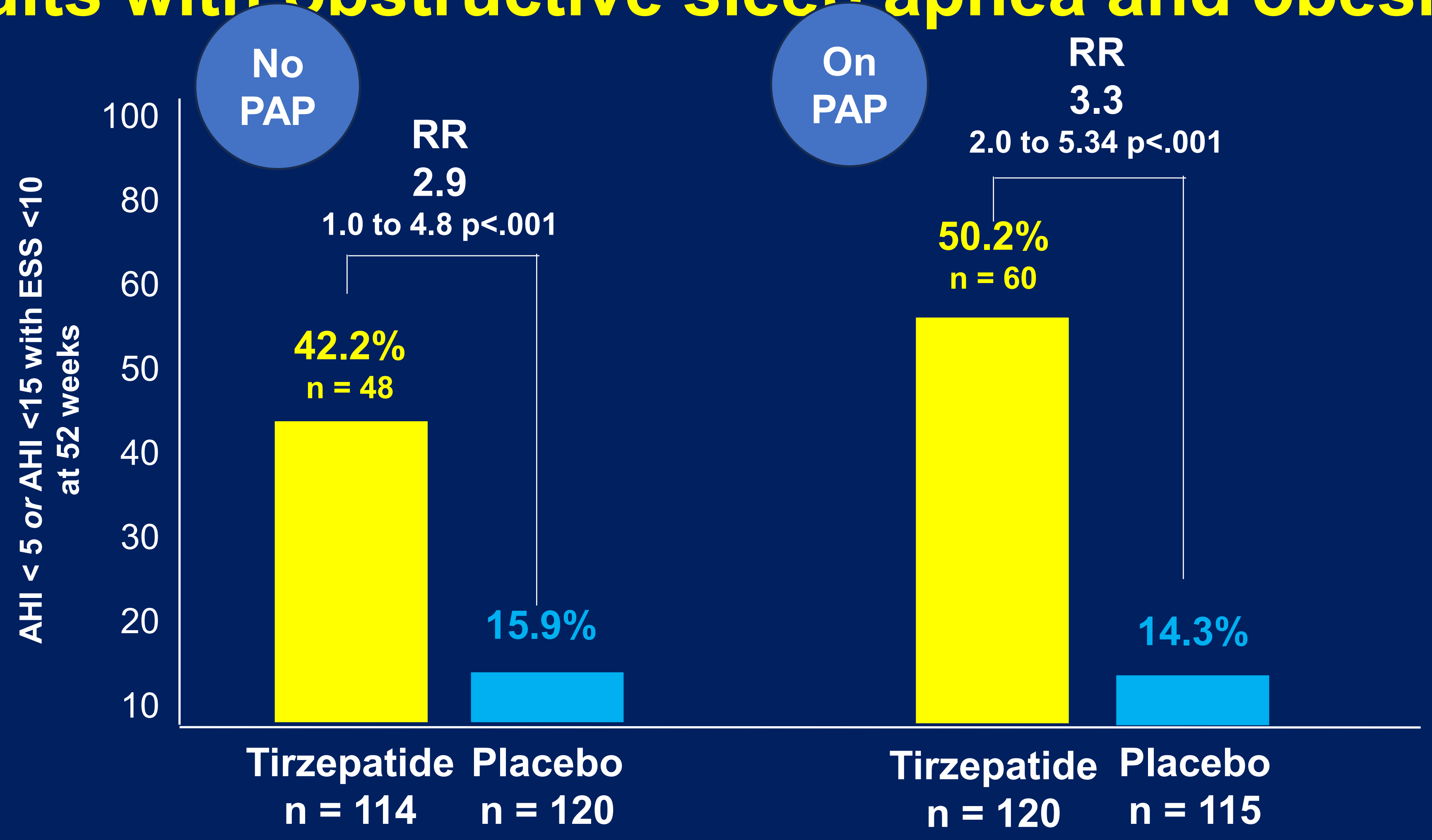
Change in the Apnea- Hypopnea Index



In both trial 1 and trial 2, tirzepatide led to a significantly greater reduction in the AHI at week 52 than placebo.

Atul Malhotra. SURMOUNT-OSA Investigators. 2024
N Engl J Med 2024;391 (13): 1193-1205. DOI: 10.1056/NEJMoa2404881

Normalized AHI with tirzepatide for the treatment of adults with obstructive sleep apnea and obesity



Atul Malhotra. SURMOUNT-OSA Investigators. 2024
N Engl J Med 2024;391 (13): 1193-1205. DOI: 10.1056/NEJMoa2404881

Observed Variability in OSA Remission Rates Post-Bariatric Surgery (Across Six Reviewed Studies)

2,310 pts with OSA
6 studies

Bariatric Surgery

Study (Citation)	OSA Remission (%)	Post-Surgery Timing	Definition of Remission
de Raaff et al. (2016)	74.1%	6–9 months	PSG/PG AHI < 15
Haines et al. (2006)	63%	Mean 11 months	No longer needing CPAP/BiPAP
Yanari et al. (2022)	51.8%	1 year	PSG AHI < 15
Peromaa-Haavisto et al. (2017)	45%	1 year	PG showing AHI < 5
Morong et al. (2014)	35.2%	7 months	PSG showing AHI < 5
Ravesloot et al. (2014)	24%	12 months	PSG/PG AHI < 5

Key Takeaway: Include a note highlighting that the reported OSA remission rates varied widely, ranging from **24% to 74.1%**. This variation is largely explained by the **heterogeneous definition of remission** used across the studies (AHI < 5, AHI < 15, or "no more need of CPAP/BiPAP")

Al Oweidat K. Bariatric surgery and obstructive sleep apnea: a systematic review and meta-analysis. Sleep Breath. 2023 Dec;27(6):2283-2294.

Prospective multicenter trial involving 132 patients diagnosed with OSA at baseline

132 pts with OSA

Bariatric surgery

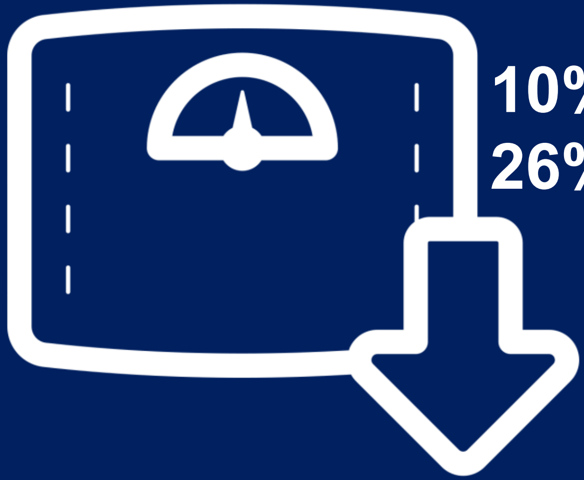
Measurement	Baseline	12 Months	Change/Significance
Total AHI (events/h)	27.8	9.9	Significant decrease ($p < 0.001$)
OSA Prevalence	71%	44%	Significant decrease ($p < 0.001$)
Mean BMI (kg/m2)	43.9	33.0	Decrease of 10.1 kg/m2 ($p < 0.001$)

Resolution/Improvement: OSA was **cured in 45%** of patients. OSA was cured or improved in **78%** (cured or moved to a milder AHI group)

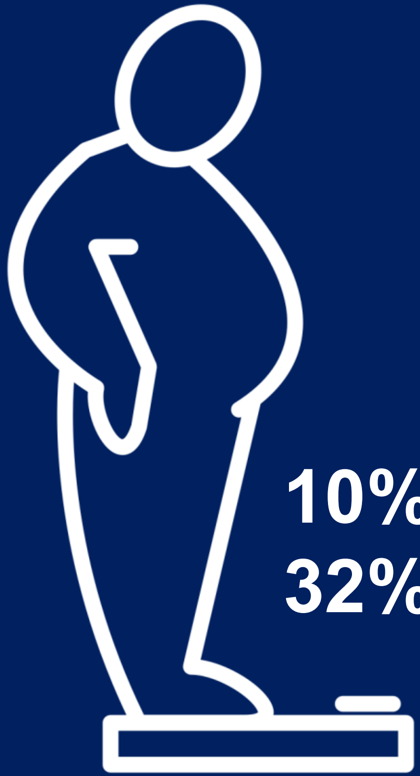
Severe OSA Reduction: The number of patients with **severe OSA was reduced from 22% at baseline to 7%** at 12 months ($p < 0.001$

Peromaa-Haavisto, P., et al. "Obstructive sleep apnea: the effect of bariatric surgery after 12 months. A prospective multicenter trial." *Sleep medicine* 35 (2017): 85-90.

OSA clinical management in context of treating comorbid obesity



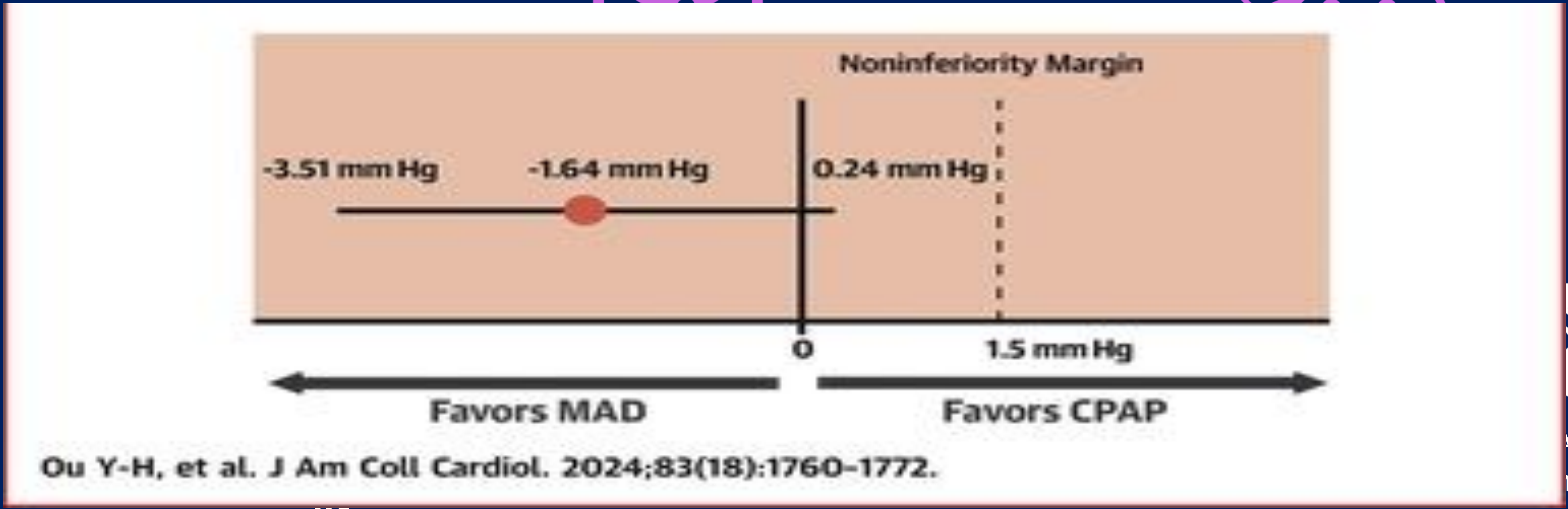
10% *decrease* in body weight
26% *decrease* in AHI



10% *increase* in body weight
32% *increase* in AHI

Gottlieb DJ, Punjabi NM. Diagnosis and Management of Obstructive Sleep Apnea: A Review. JAMA. 2020;323(14):1389–1400. doi:10.1001/jama.2020.3514

Mandibular advancement device versus CPAP in lowering 24-hour blood pressure in patients with obstructive sleep apnea



pts

AP
nent

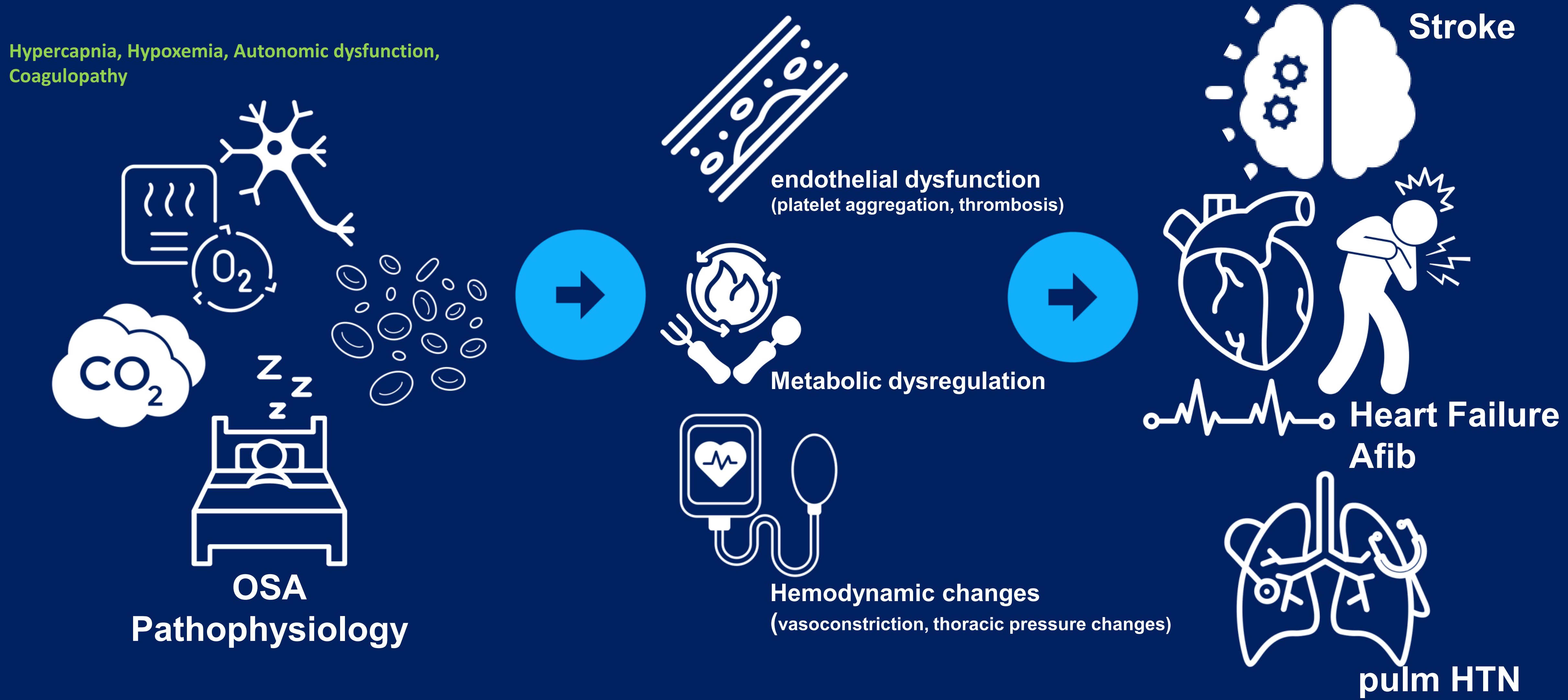
mean age 61 years
♂ 85%; ♀ 15%

follow up

Adherence	MAD > 6hours	CPAP > 6 hours
	56.5%	23.2%

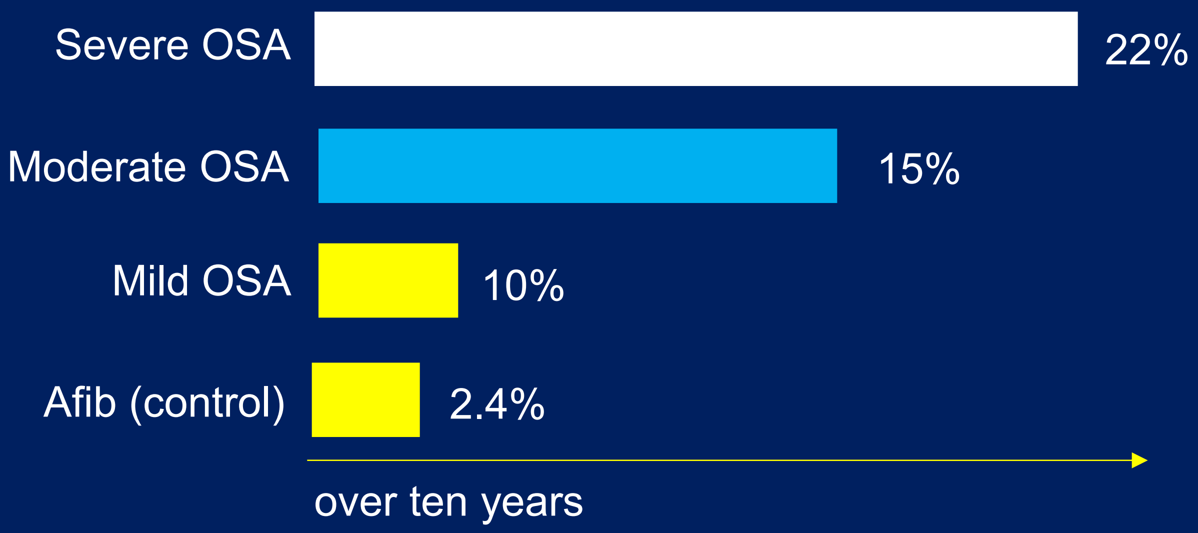
Ou, Y, Colpani, J, Cheong, C. et al. Mandibular Advancement vs CPAP for Blood Pressure Reduction in Patients With Obstructive Sleep Apnea. *JACC.* 2024 May, 83 (18) 1760–1772.

Cardiovascular Implication of Sleep Apnea



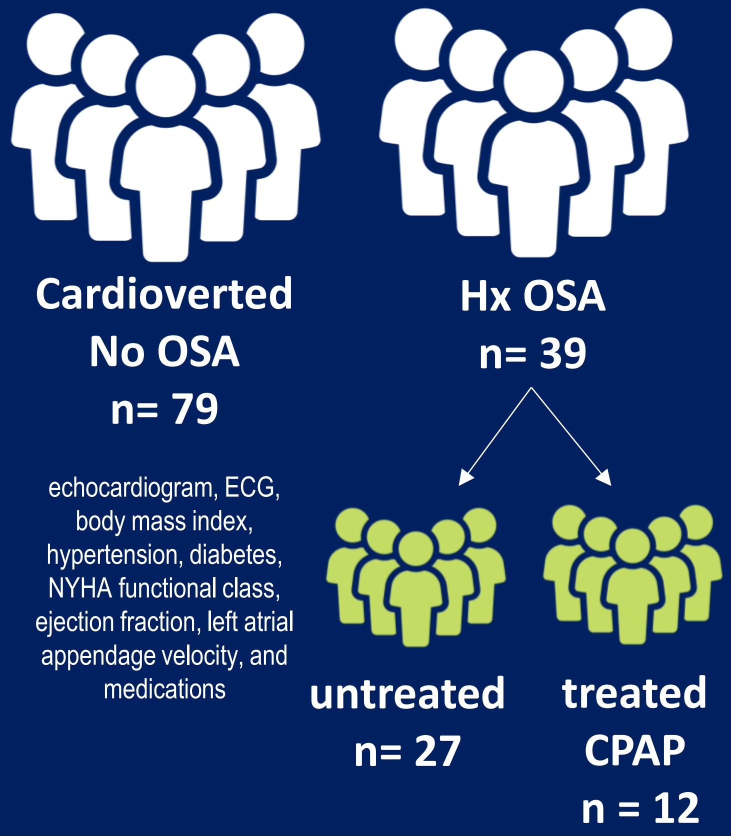
Sanchez de la Torre, M. Obstructive sleep apnea and cardiovascular disease. The Lancet, Respiratory. March 2013, 1(1), 61- 72.

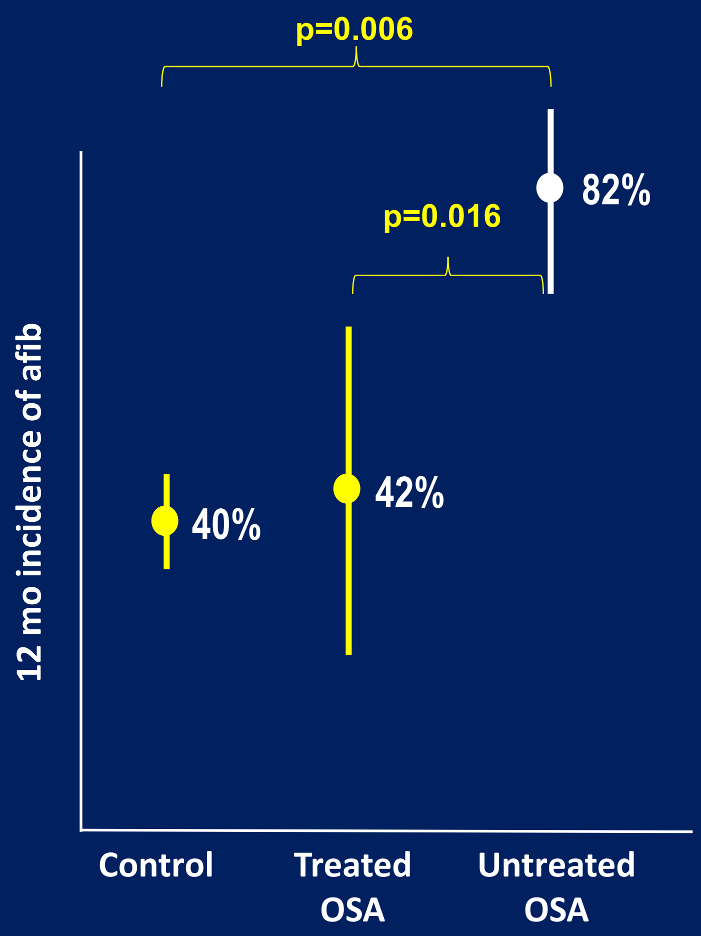
Incidence of atrial fibrillation by OSA severity



Gami, A, Hodge, D, Herges, R. et al. Obstructive Sleep Apnea, Obesity, and the Risk of Incident Atrial Fibrillation. J Am Coll Cardiol. 2007 Feb, 49 (5) 565–571.

Recurrence of atrial fibrillation after cardioversion

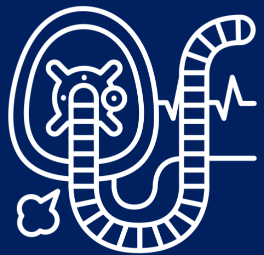




Kanagala R. Obstructive sleep apnea and the recurrence of atrial fibrillation. Circulation. 2003 May 27;107(20):2589-94.

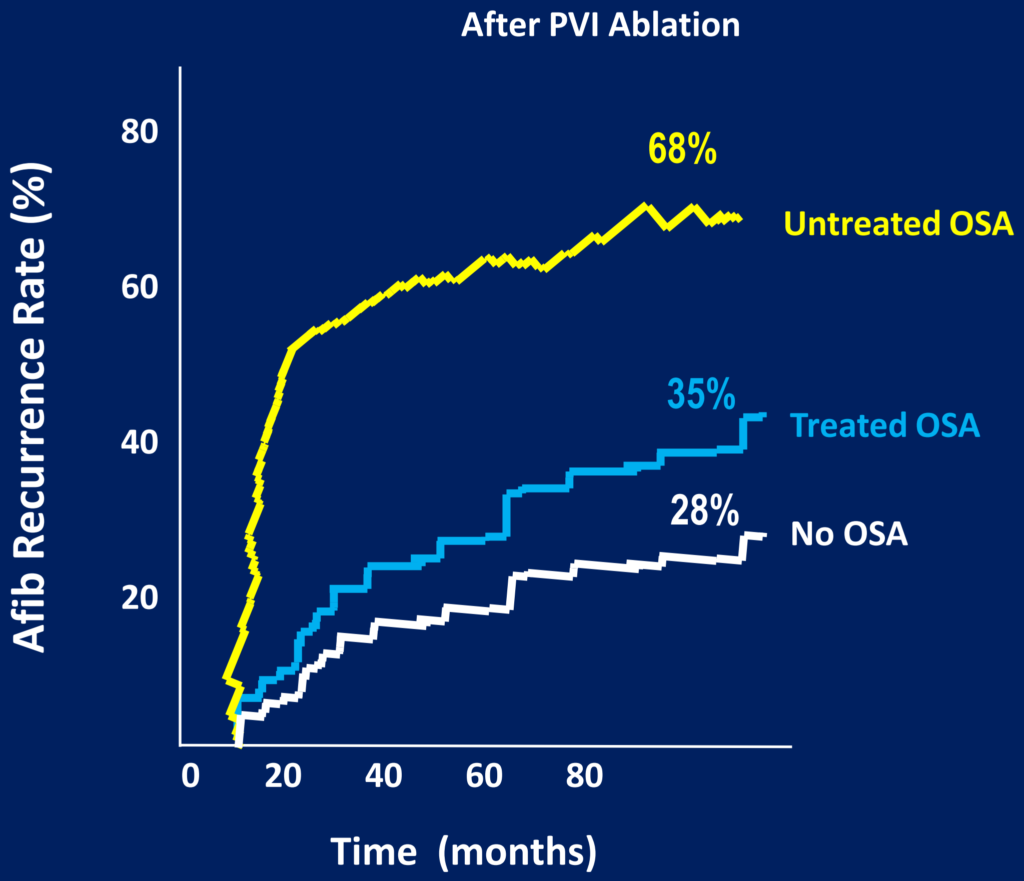
Recurrence of atrial fibrillation after cardioversion vs PV ablation

720 pts
PVI for AF



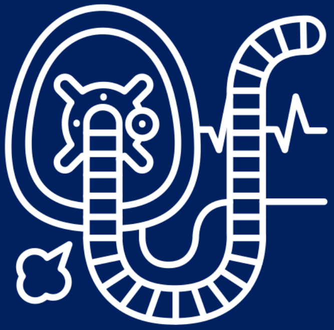
OSA status / CPAP treatment

Cardiac structure
magnetic resonance (CMR)



Neilan TG. Effect of sleep apnea and continuous positive airway pressure on cardiac structure and recurrence of atrial fibrillation. J Am Heart Assoc. 2013 Nov 25;2(6):e000421

Continuous positive airway pressure improves blood pressure and serum cardiovascular biomarkers in obstructive sleep apnea and hypertension



92 subjects (75% male) age 51±8 years and apnea–hypopnea index 40±8 events/h, taking an average of 3.4 antihypertensive drugs) were randomized.

(1:1)

CPAP
n= 46

35% ♂
BMI 30± 5
ESS 16 ± 4
ODI/AHI 45 ± 18

vs.

36% ♂
BMI 31± 5
ESS 6 ± 4
ODI/AHI 41 ± 17

No CPAP
n= 46

Biomarker parameters

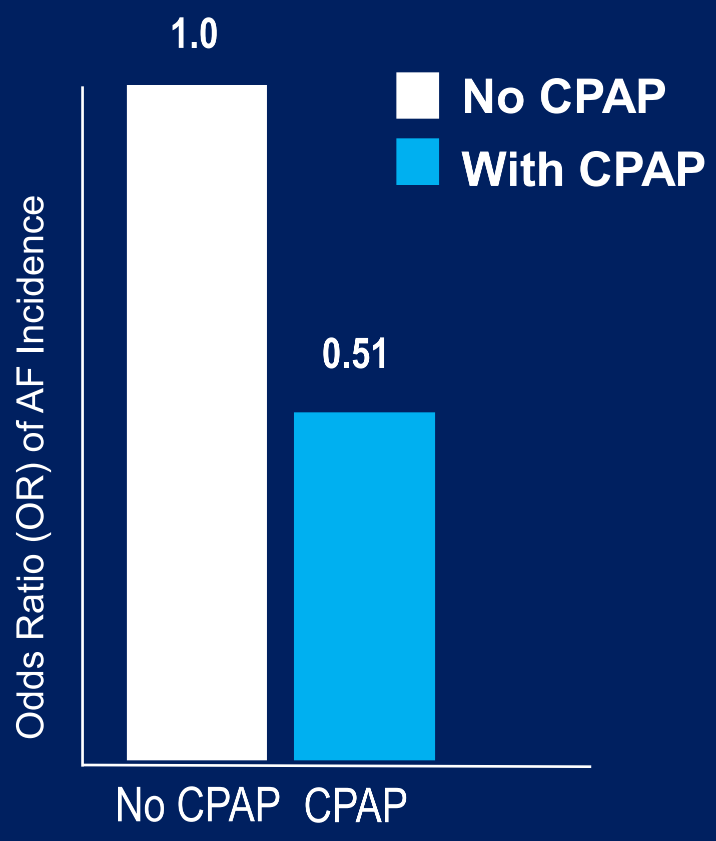
Troponin I pg·mL^{-1}	4.0 (2.5–6.7)	5.0 (3.2–8.7) p=0.006
BNP pg·mL^{-1}	19.4 (10.9–37.8)	19.4 (10.1–33.8) p=0.036
CRP ng·mL^{-1}	5.4 (1.6–8.9)	4.2 (1.5–8.7)
HFABP ng·mL^{-1}	5.5 (2.4–33.4)	4.1 (2.6–8.2)
AOPPs µM	130 (39–495)	270 (34–519)

Serum troponin I (mean difference −1.74 (95% CI −2.97–−0.50) pg·mL−1; p=0.006) and brain natriuretic peptide (−9.1 (95% CI −17.6–−0.6) pg·mL−1; p=0.036) were significantly reduced in CPAP compared with the control group.

Continuous positive airway pressure improves blood pressure and serum cardiovascular biomarkers in obstructive sleep apnea and hypertension Eur Resp Journal 2021; 58 (5):

Meta analysis of CPAP as a therapy for Atrial Fibrillation in OSA

Groups	Odds Ratio (OR) of Developing AF	Interpretation/Result
Non-CPAP Users (Control Group)	1.00 (Baseline Odds)	Represents the expected risk of AF development in untreated OSA patients.
CPAP Users (Intervention Group)	**0.51**	The odds of developing AF were reduced by approximately half (49%) compared to non-users.



The meta-analysis, which included a total of 6,523 patients, concluded that patients treated with CPAP showed a **significant positive reduction in AF complications**.

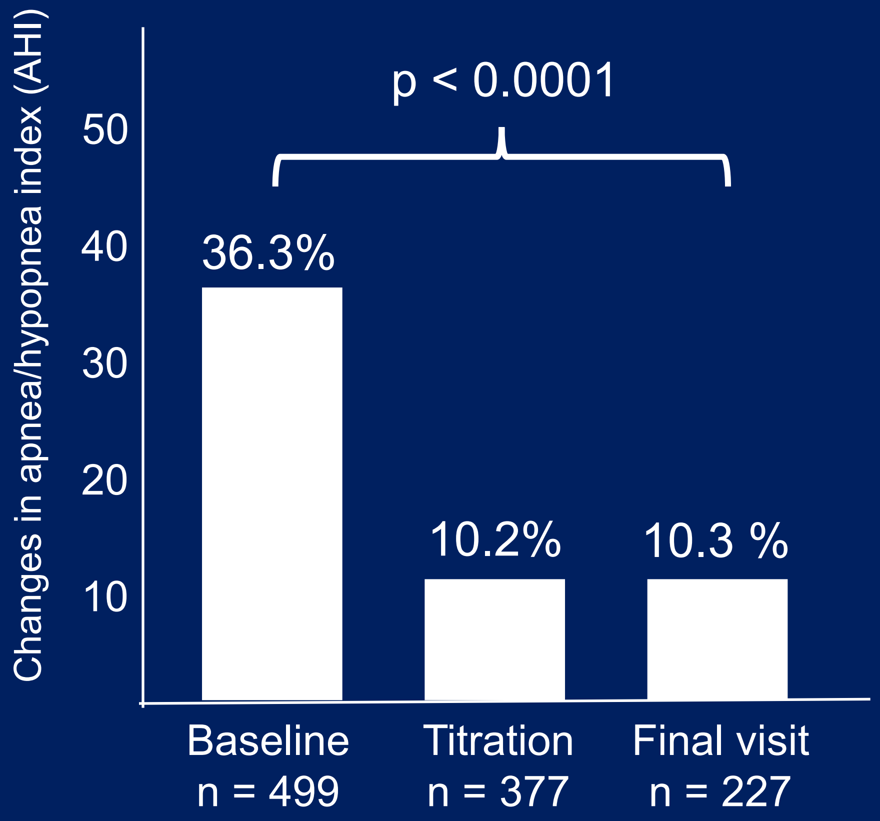
- **CPAP users showed a decrease in the incidence of AF (OR, 0.51)**
- The statistical finding (OR = 0.51; 95% CI, 0.27–0.97; p = 0.04) demonstrates that CPAP is efficacious for mitigating AF in OSA patients

Affas Z. Continuous positive airway pressure reduces the incidence of atrial fibrillation in patients with obstructive sleep apnea: A Meta-Analysis and Systematic Review. Spartan Med Res J. 2022 Sep 6;7(2):34521.

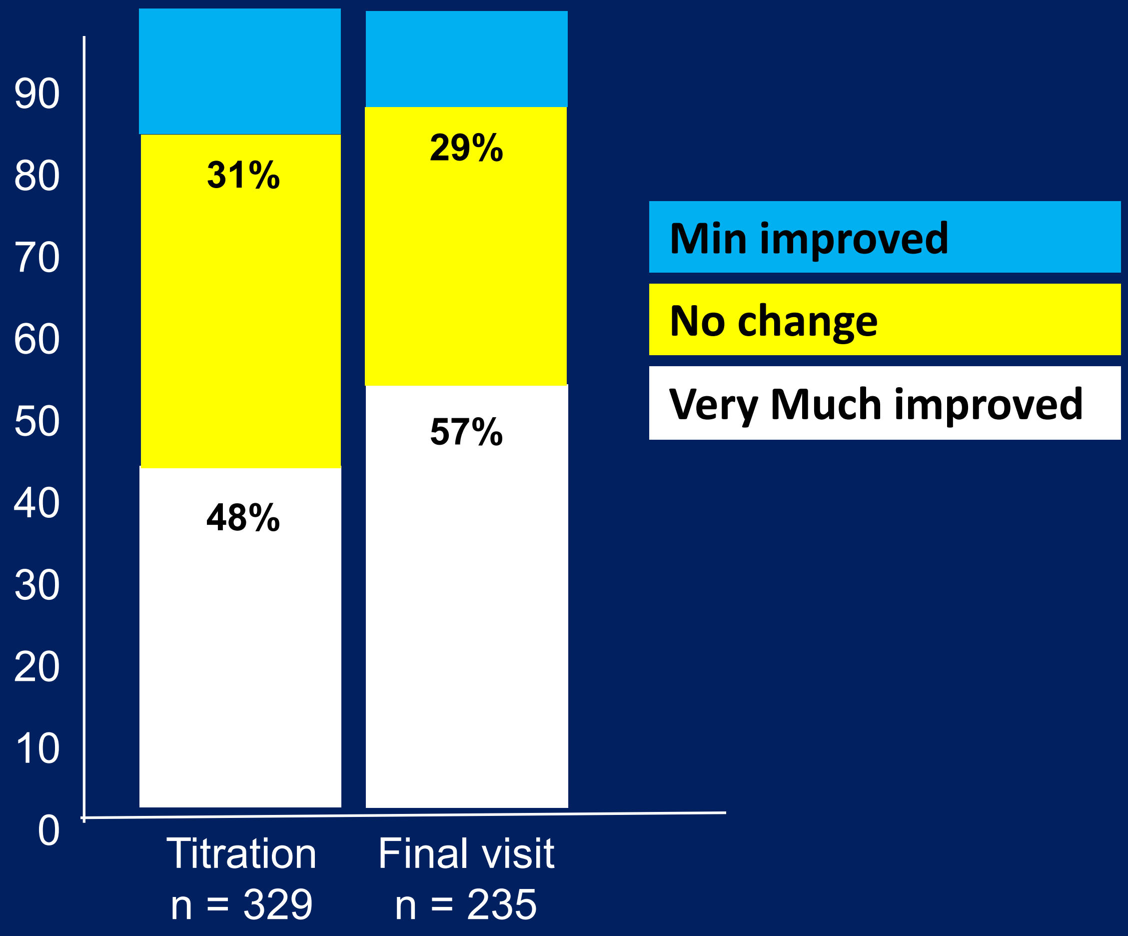
Inspire device for refractory sleep apnea patients

- Candidates:
  - Intolerance of PAP
  - AHI > 15/hr
  - BMI < 35
- Contraindications:
  - Significant central events
  - Paralysis or nerve damage
  - Significant cardiopulmonary disease that make risk of anesthesia prohibitive
  - Devise adherence

Hypoglossal nerve stimulation in OSA. The ADHERE registry



Changes in (AHI) from baseline to post-titration and final visit results



Clinical Global Impression of the Intervention – Improvement (CGI-I) rated by the physician at post-titration and final visit.

Heiser C, Steffen A, Boon M, et al. ADHERE registry investigators. Post-approval upper airway stimulation predictors of treatment effectiveness in the ADHERE registry. Eur Respir J. 2019 Jan 3;53(1):1801405. PMID: 30487205; PMCID: PMC6319796.

Summary

- Sleep apnea is underdiagnosed and untreated
- CPAP is modestly effective in lowering BP, especially in patients with resistant hypertension
- Risk reductions are observed in those who were CPAP adherent
- Despite consistent date in observation studies, RCTs of CPAP shows evidence of reduced Afib recurrence
- Hypoglossal nerve stimulation should not be used as first line therapy
- Medications such as Carbonic anhydrase inhibitor and SSRI may help reduced the burden of OSA
- Weight loss is helping in treating sleep apnea

Pharmacological Therapy in OSA

- Upper air collapsibility
- Arousal
- Respiratory Control
- Sleepiness

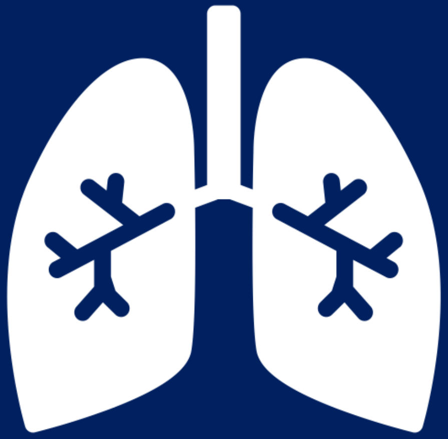
Drug promoting wakefulness

Pitolisant
Solriamfetol
Modafinil
Armodafinil

Drug target Upper airway tone

Atomoxetine/Oxybutynin
Dronabinol
Reboxetine/Butylbromide

Drug target Loop gain



Acetazolamide
Sulthiame

Atomoxetine (Strattera) and Oxybutynin reduced OSA severity

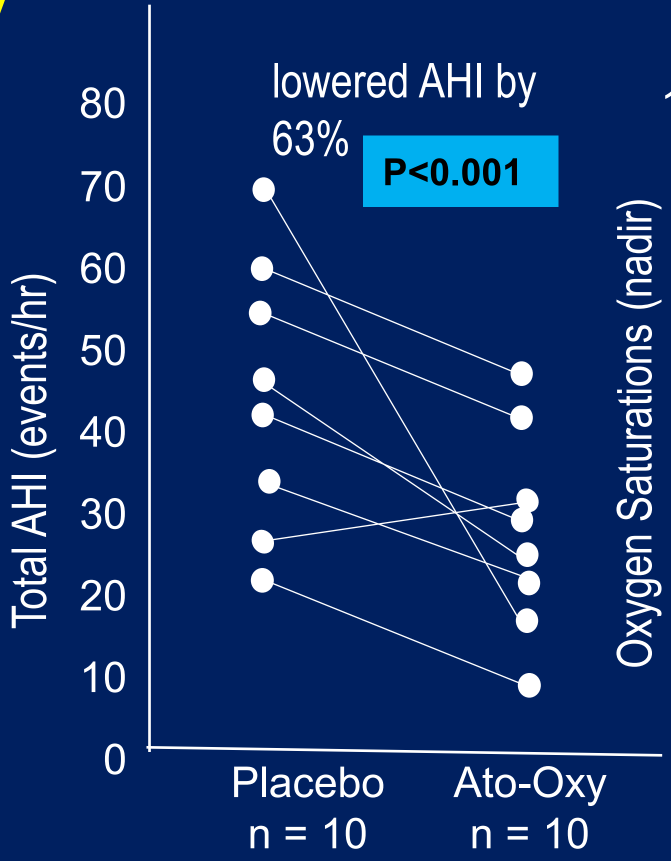
n = 20
randomized, placebo-controlled, double-blind, crossover trial
comparing 80 mg atomoxetine plus 5 mg oxybutynin to control

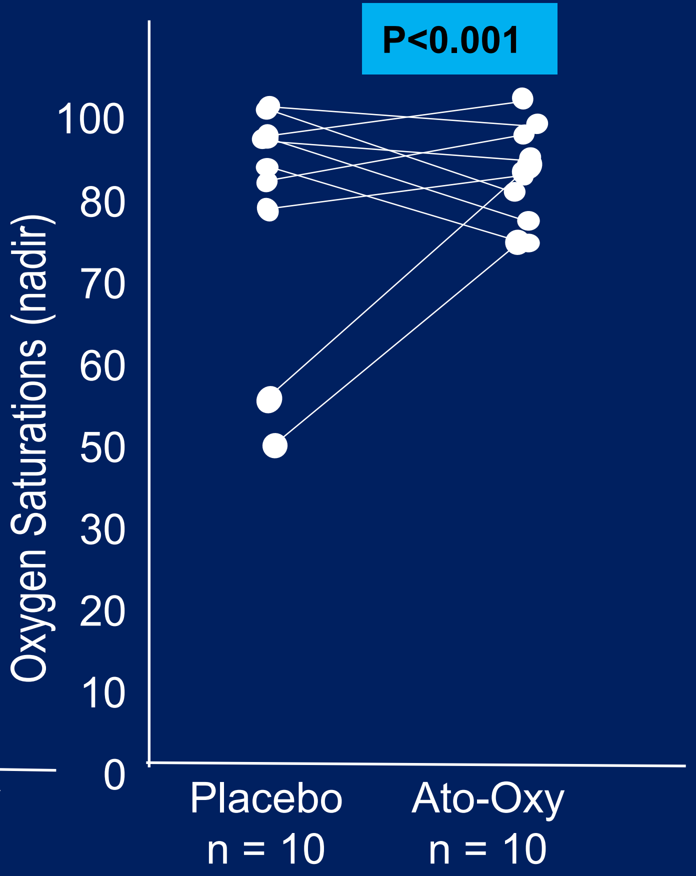
n = 10

n = 10

body mass index was 34.8 (30.0-40.2) kg/m^2

median age was 53 (46-58) years



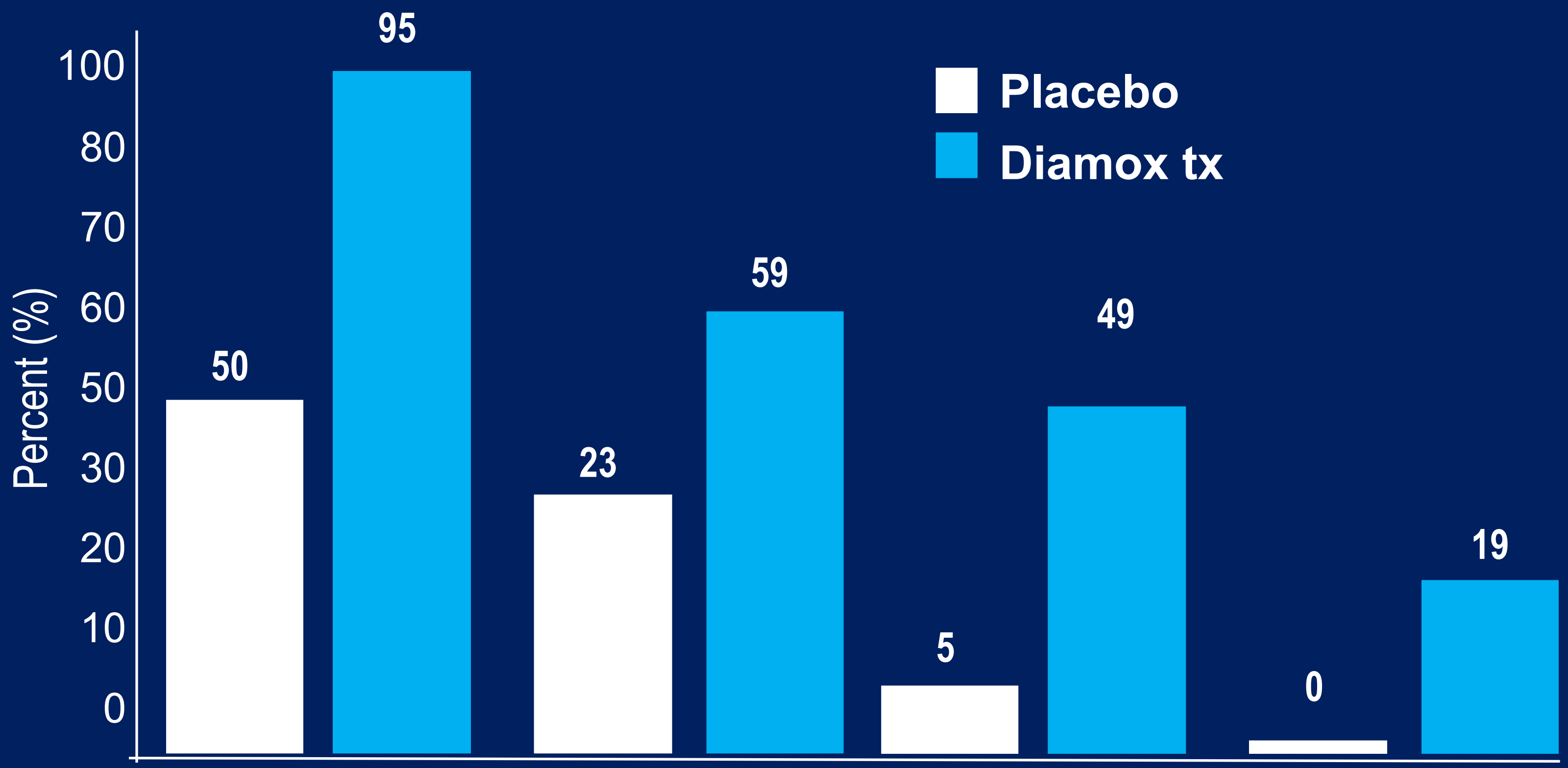


Individual data showing the effect of atomoxetine plus oxybutynin (ato–oxy) on (A) apnea–hypopnea index (AHI). A total of 19/20 subjects had a reduction in AHI

Rosenberg R, Abaluck B, Thein S. Combination of atomoxetine with the novel antimuscarinic aroxybutynin improves mild to moderate OSA. *J Clin Sleep Med*. 2022;18(12):2837–2844.

Carbonic anhydrase inhibition for sleep apnea
Our 4-week, randomized, placebo-controlled, double-blind dose-guiding study

♀♂patients with inability to use CPAP
Age 18 - 75 years,
BMI of ⩾20 kg/m^2 and ⩽35 kg/m^2,
AHI of ⩾15 (mean of two recordings each with an AHI ⩾10 at baseline),
Epworth Sleepiness Scale > 6

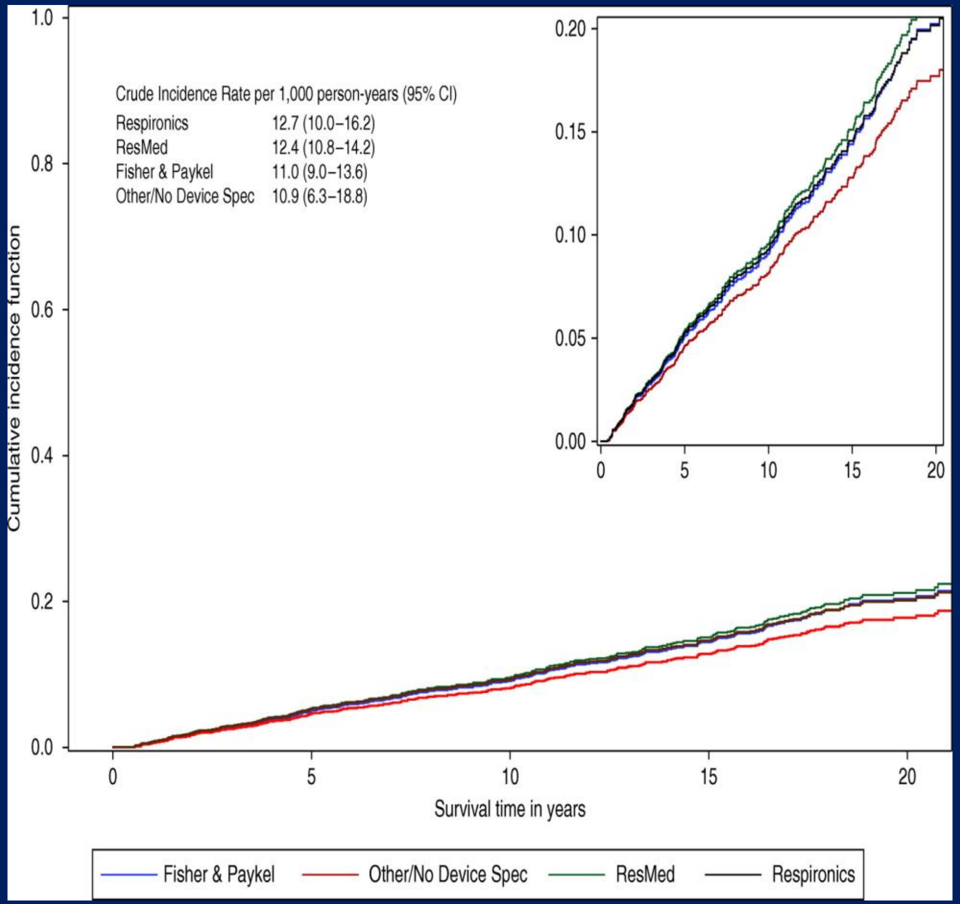


Proportions of patients with reductions of 5%, 30%, 40%, and 60% in the apnea–hypopnea index in the active and placebo groups. Results are from paired night recordings in 46 patients treated with sulthiame (STM) (200 or 400 mg) and 22 patients receiving placebo.

Jan Hedner; Kaj Stenlöf; Ding Zou et al.
Am J Respir Crit Care Med 2051461-1469.

Updates in Recalls : PAP Recall

- Phillips Respironics
- PAP recall worldwide (50% in US)
- Involves approximately 5.5 million machines
  - Started June 2021
- Involves a polyester-based polyurethane foam that acts as a sound insulator which may degrade over-time
  - Headaches, airway irritation, cough, chest pressure/pain, sinus issues
  - ? Cancer ?



Estimated cumulative incidence of incident cancer by positive airway pressure device manufacturer. Crude incidence rate per 1,000 person-years (95% CI): Philips Respironics: 12.7 (10.0–16.2); all non–Philips Respironics devices combined: 11.9 (10.6–13.3). CI = confidence interval; Spec = specification

Kendzerska, Tetyana, et al. "An association between positive airway pressure device manufacturer and incident cancer? A secondary data analysis." American Journal of Respiratory and Critical Care Medicine 204.12 (2021): 1484-1488.