



**Brigham and Women's Hospital**  
Founding Member, Mass General Brigham

# Obstructive Sleep Apnea

**Rohit Budhiraja, MD**

**Director, BWH Sleep Disorders Clinic**

Divisions of Sleep and Circadian Disorders  
And Pulmonary and Critical Care Medicine

Department of Medicine

Brigham and Women's Hospital

**Assistant Professor of Medicine**

**Harvard Medical School, Boston, MA**





- Med School @ **All India Institute of Medical Sciences**, India
- IM Residency @ **Upstate Medical University**, Syracuse, NY
- Pulm/CC Fellowship @ **Tufts Medical Center**, Boston, MA
- Sleep Fellowship @ **Henry Ford Hospital**, Detroit, MI
- **Director, BWH Sleep Disorders Clinic**
- **Clinical and Research interest: OSA epidemiology and outcomes, CPAP**

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- Conflict of Interest: None
  - Disclosures-None





OSA in  
Pulmonary  
Disorders

Endotypes

Less well-  
known  
symptoms

Sleep  
Studies

PAP therapy

Other  
therapies

# Prevalence of OSA: Adults 30–70 years of age

Severity of OSA	Prevalence (%)
None (AHI <5)	67.3
Mild (AHI 5–14 )	21.4
Moderate to Severe (AHI ≥15)	11.3

# Prevalence of Significant SDB in Cardiovascular Disease

30% of cardiac disease patients

50% of CHF patients

60% of acute MI patients

60% of stroke survivors

83% of drug resistant hypertension patients

# Sleep Apnea and Obstructive Lung Disease

## OSA

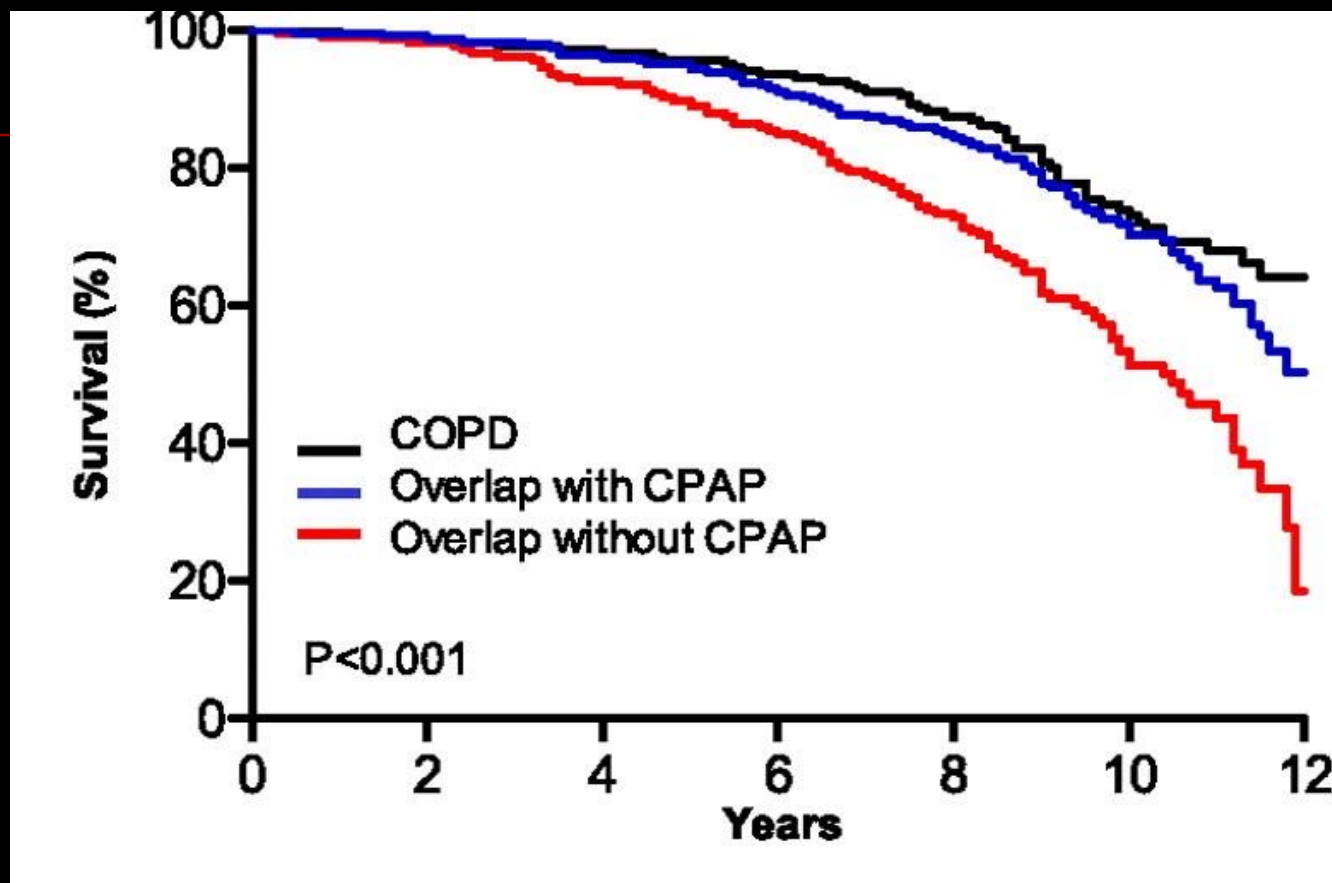
- Hypoxia
- Inflammation
- Worse GERD from negative intrathoracic pressure
- Nasal congestion from PAP therapy
- Poor sleep contributing to mood disturbances: smoking

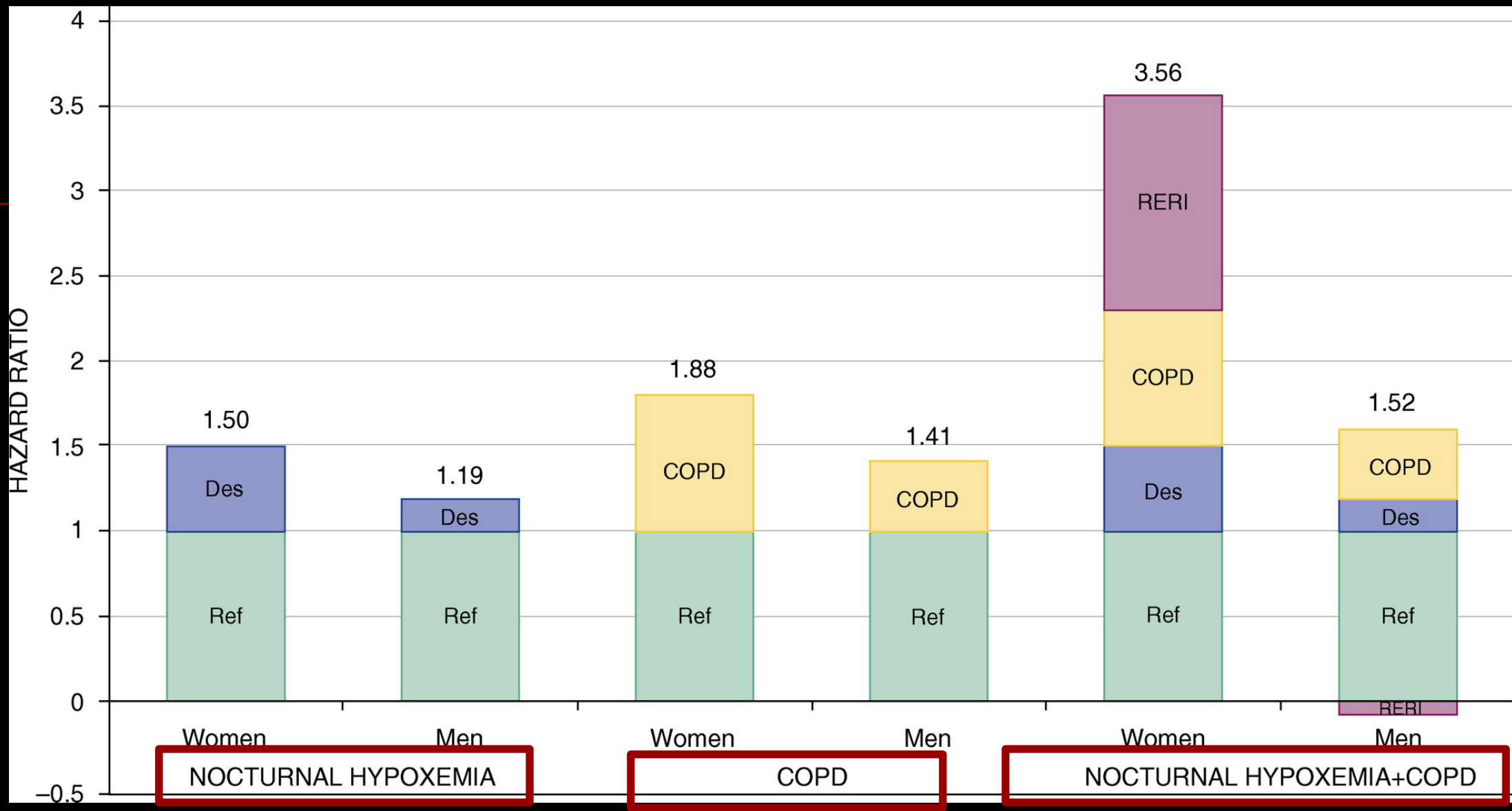
## COPD

- Loss of elastic recoil: increased upper airway collapsibility
- Increased upper airway edema from cor pulmonale

## Asthma

- Augmented inspiratory negative intraluminal pressure: pharyngeal airway collapse





# Treatment of Nocturnal Asthma

Optimize medical management (Steroids, LABA, LTI).

**Evaluate for and treat Sleep Apnea.**

Diagnose and treat GERD.

Diagnose and treat rhinitis.

Risk factor modification

# Idiopathic Pulmonary Fibrosis

AHI was <5 in  
14 (41%)

AHI 5–15 in 15  
(44%)

59%

AHI  $\geq$ 15/h in 5  
(15%)

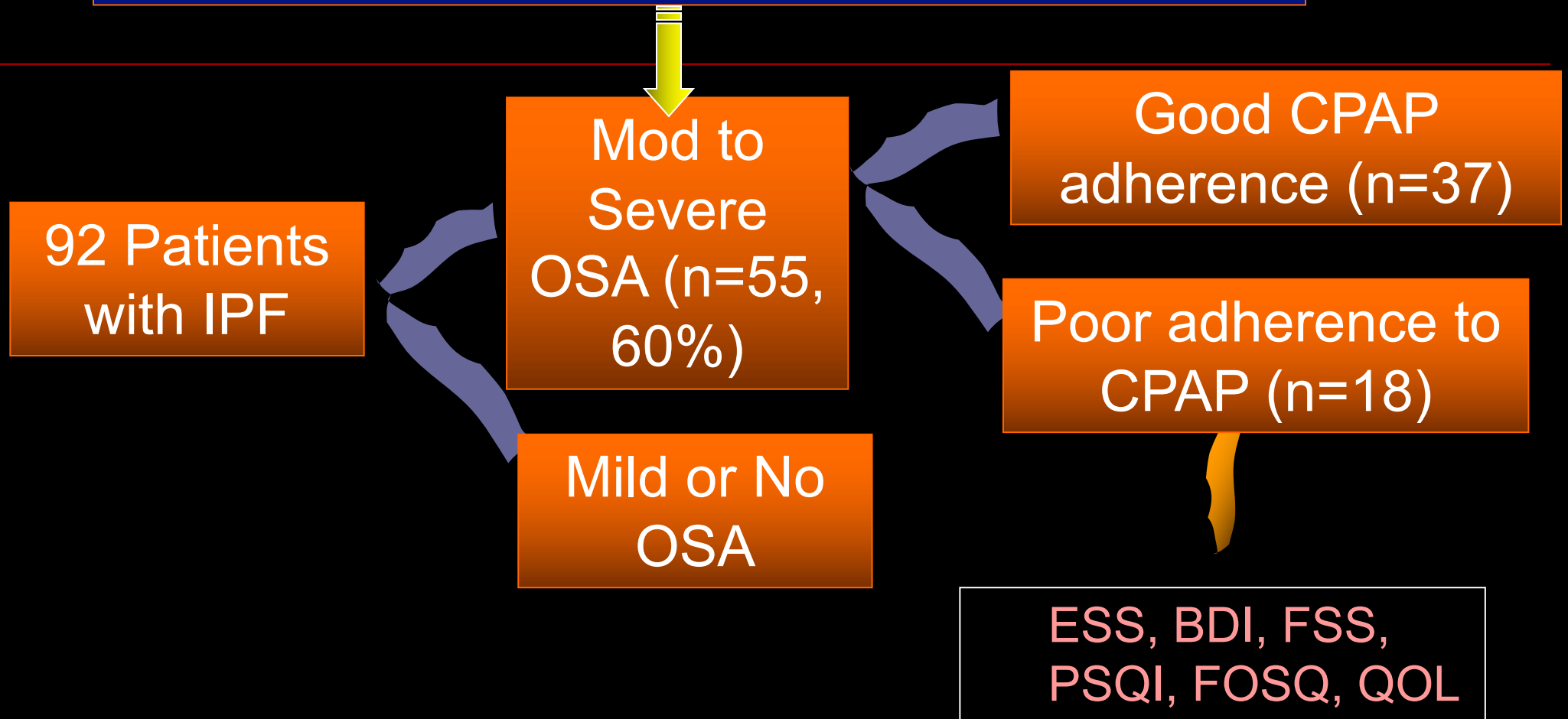
AHI was <5 in  
14 (12%)

AHI 5–15 in 10  
(20%)

88%

AHI  $\geq$ 15/h in 34  
(68%)

Comparison of outcomes after 1 year  
based on adherence to CPAP therapy



# Good CPAP compliance group

ESS Epworth  
Sleepiness Scale

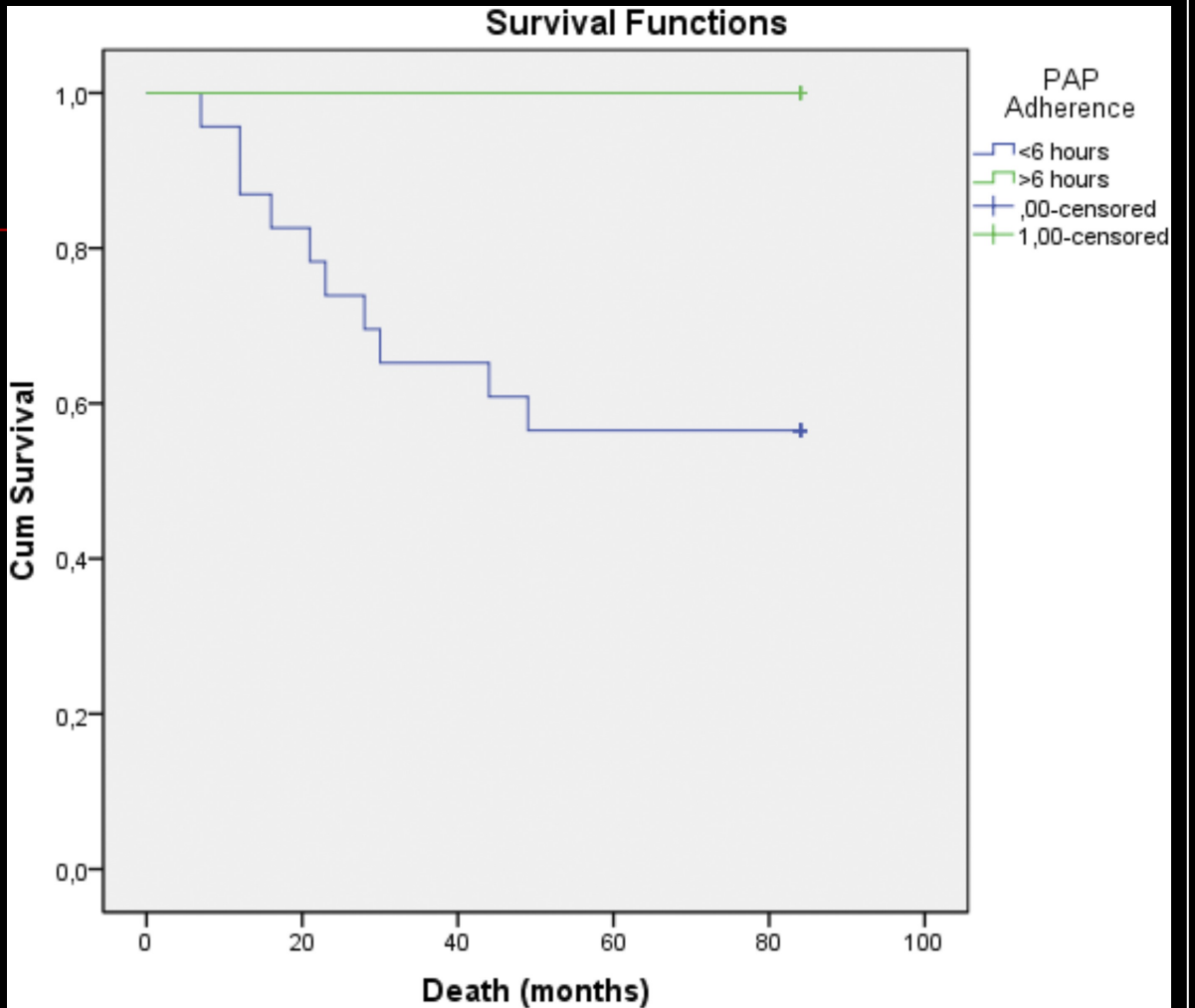
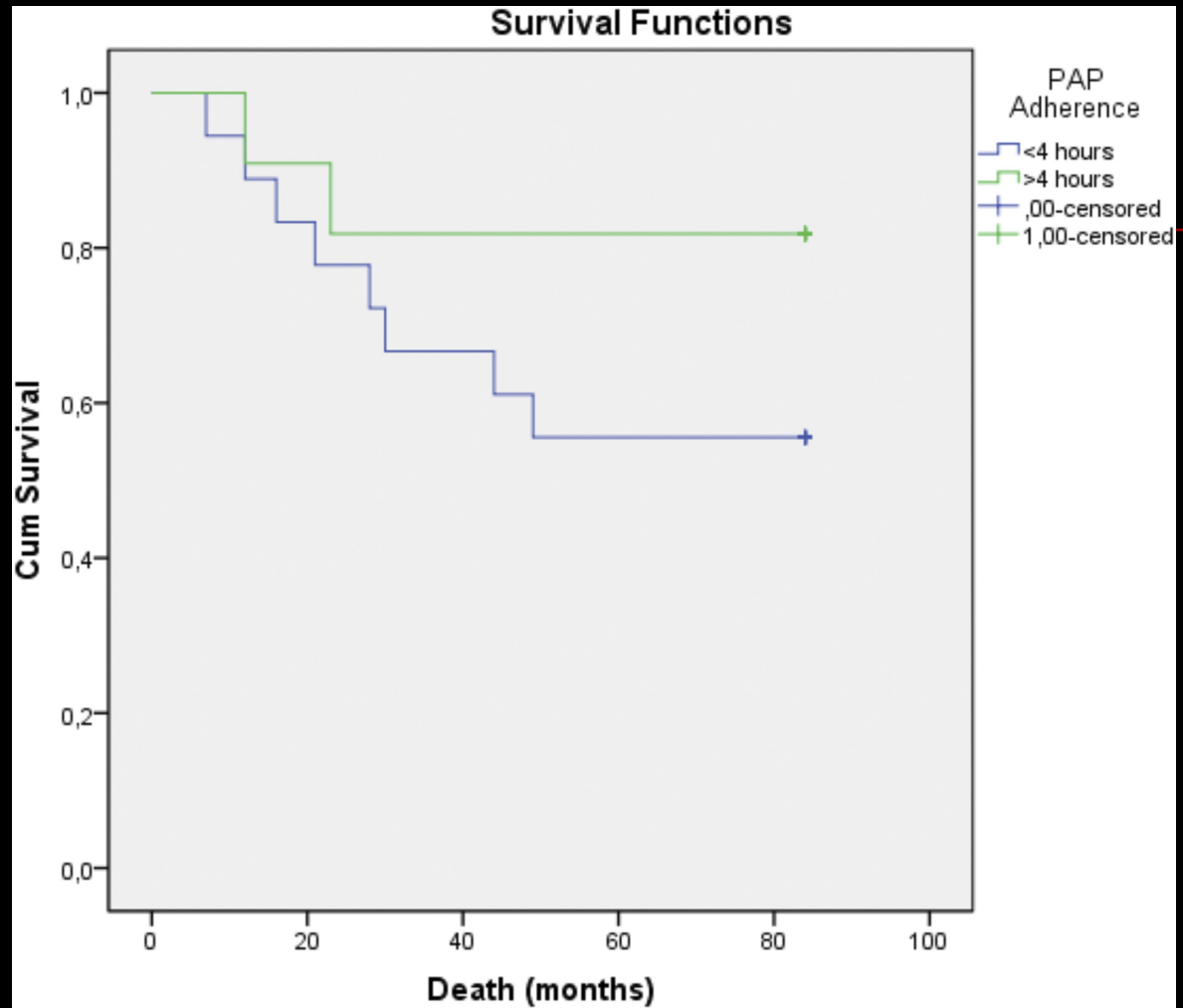
BDI Beck Depression  
Inventory

PSQI Pittsburgh Sleep  
Quality Index

FSS Fatigue Severity Scale

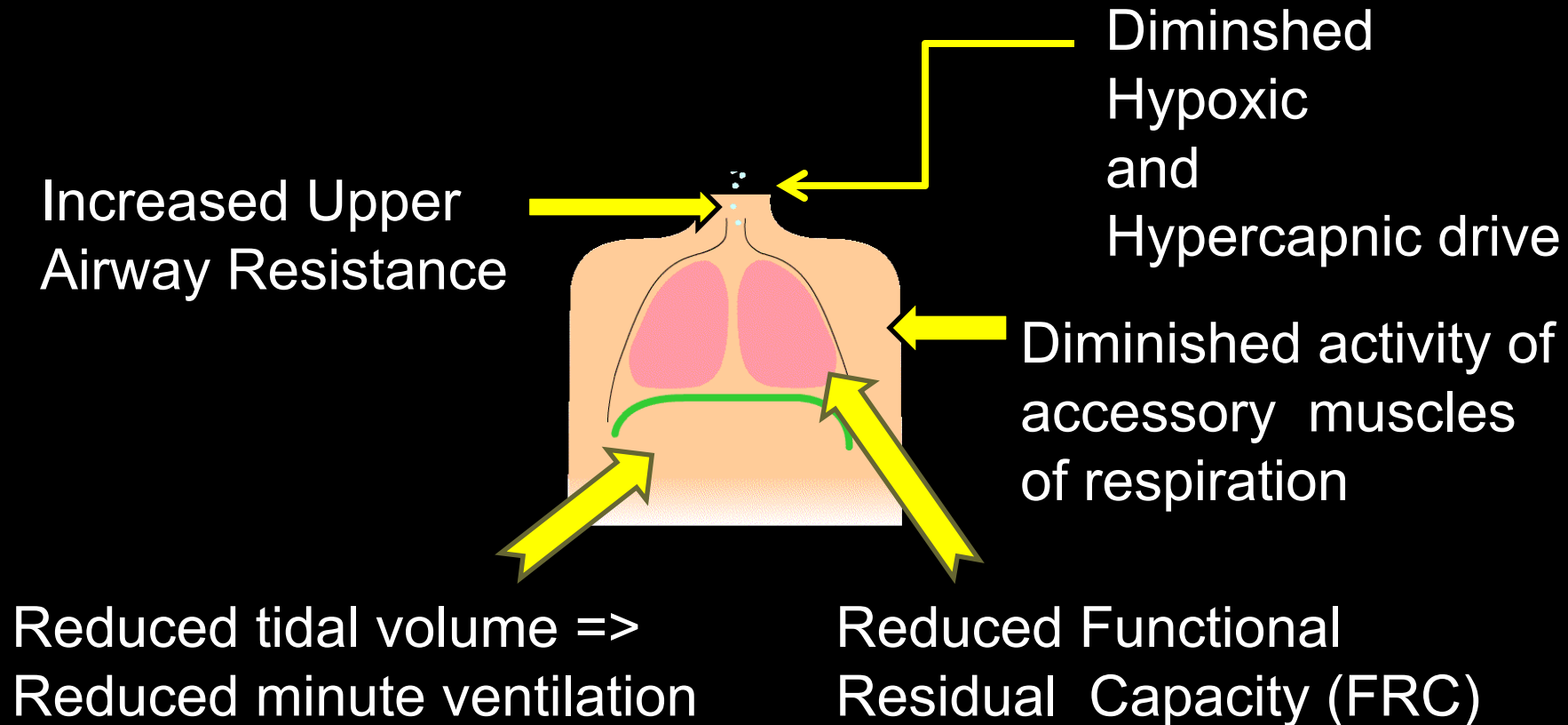
SF-36 Short-Form 36 Health  
Survey

FOSQ Functional Outcomes  
of Sleep Questionnaire

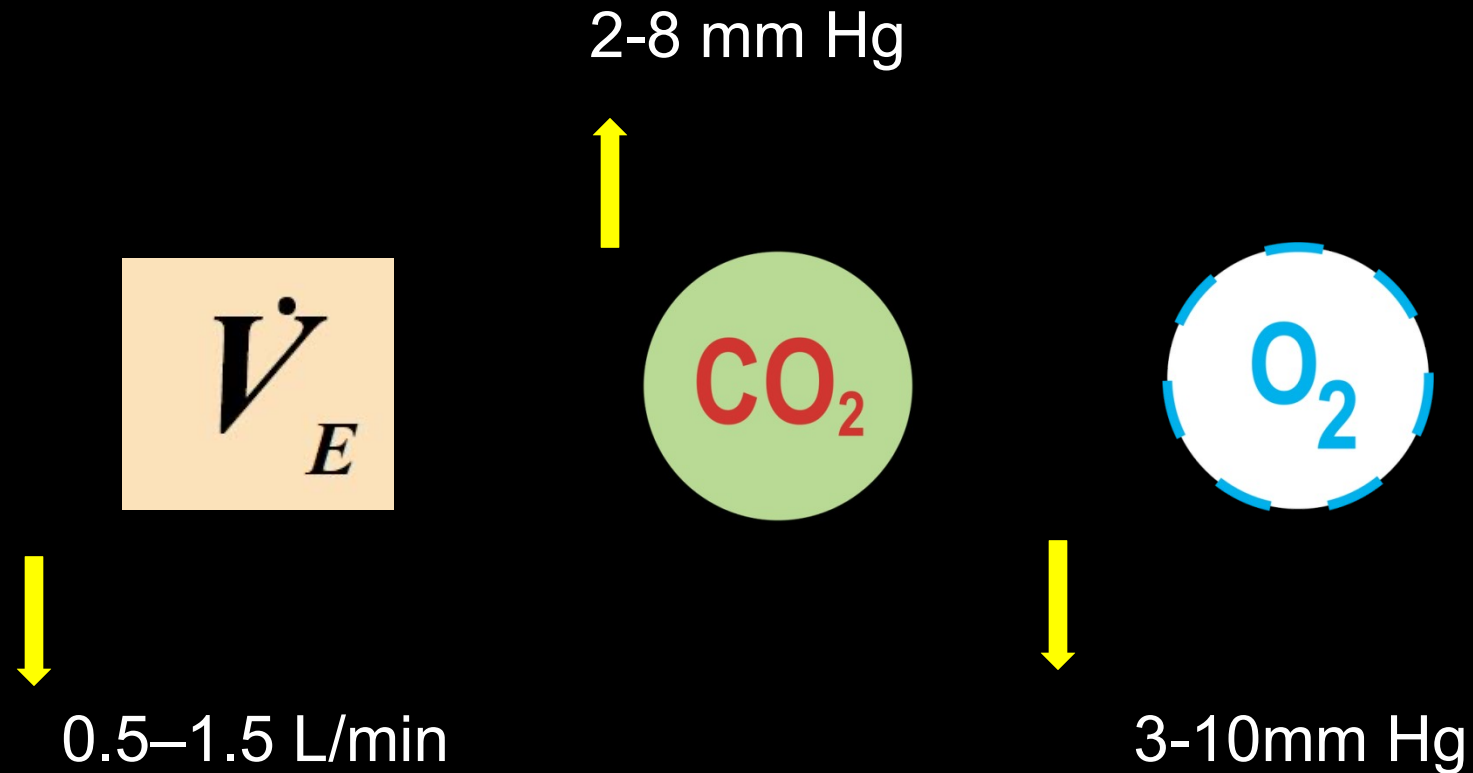


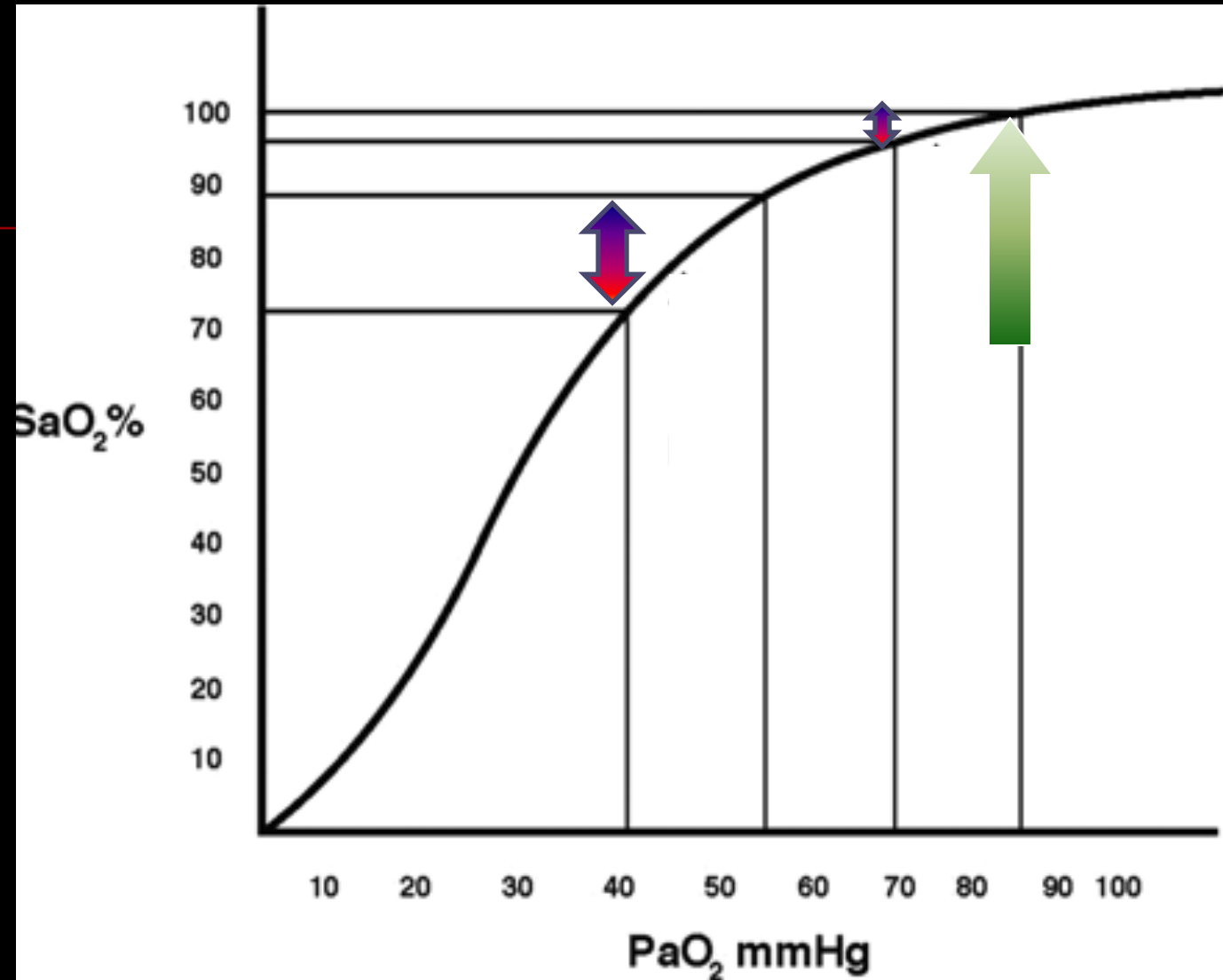
Papadogiannis, George, et al. "Patients with idiopathic pulmonary fibrosis with and without obstructive sleep apnea: differences in clinical characteristics, clinical outcomes, and the effect of PAP treatment." *Journal of Clinical Sleep Medicine* 17.3 (2021): 533-544.

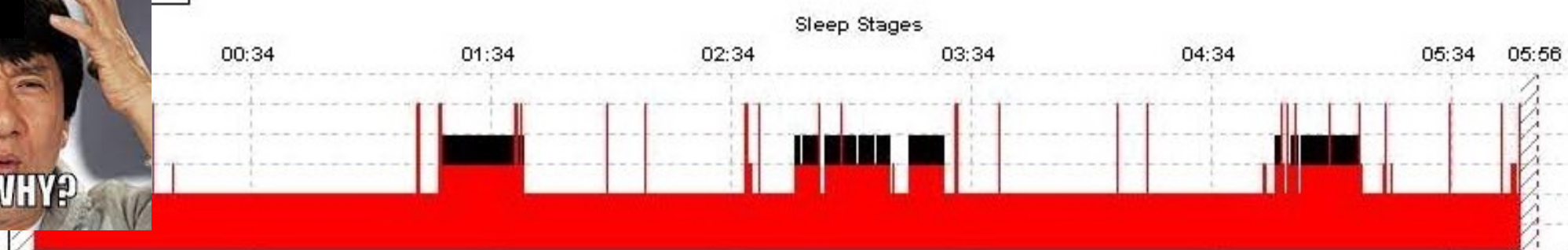
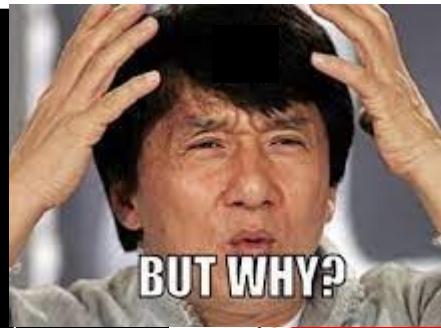
# Physiological Changes during Sleep



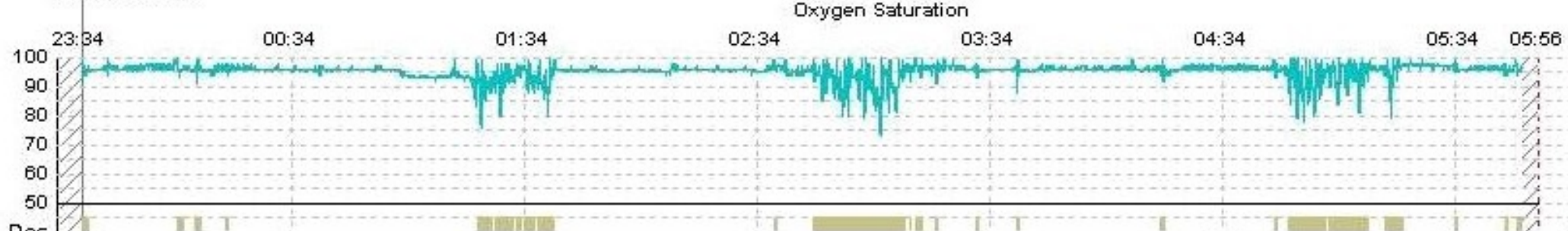
# Changes during Sleep



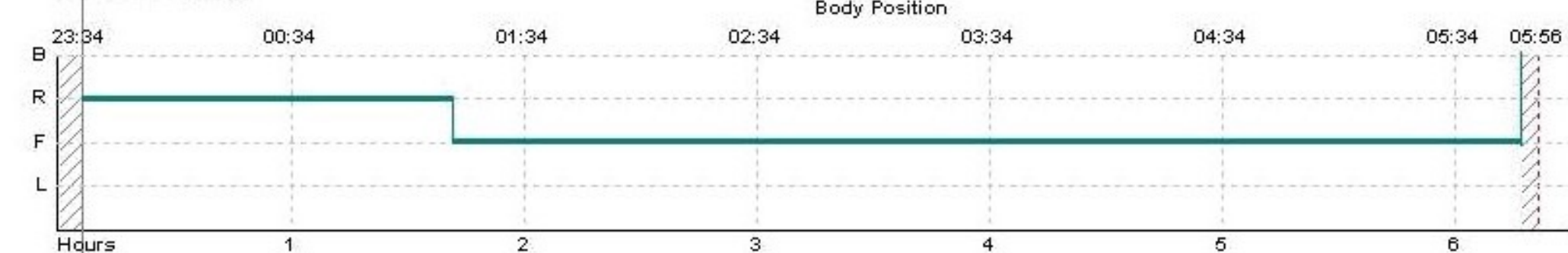




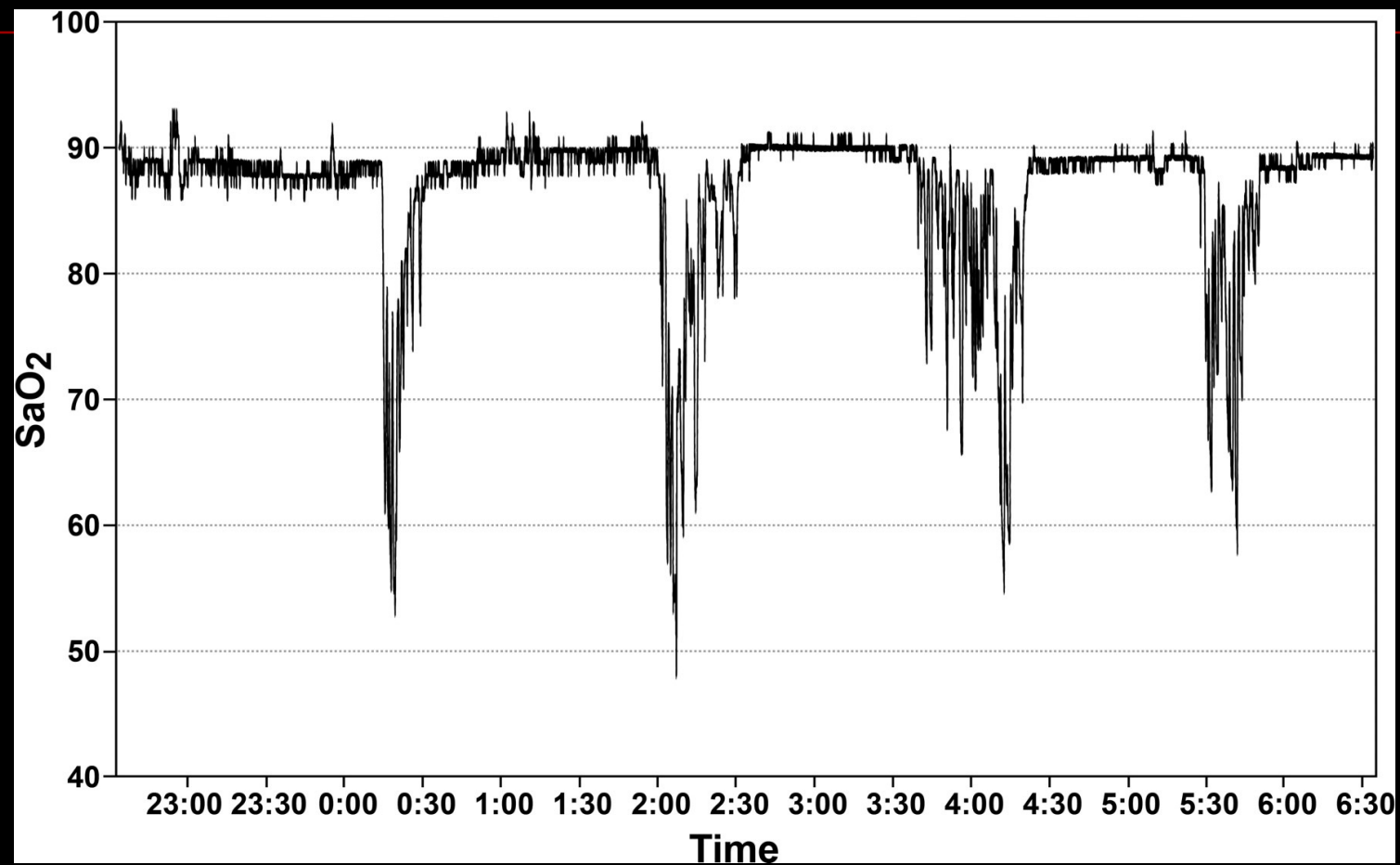
Hours 1 2 3 4 5 6  
Epoch: 13  
Stage: Awake



Des  
Hours 1 2 3 4 5 6  
Epoch: 13  
Max: 99% Min: 95%



# Nocturnal Oximetry in Lung Disease



# Nocturnal Hypoxemia



Decreased daytime energy levels



Impaired social and physical functioning

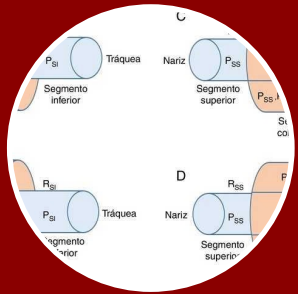
# Obesity and OSA

10% weight gain: 32% increase in AHI

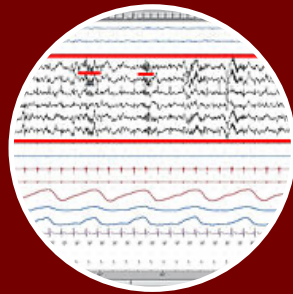
10% weight loss: 26% decrease in AHI

20-40% are not obese

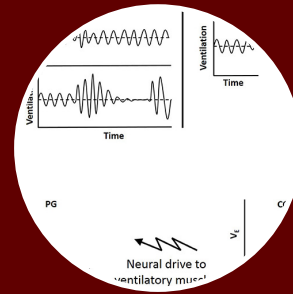
# Sleep Apnea Endotypes (PALM)



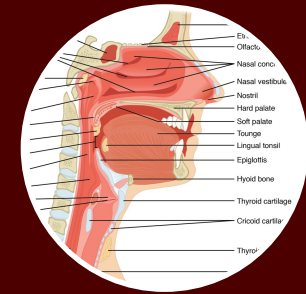
Pharyngeal  
Critical Closing  
**P**ressure ( $P_{crit}$ )



(Low) **A**rousal  
Threshold



(High) **L**oop  
Gain

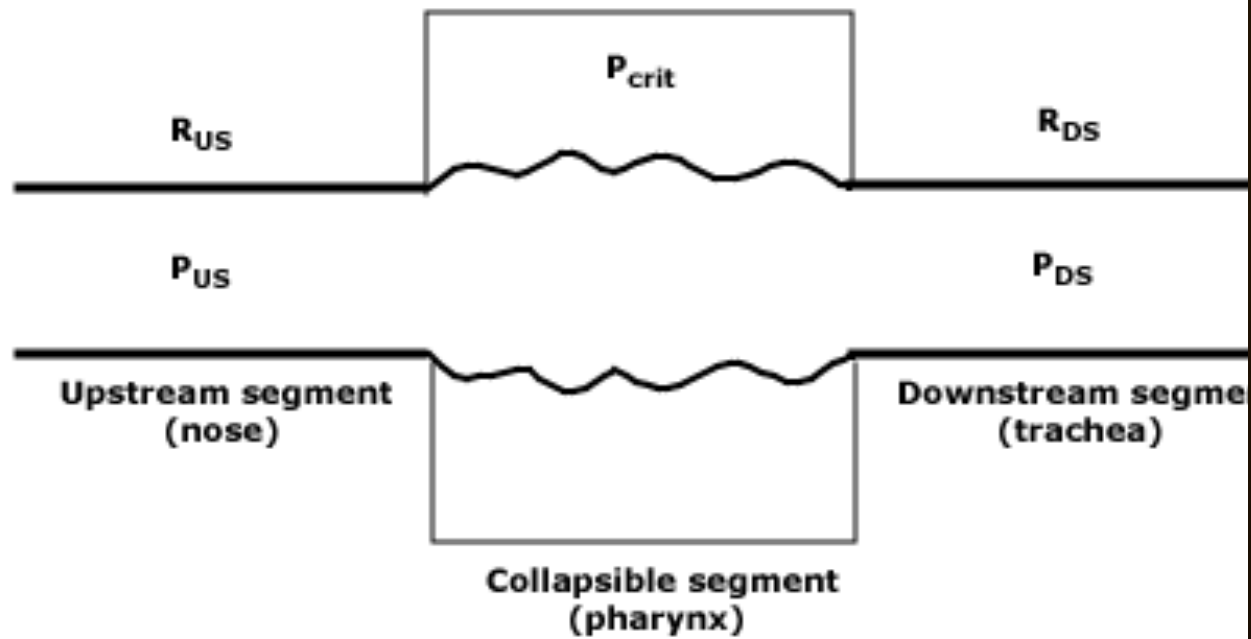


(Poor) Upper  
Airway **M**uscle  
Function

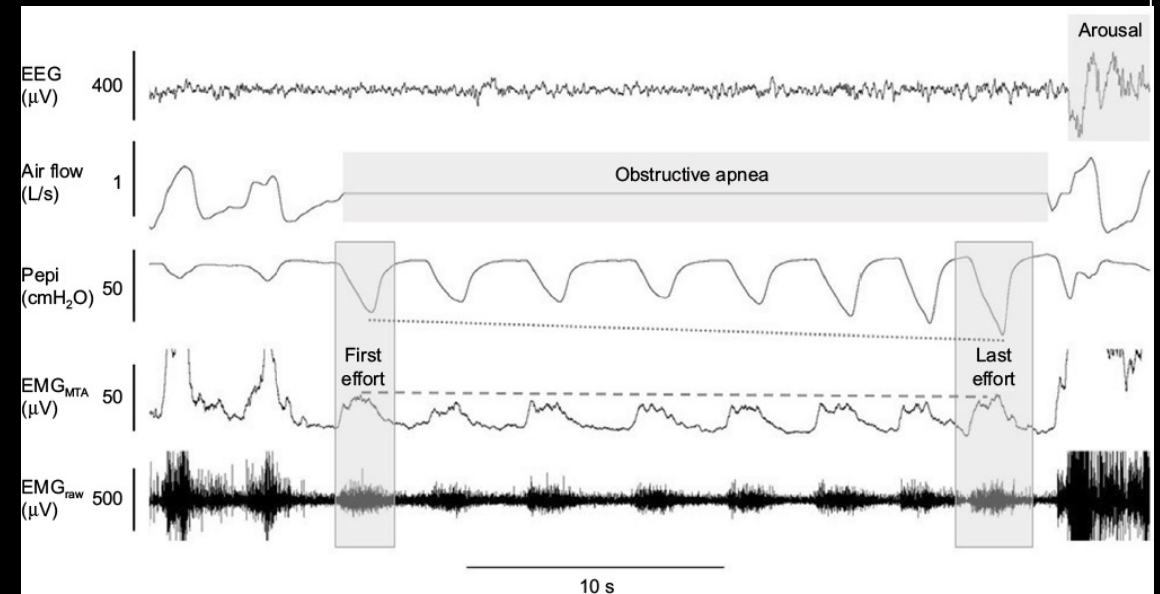
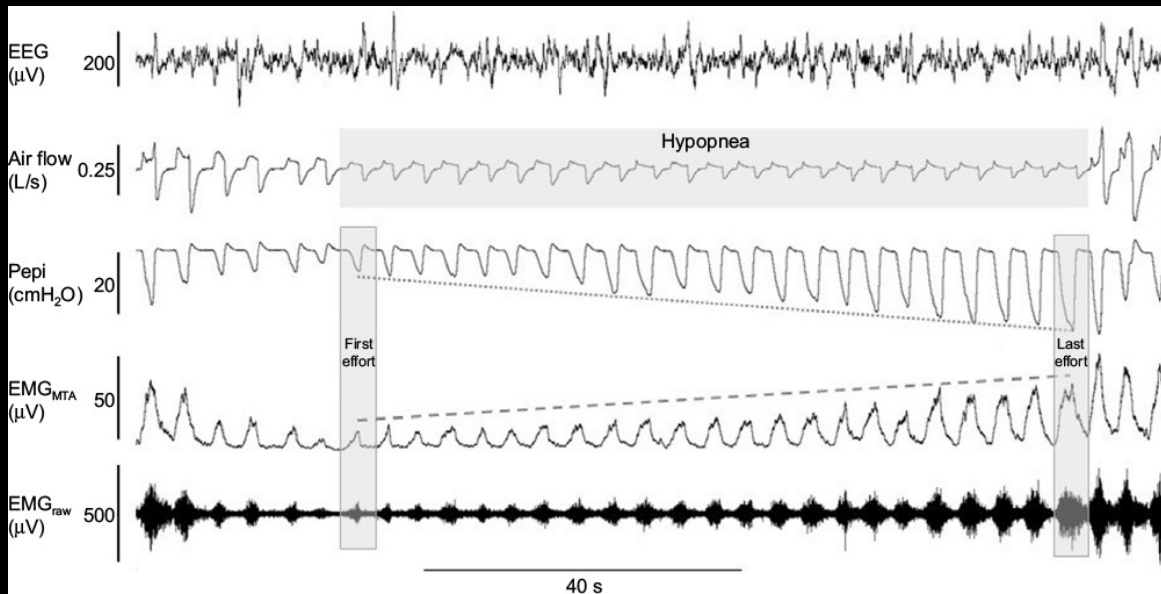


# P<sub>crit</sub>

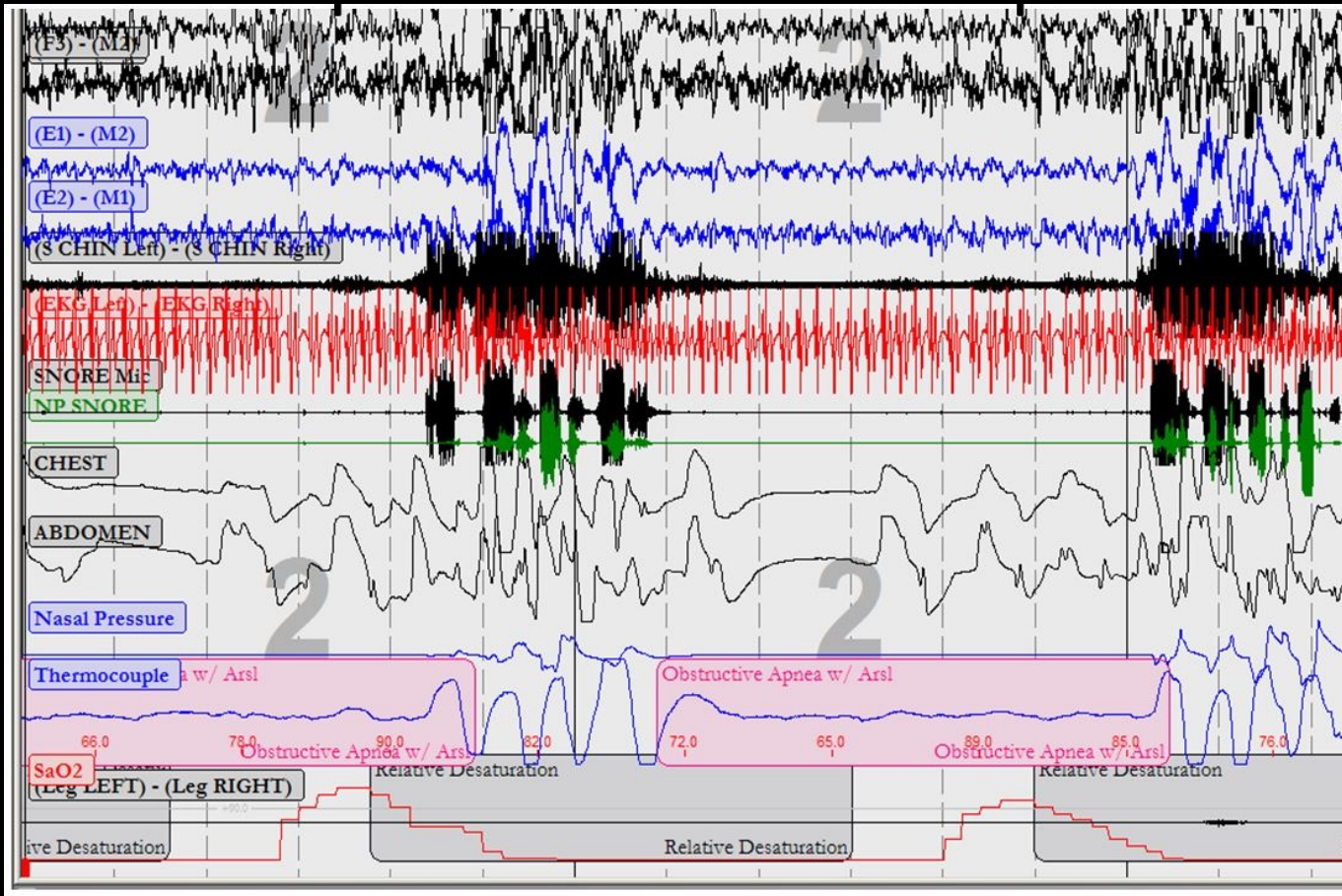
Starling Resistor Model of Upper Airway



# Normal versus diminished genioglossus activation



# Low Arousal Threshold



Prior to GG  
recruitment

Prevents deeper,  
more stable stages

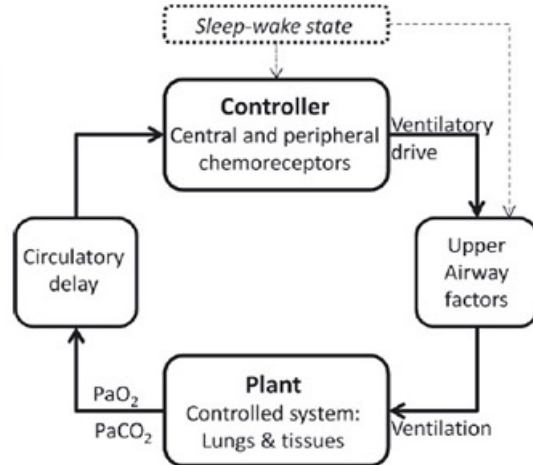
Destabilizes  
breathing patterns

# Loop Gain

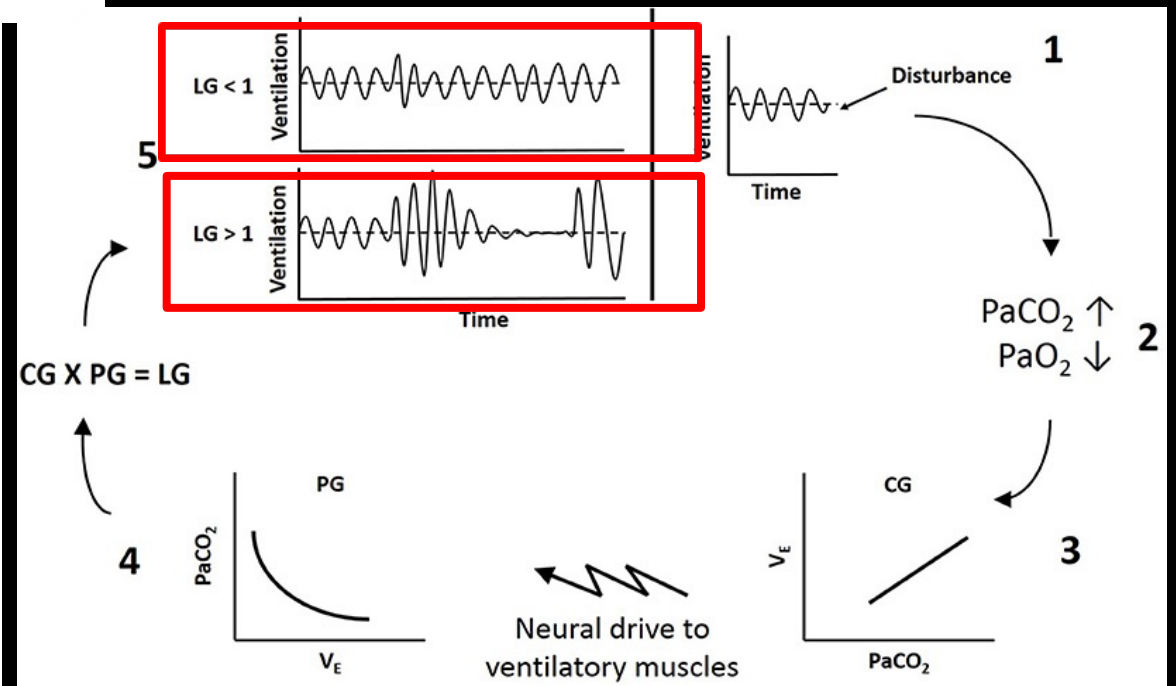


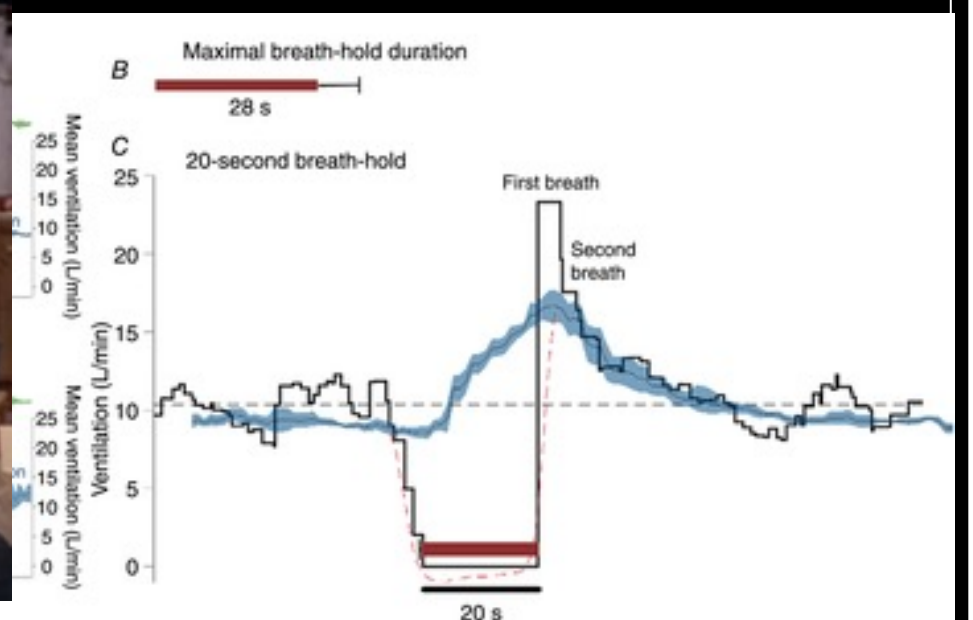
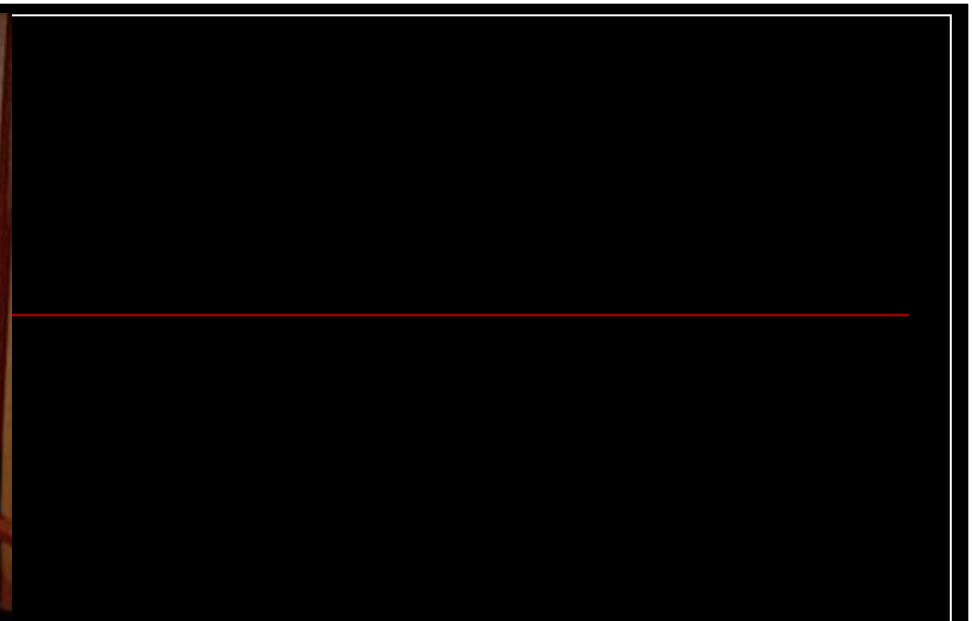
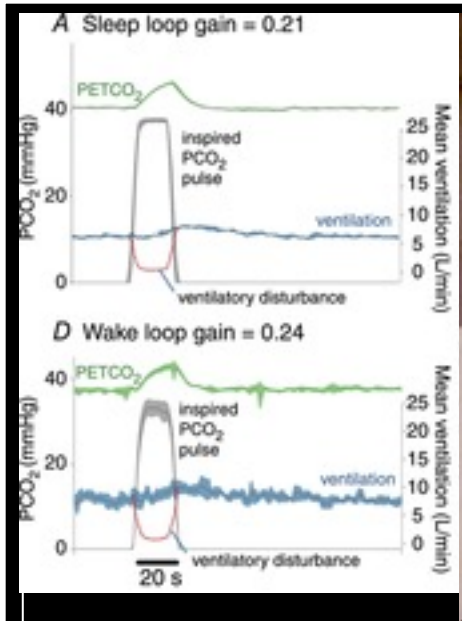
Loop-gain theory:

$$\text{Loop gain} = \frac{\text{Response to disturbance}}{\text{Disturbance}}$$



Burgess KR. J Physiol. 2012;590:1781-1782.





Messineo L, Taranto-Montemurro L, Azarbarzin A, Oliveira Marques MD, Calianese N, White DP, Wellman A, Sands SA. Breath-holding as a means to estimate the loop gain contribution to obstructive sleep apnoea. *The Journal of physiology*. 2018 Sep;596(17):4043-56.

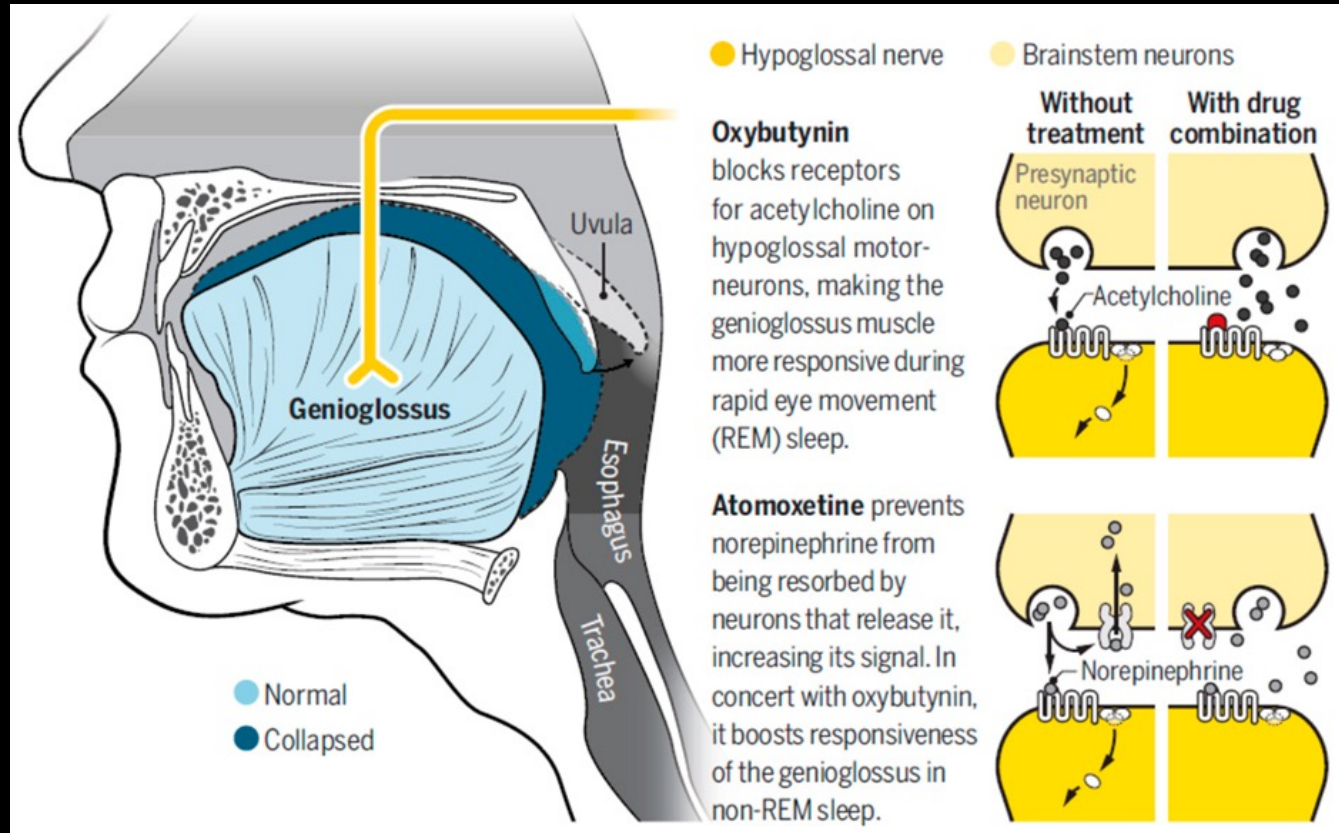
## Arousal Threshold

- Hypnotics
- ?Treat underlying anxiety/  
depression/PTSD

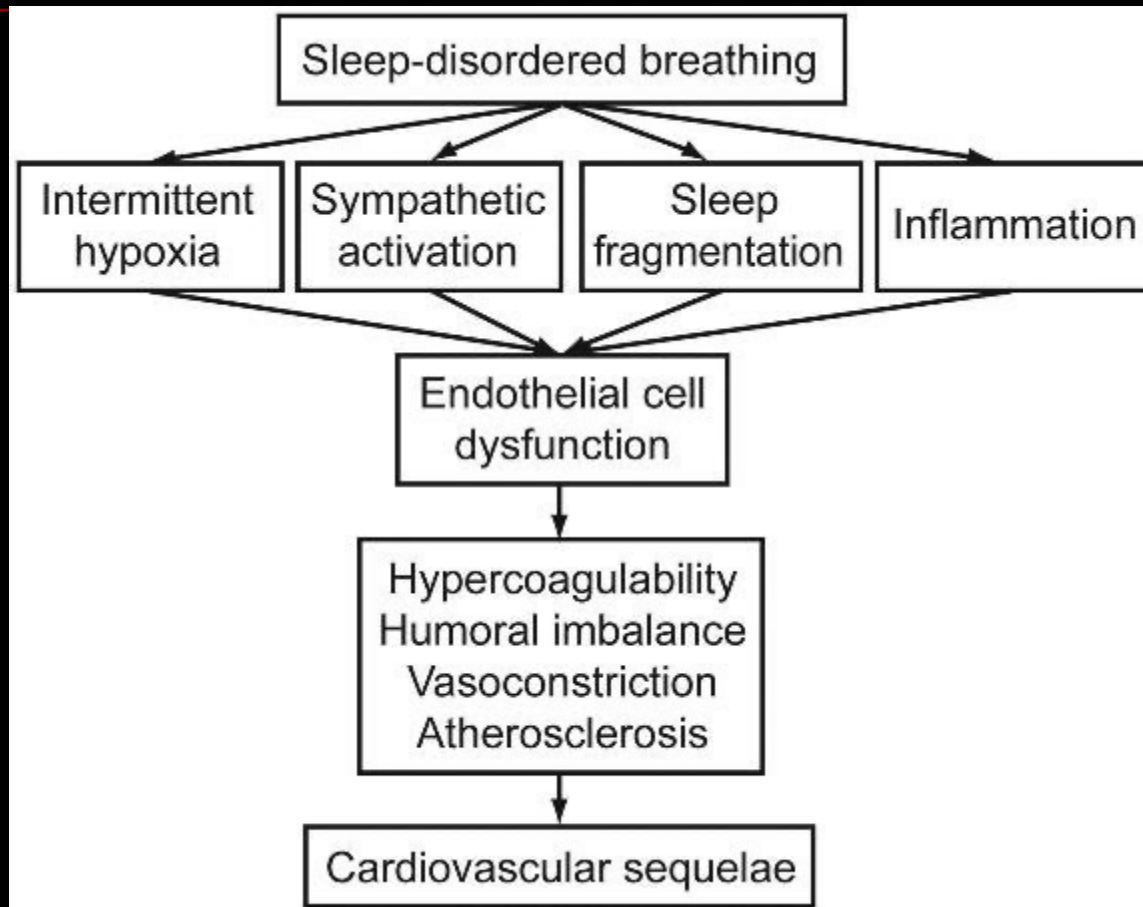
## Loop Gain

- Acetazolamide
- Oxygen
- Non vented masks
- ?PAP

# Upper Airway Muscle Dysfunction



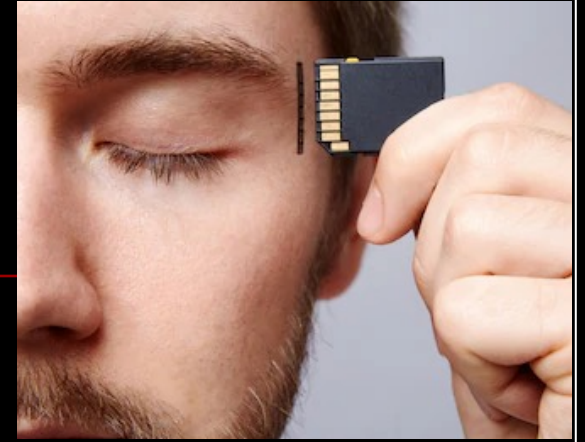
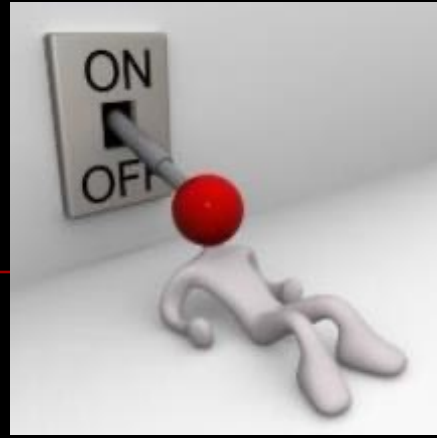
# Sleep-Disordered Breathing and Cardiovascular Disorders



Budhiraja, Rohit, and Stuart F. Quan "Sleep-disordered breathing and cardiovascular disorders." *Respiratory care* 55.10 (2010): 1322-1332.

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# Symptoms of OSA



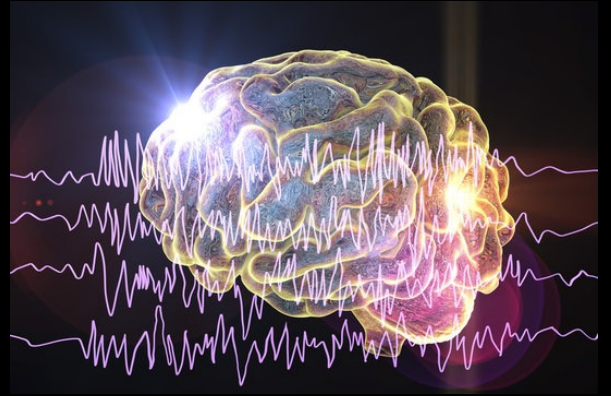
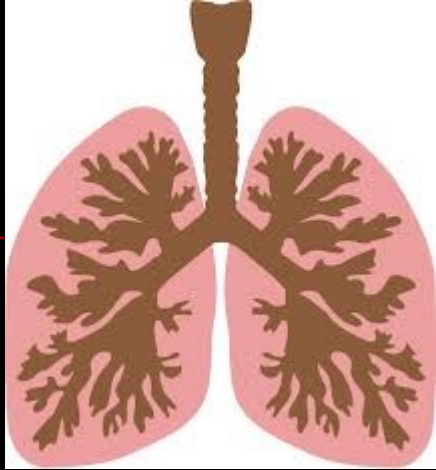
Type 1: full attended PSG ( $\geq 7$  channels) in-lab

Type 2: full unattended PSG ( $\geq 7$  channels)

Type 3: limited channel devices (usually using 4–7 channels)

Type 4: limited channel devices using oximetry and/or fewer of the parameters





# Home Study

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**Non-inferior outcomes in  
CPAP acceptance and  
functional improvements**

# Apnea-Hypopnea index (AHI)

AHI (/hr)	Severity
5-15	Mild
>15-30	Moderate
>30	Severe



Verdict on  
treating Mild  
Sleep Apnea?

# Treatment of Mild OSA

Treatment may improve **sleepiness** and **quality of life**.

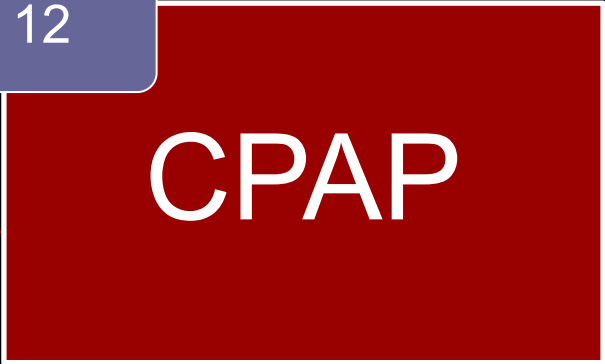
Limited or inconsistent evidence pertaining to the impact of therapy on **neurocognition, mood, vehicle accidents, cardiovascular events, stroke, and arrhythmias**.

Chowdhuri, S., Quan, S.F., Almeida, F., Ayappa, I., Batool-Anwar, S., Budhiraja, R., Cruse, P.E., Drager, L.F., Griss, B., Marshall, N. and Patel, S.R., An official American Thoracic Society research statement: impact of mild OSA in adults. *American journal of resp and critical care medicine*, 2016 193(9), e37-e54.



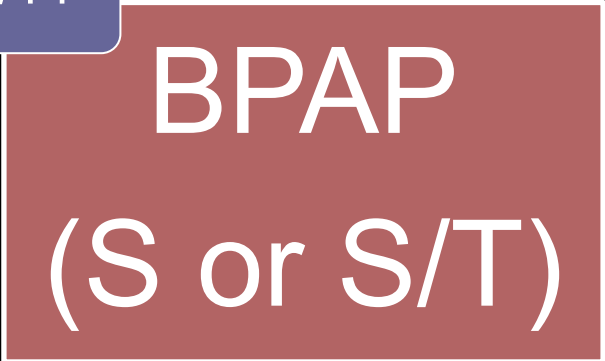
**A new guest in the bedroom...**

12

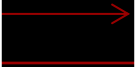


5-15

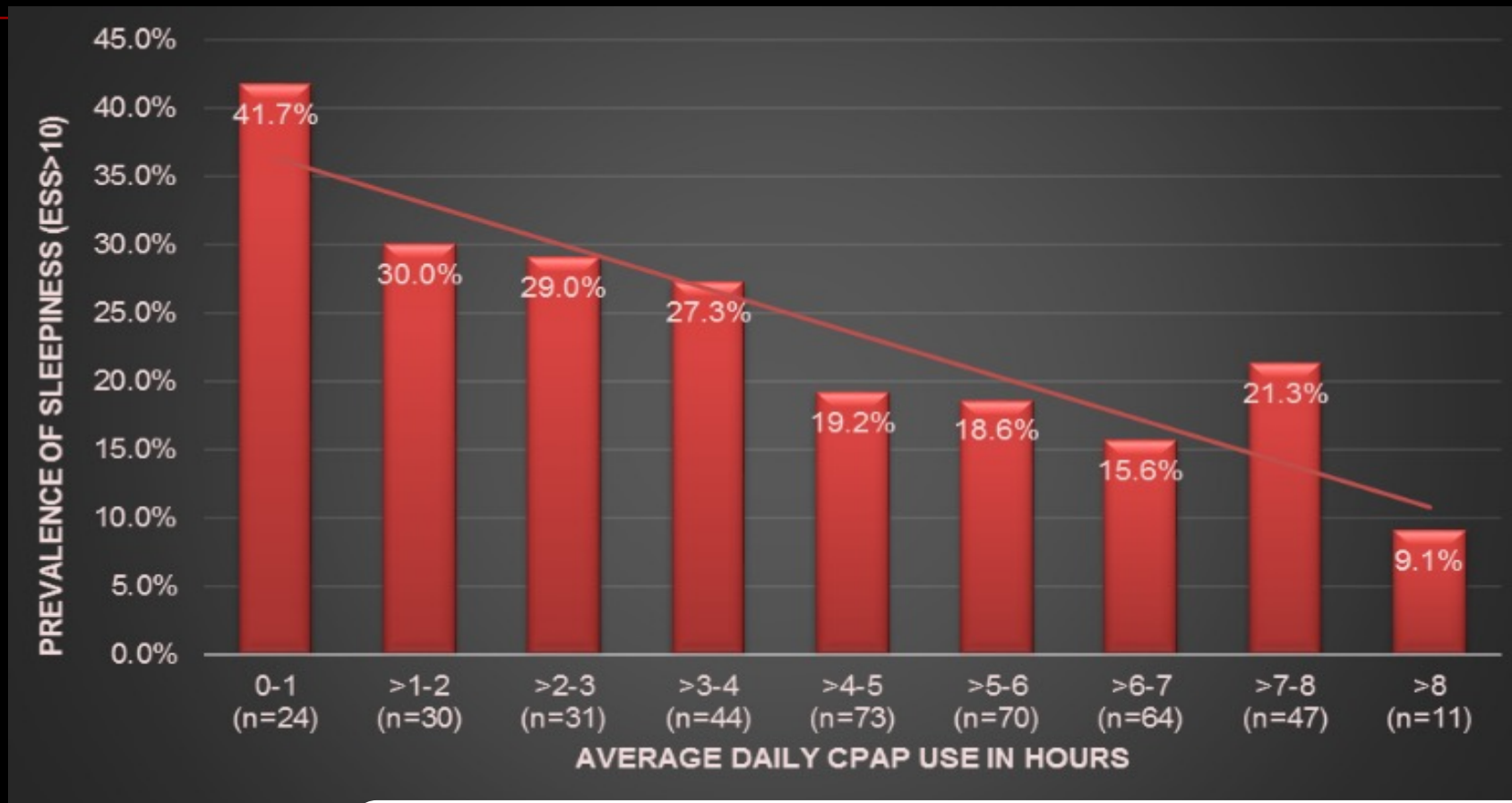
22/14



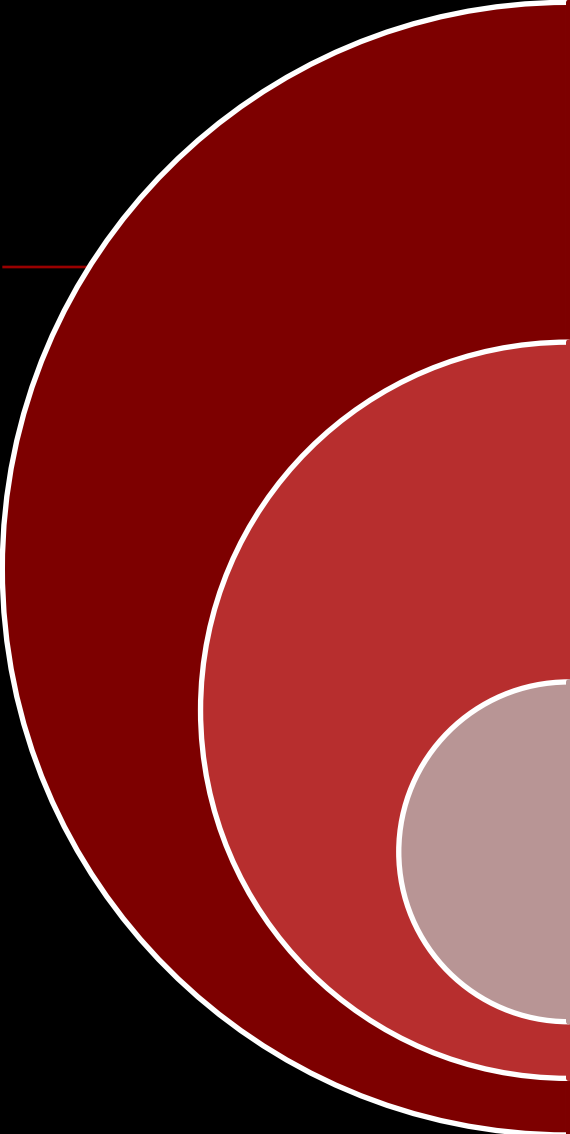
EPAP 4-15  
PS: 0-20  
Rate: Auto



# Improvement in Sleepiness with CPAP



Budhiraja, Rohit, et al. "Predictors of sleepiness in obstructive sleep apnoea at baseline and after 6 months of continuous positive airway pressure therapy." *European Respiratory Journal* 50.5 (2017): 1700348.



Barbé et al: Effect of CPAP on the incidence of HTN and cardiovascular events in nonsleepy patients with OSA, JAMA(2012),: No significant difference, CV benefit with CPAP >4 h/day

Peker et al: Effect of positive airway pressure on cardiovascular outcomes in coronary artery disease patients with nonsleepy obstructive sleep apnea: AJRCC(2016), : No significant difference, significant CV risk reduction with CPAP >4 h/day

McEvoy *et al.*, CPAP for prevention of cardiovascular events in obstructive sleep apnea, NEJM, 375 (2016): No significant difference, lower risk of cerebral event with CPAP >4 h/day

# Effect of CPAP on CV outcomes

## Adherence Analysis

Patients who used CPAP for  $\geq 4$  h/night did achieve significant cardiovascular benefits with an incidence density ratio 0.72 [0.52-0.98;  $p = 0.04$ ]

## Randomized Intervention with CPAP in Coronary Artery Disease and Obstructive Sleep Apnea (RICCADSA) trial

AHI  $\geq 15$  events/h randomized to CPAP (n = 86) or no-CPAP (n = 85).

The incidence of MACCE did not differ in intention-to-treat population.

On-treatment analysis showed a **significant risk reduction in those who used CPAP for  $\geq 4$**  vs.  $<4$  h/day or did not receive treatment (adjusted hazard ratio [HR] 0.17; 95% confidence interval [CI] 0.03–0.81;  $p = 0.03$ ).

# Objective Adherence

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## Use of PAP devices for

4 or more hours per night on  
70% of nights

Consecutive 30-day period any time  
during the first 3 months

CPAP is uncomfortable

It's the most effective therapy

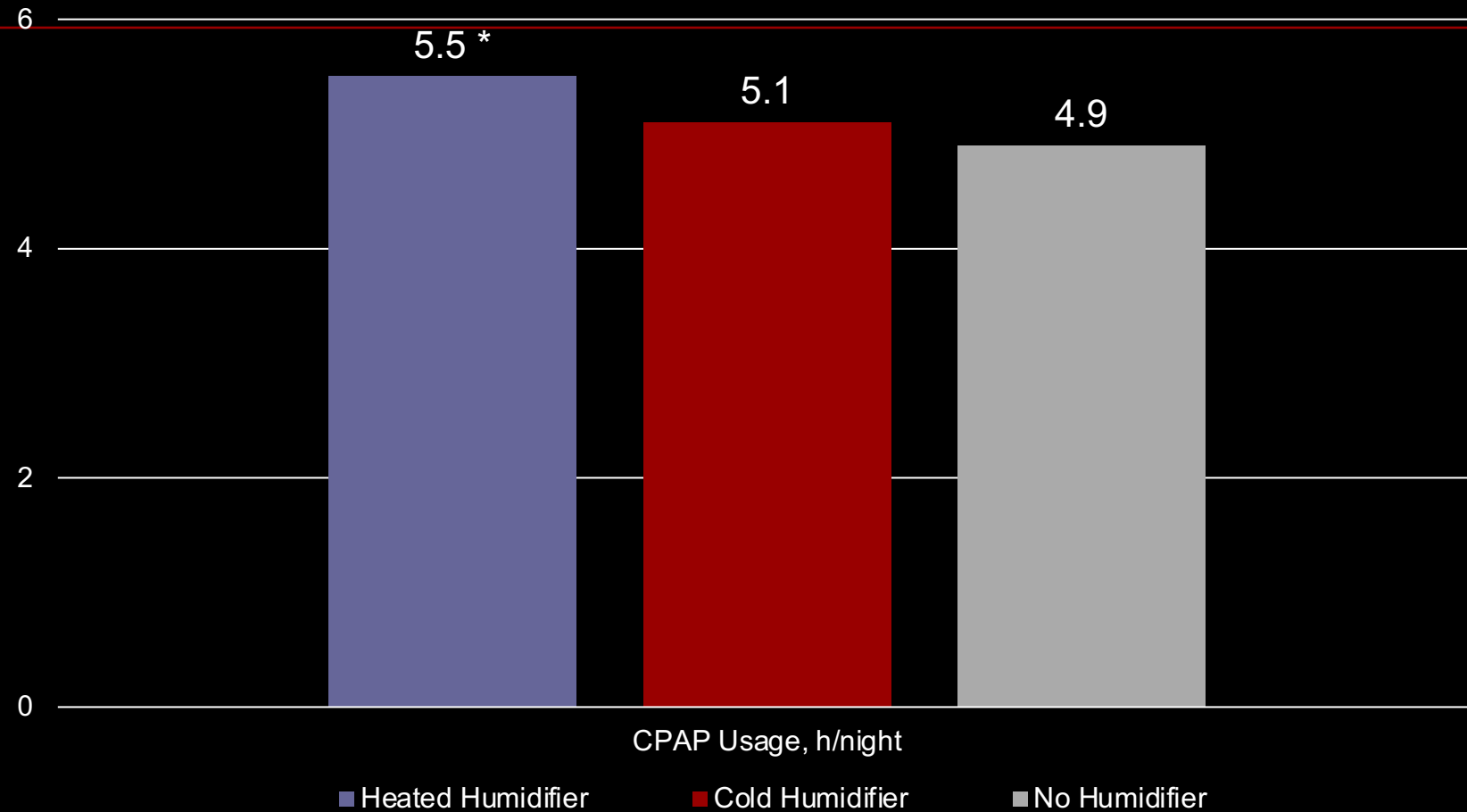


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**“My nose gets congested/ dry”**



# Heated Humidification and CPAP use



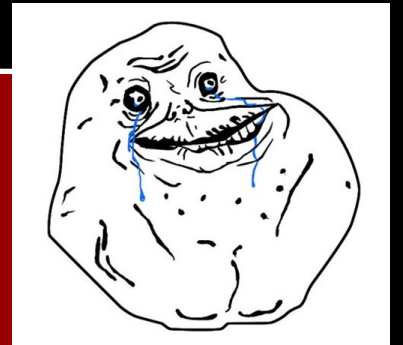
Massie, Clifford A., et al. "Effects of humidification on nasal symptoms and compliance in sleep apnea patients using continuous positive airway pressure." *Chest* 116.2 (1999): 403-408.

# Aerophagia

Swallowing of air with  
CPAP use.

More common in those  
with GERD

Bloating  
Gastric distension  
Flatulence  
Belching,  
Stomach Ache





Add incline while sleeping



Treat GERD



Dietary advice: avoid chewing gum and carbonated drinks



Simethicone/  
Activated Charcoal tablets



Consider decreasing pressure or APAP

# Factors Associated with Adherence at 6-Months

Variable	T	P
Age	3.6	<0.001
AHI	2.2	0.03
Anxiety	-2.2	0.02
Decrease in ESS Scores	3.11	0.002

R Budhiraja, et al. CPAP Adherence in Obstructive Sleep Apnea,  
*Journal of Clinical Sleep Medicine, Vol. 12, No. 3, 2016*

# Anxiety

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Nasal Masks

Wear the CPAP while awake

PATIENT EDUCATION

Cognitive behavior therapy

Anxiety medications

## Participants with Good Adherence

The prevalence of ESS >10 after 6m of CPAP 18.1%

Higher in those with baseline excessive sleepiness

No other variables were significantly associated with odds of sleepiness

# Treatment-Emergent Central (Complex) Sleep Apnea

Patient being  
treated for  
OSA

Application of  
CPAP (or  
other therapy)

Develops  
Central Sleep  
Apnea

# Treatment-Emergent Central Sleep Apnea (TECSA)

Seen in **5-15% of titrations**, Spontaneously resolves in most by 3 m

**High loop gain, Low pCO<sub>2</sub> levels** increase the risk

**More central and mixed apneas on the diagnostic study, higher rates of comorbid heart failure, stroke, narcotic use**

**ASV** appears superior to BPAP-ST for the long-term treatment of persistent CSA.

Cassel, et al. "A prospective polysomnographic study on the evolution of complex sleep apnoea." *European Respiratory Journal* 38.2 (2011): 329-337.

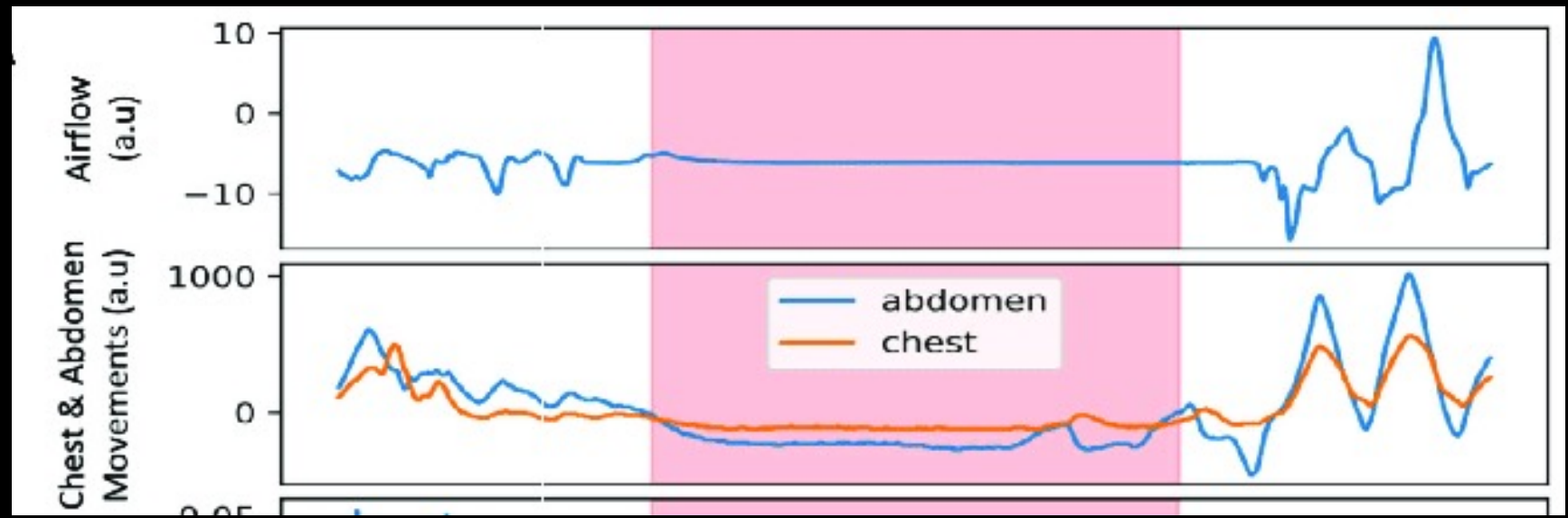
Moro, Marilyn, et al. "Clinical predictors of central sleep apnea evoked by positive airway pressure titration." *Nature and science of sleep* 8 (2016): 259.

Dellweg, Dominic, et al. "RCT of NPPV versus servoventilation in patients with CPAP-induced central sleep apnea." *Sleep* 36.8 (2013): 1163-1171.

Obstructive



Central/ Mixed





Insufficient Sleep Time



Persistent disease



Inadequate CPAP use



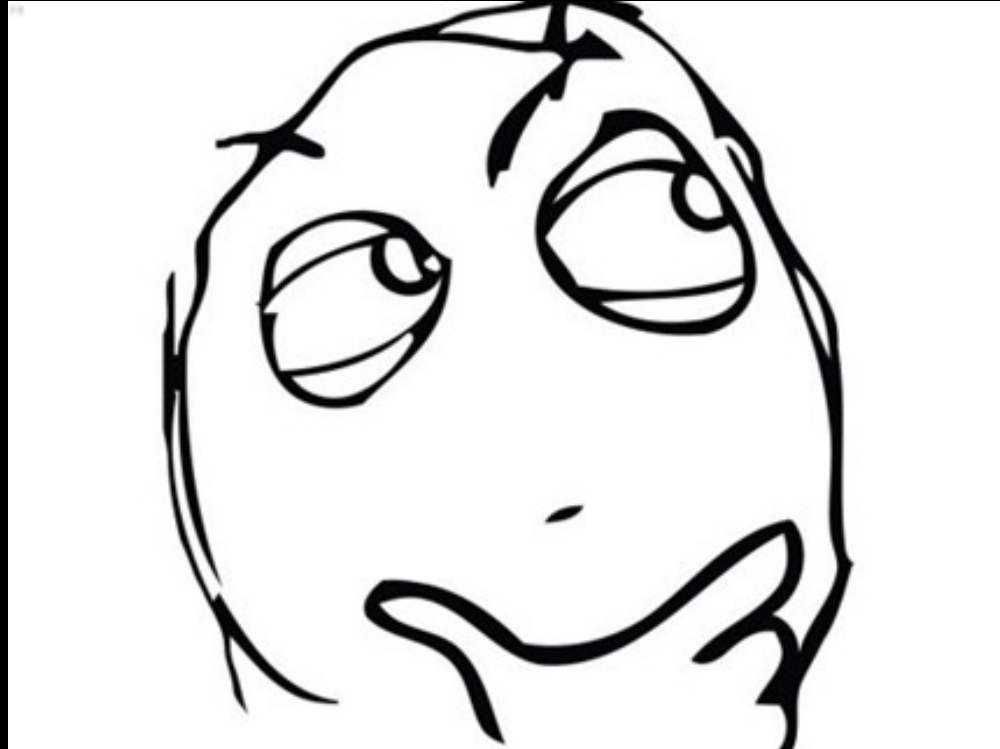
Associated depression

Stimulants



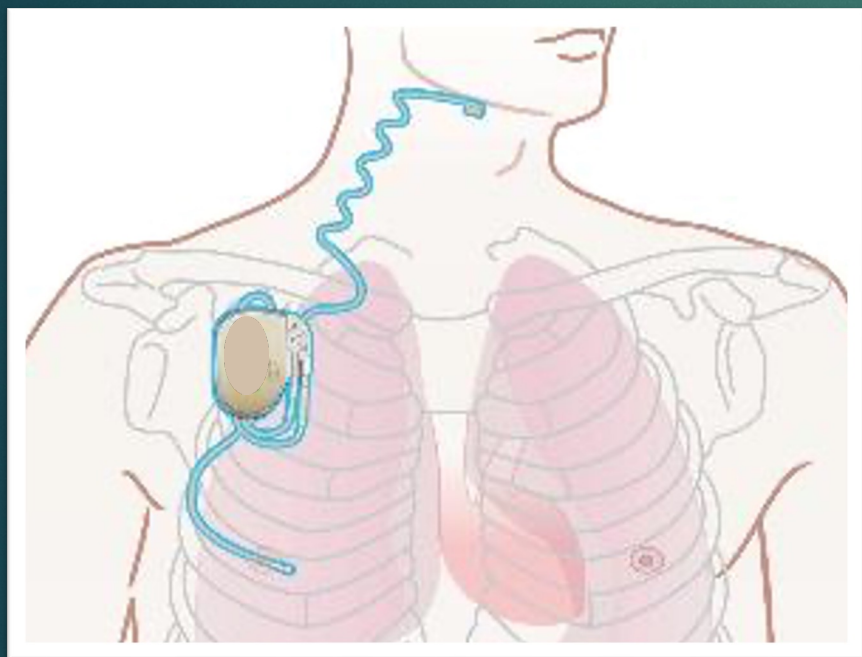
Medications: Psych/ Neuro/ Cardio/ Anti-allergy

What else do you got?





# Hypoglossal Nerve Stimulation



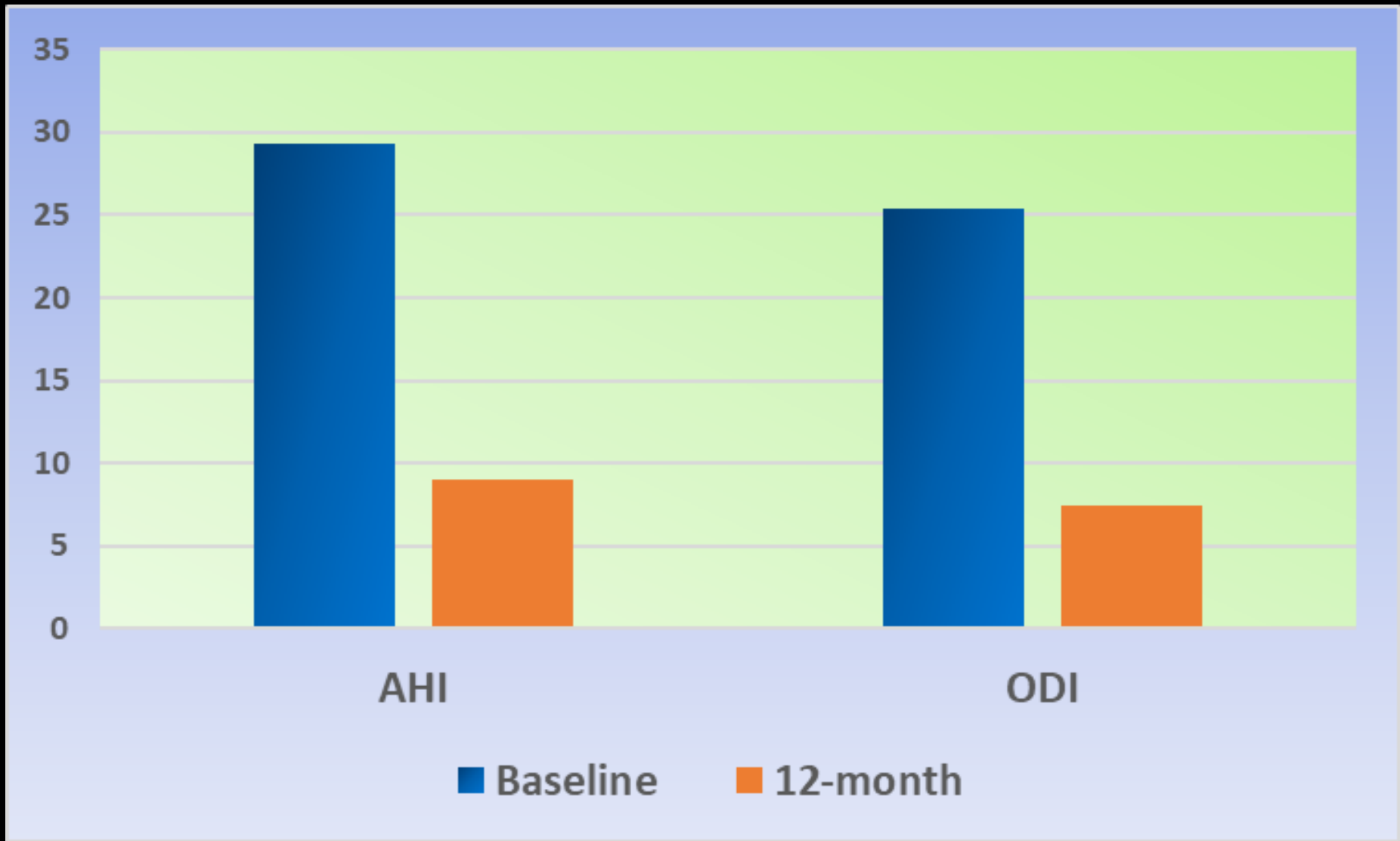
Stimulation  
lead

Generator

Sensing  
lead

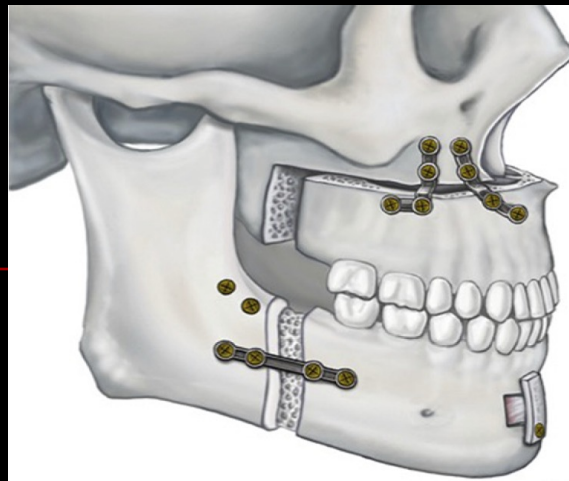


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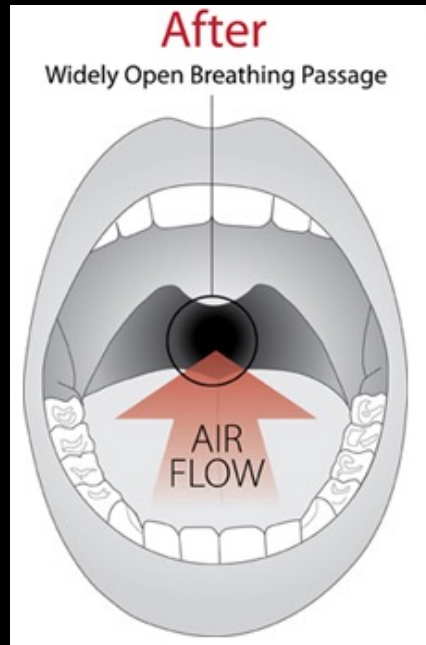
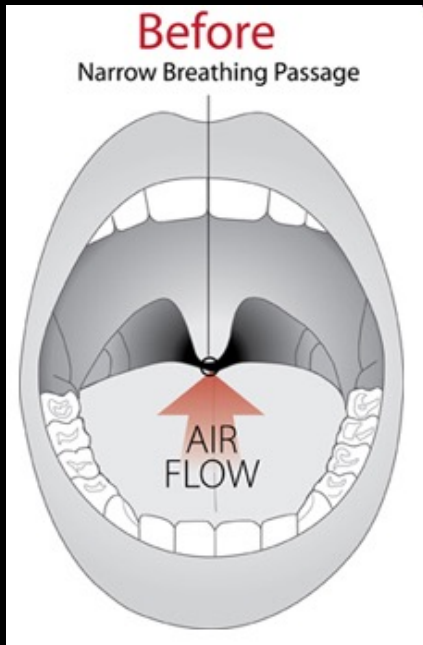


Strollo Jr, Patrick J., et al. "Upper-airway stimulation for OSA." NEJM 370.2 (2014): 139-149.

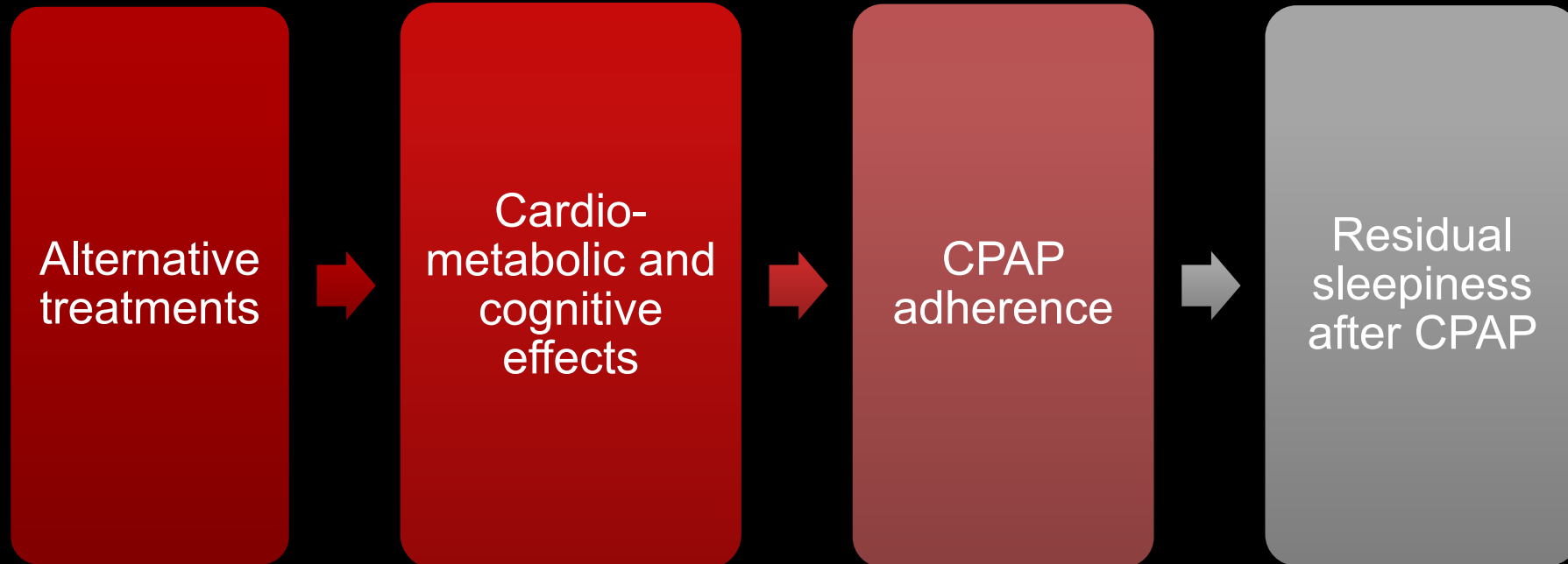
# Surgery



# Didgeridoo



# Gaps in OSA Knowledge



# Big Data

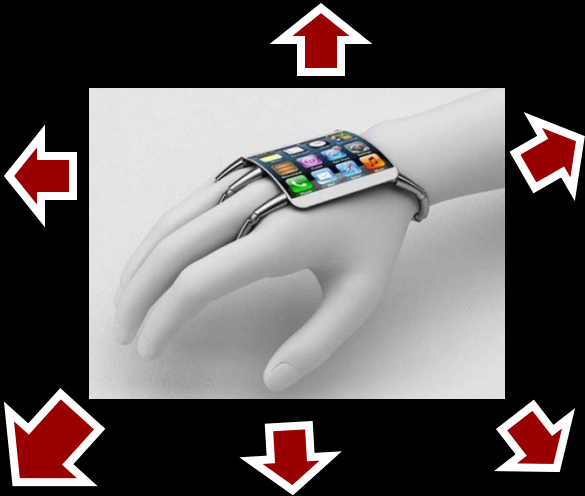
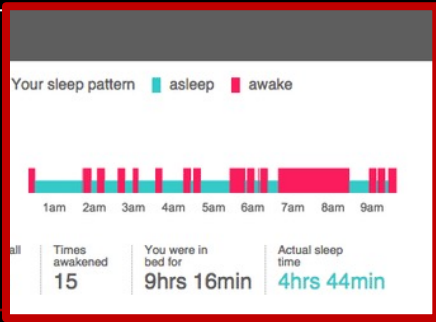
Voluminous databases with numerous datapoints

Allow exploration of the effects of individual differences and complex interactions

Facilitate identification and management of individuals according to their unique characteristics

“Personalizing” medicine or pursuing “Precision” medicine





# Question 1

What is the benefit of APAP over CPAP?

- Better sleep quality
- Better control of AHI
- A greater improvement in hypoxemia
- Lower mean airway pressure

# Question 1

## What is the benefit of APAP over CPAP?

- Better sleep quality
- Better control of AHI
- A greater improvement in hypoxemia
- Lower mean airway pressure (may help with comfort, aerophagia)

## Question 2

Which of the following breathing disorders is usually less severe in rapid eye movement (REM) sleep compared to non-rapid eye movement (NREM) sleep?

- Hypoxemia in COPD
- Obstructive Sleep Apnea
- Treatment Emergent Central Sleep Apnea
- Obesity Hypoventilation

## Question 2

Which of the following breathing disorders is usually less severe in rapid eye movement (REM) sleep compared to non-rapid eye movement (NREM) sleep?

- Hypoxemia in COPD
- Obstructive Sleep Apnea
- Treatment Emergent Central Sleep Apnea (Loop gain during REM sleep is lower compared to loop gain during NREM sleep.)
- Obesity Hypoventilation

# Key Points



Sleep Apnea in  
Lung disorders

Obesity AND  
Anatomy AND  
Physiology

'Other' Symptoms

Monitor and  
Improve CPAP  
Adherence

Other treatments  
MAD, HNS,  
Positional,  
Surgical

Treat Overall  
Sleep

# References

- Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, Marcus CL, Mehra R, Parthasarathy S, Quan SF, Redline S. Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events: deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. *Journal of clinical sleep medicine*. 2012 Oct 15;8(5):597-619.
- Peppard, Paul, et al. "Increased prevalence of SDB in adults." *Am journal of epidemiology* 177.9 (2013): 1006-1014
- Budhiraja R, Siddiqi TA, Quan SF. Sleep disorders in chronic obstructive pulmonary disease: etiology, impact, and management. *Journal of Clinical Sleep Medicine*. 2015 Mar 15;11(3):259-70.
- Marin J. *AJRCCM* 2010;182:325–31
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The woods are lovely, dark and deep.  
But I have promises to keep,  
And miles to go before I sleep,  
And miles to go before I sleep.

Robert Frost