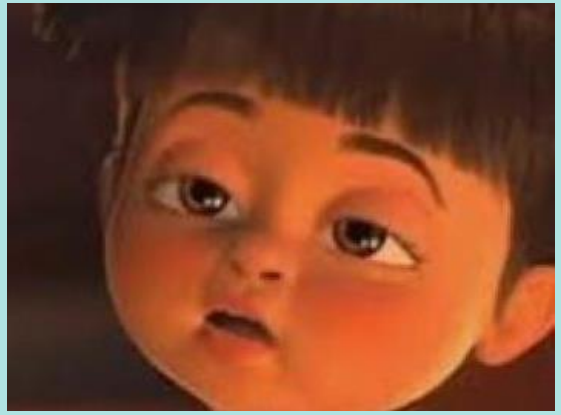
Brigham and Women's Hospital
Founding Member, Mass General Brigham

Obstructive Sleep Apnea



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Department of Medicine
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- 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

- Conflict of Interest: None
- Disclosures-None

OSA in Pulmonary Disorders

Endotypes

Less well appreciated symptoms

Sleep Studies

PAP therapy

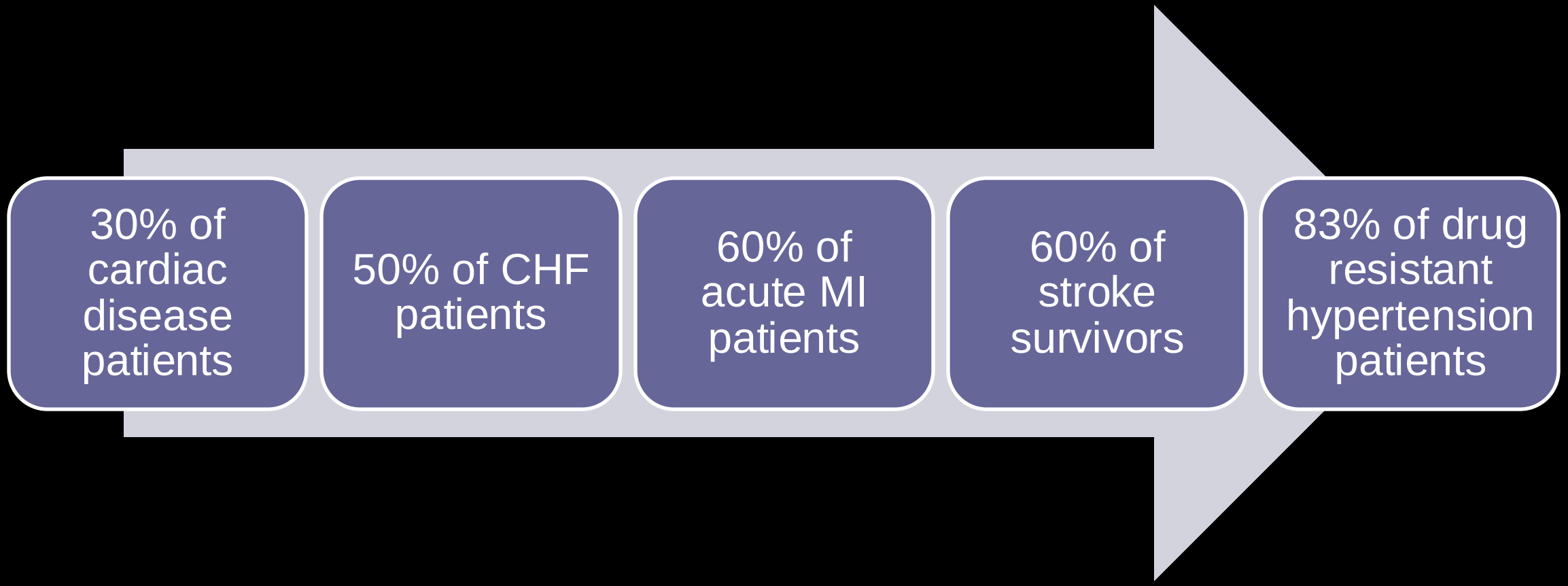
Other therapies

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

Peppard, Paul, et al. "Increased prevalence of SDB in adults." Am journal of epidemiology 177.9 (2013): 1006-1014.

Prevalence of Significant SDB in Cardiovascular Disease



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

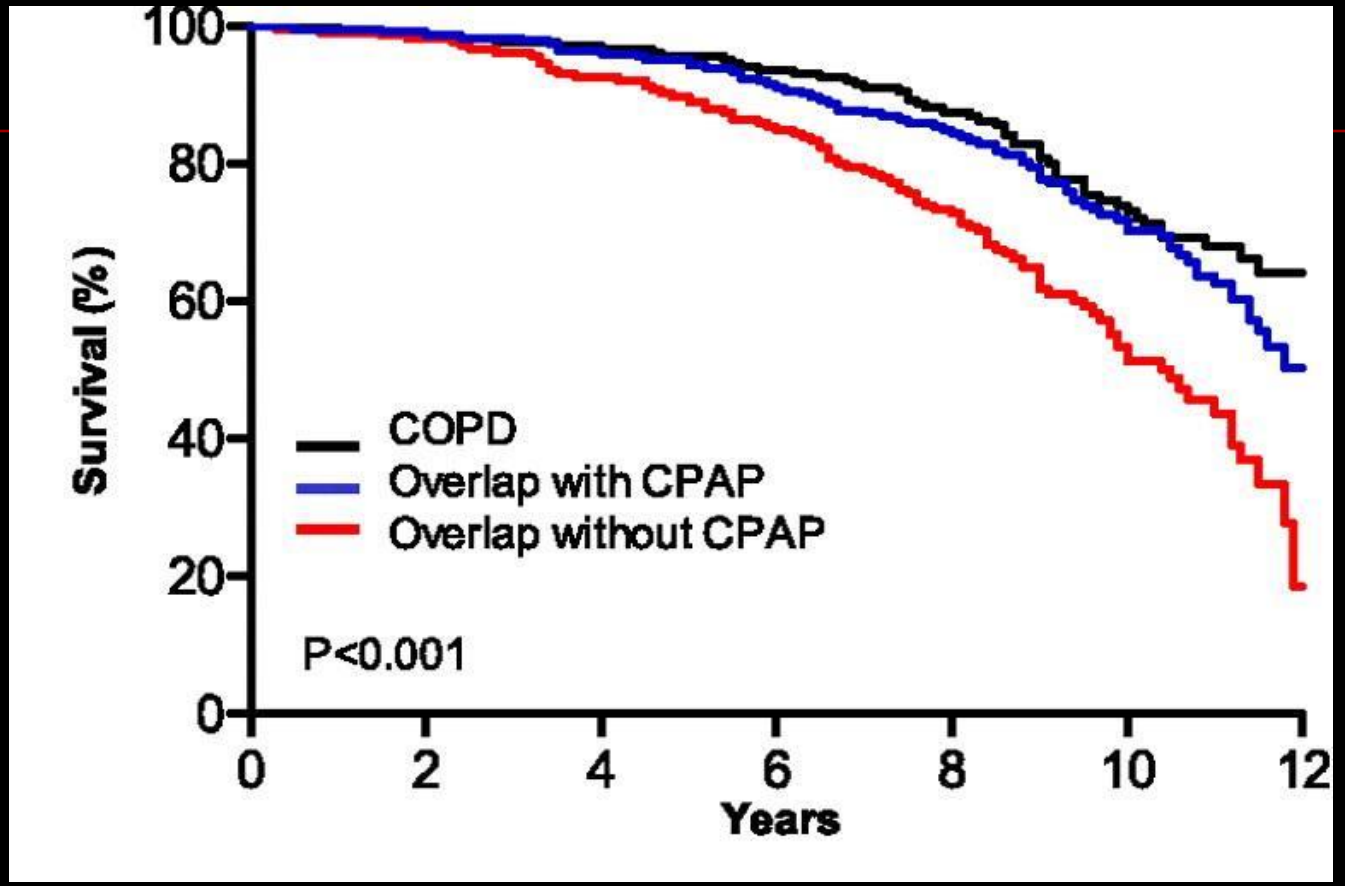
COPD

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

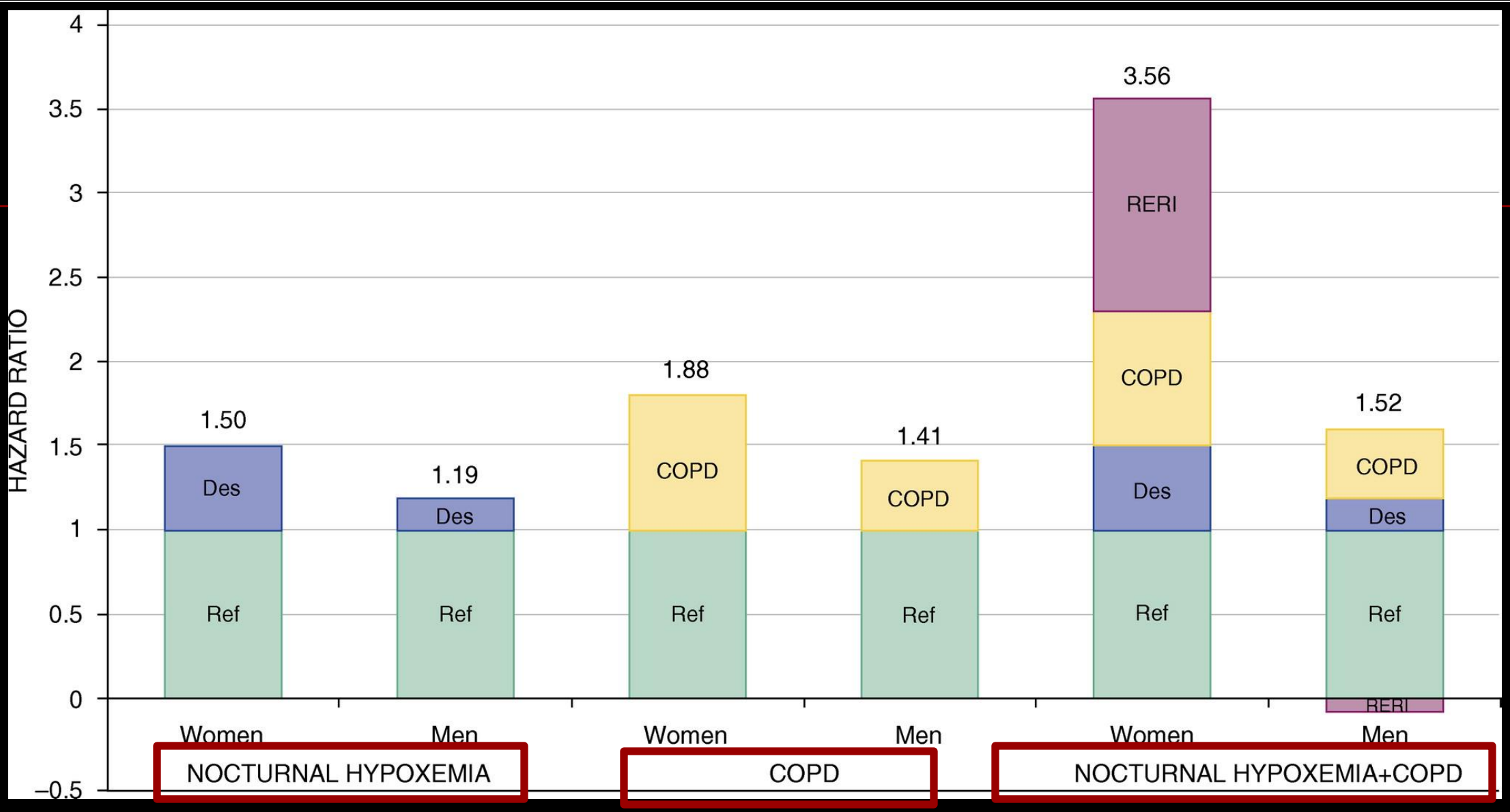
Asthma

- Augmented inspiratory negative intraluminal pressure: pharyngeal airway collapse

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.



Published in: Tetyana Kendzerska; Richard S. Leung; Shawn D. Aaron; Najib Ayas; Jacqueline S. Sandoz; Andrea S. Gershon; *Annals ATS* 1671-81.

DOI: 10.1513/AnnalsATS.201802-136OC Copyright © 2019 by the American Thoracic Society

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 ≥15/h in 5 (15%)

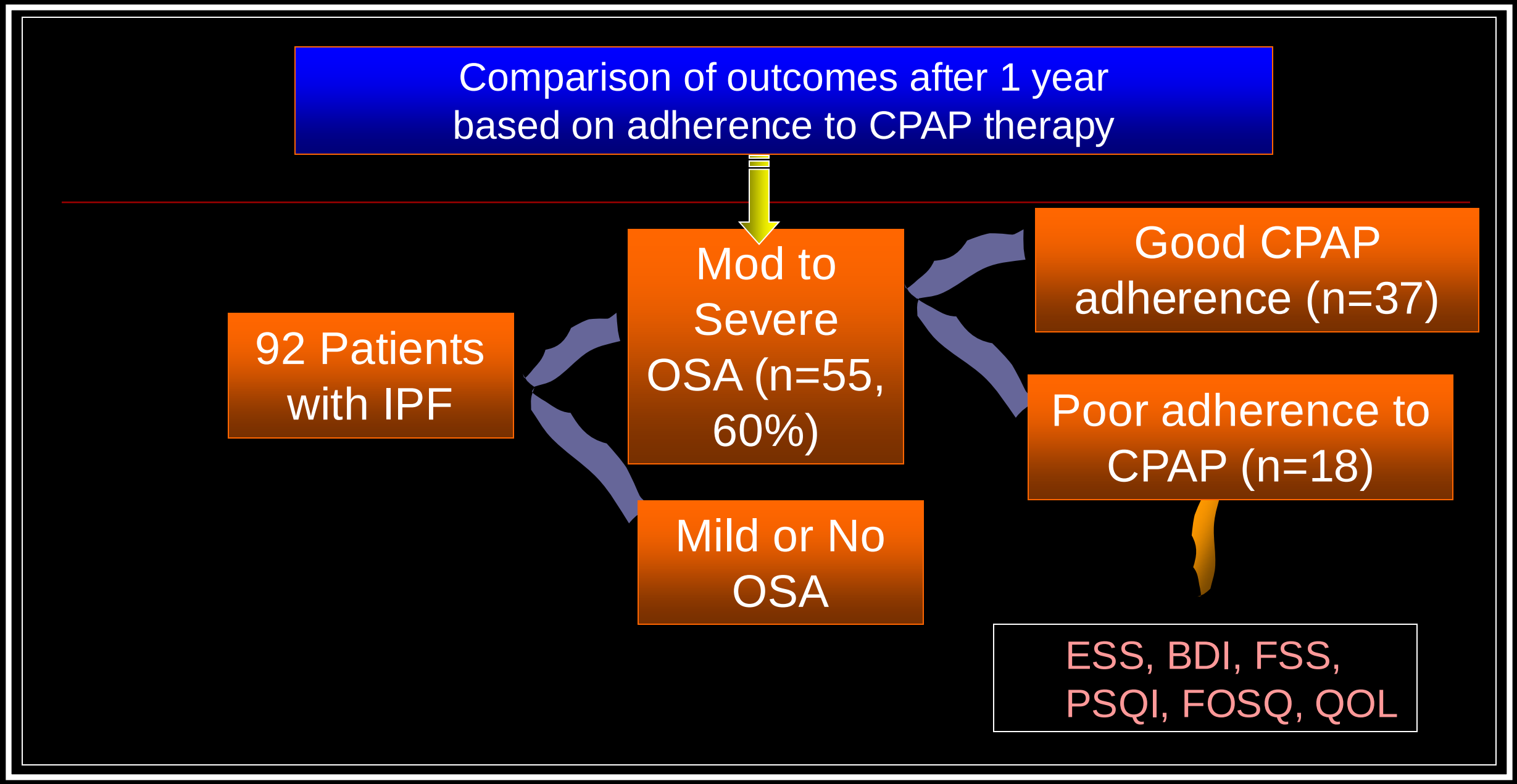
AHI was <5 in 14 (12%)

AHI 5–15 in 10 (20%)

88%

AHI ≥15/h in 34 (68%)

Mermigkis , Sleep Breath (2010) 14:387–390; Lancaster Chest. 2009 Sep;136(3):772-8

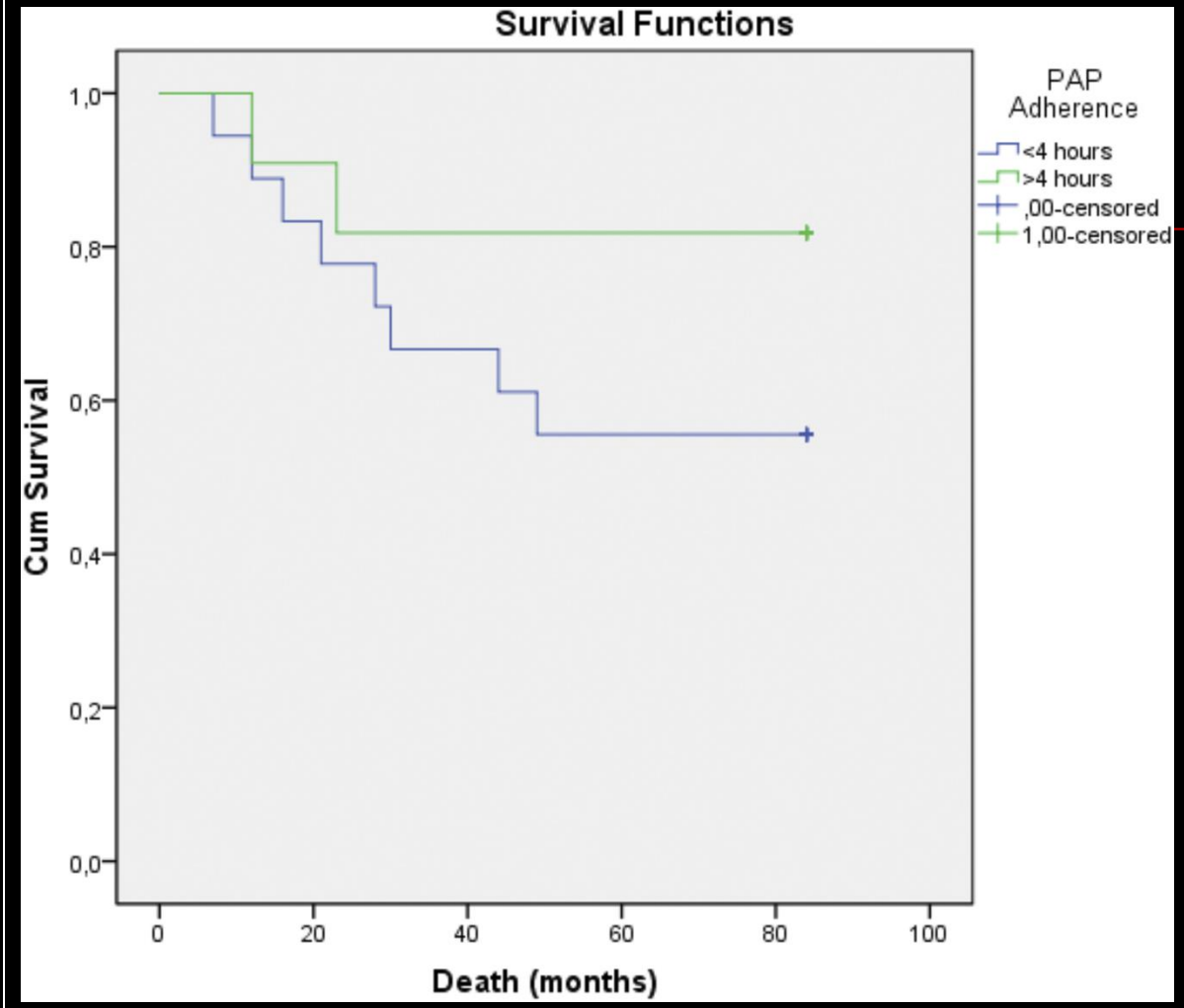


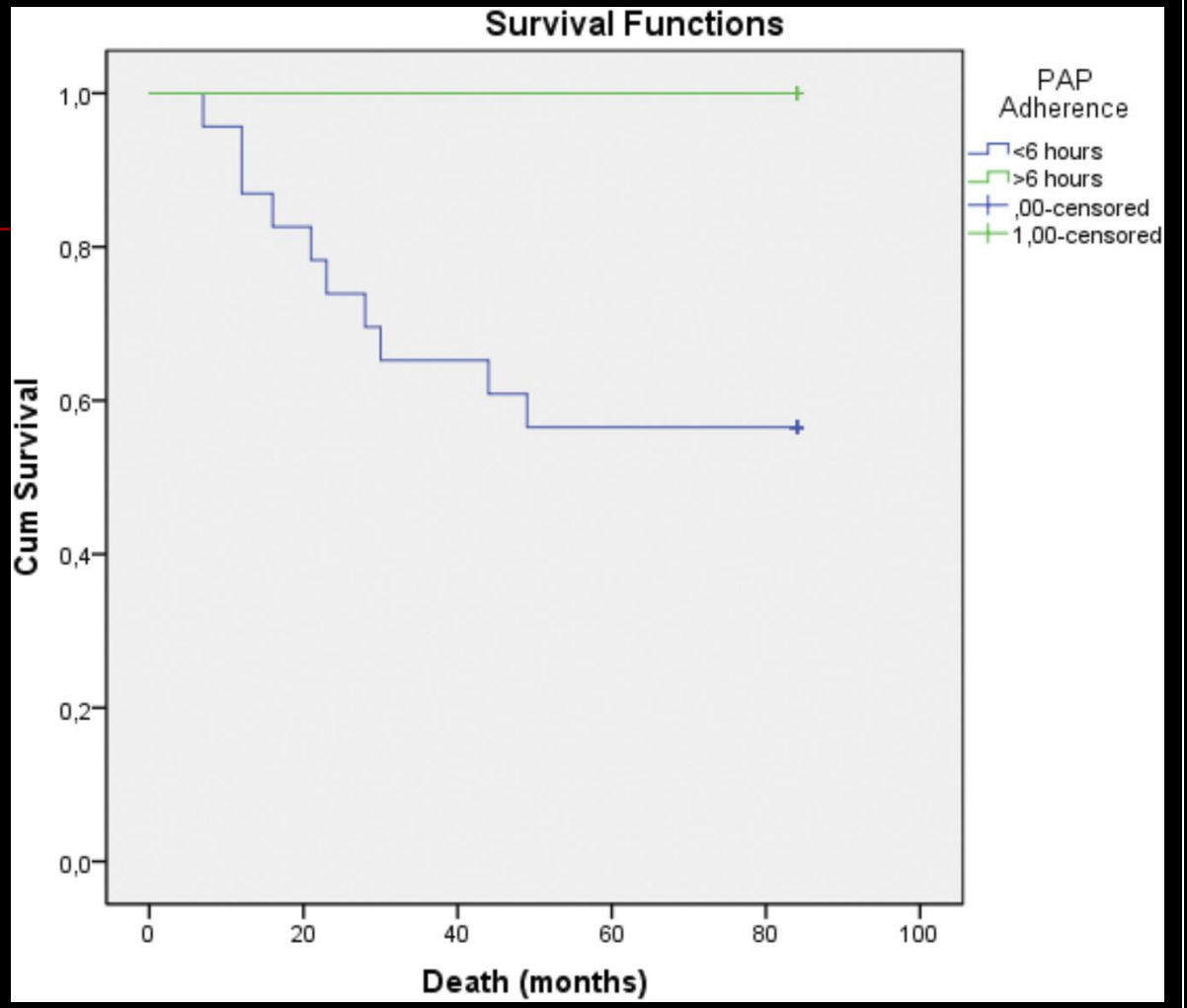
Mermigkis, Charalampos, et al. "Obstructive sleep apnea should be treated in patients with idiopathic pulmonary fibrosis." *Sleep and Breathing* 19.1 (2015): 385-391.

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

Mermigkis, Charalampos, et al. "Obstructive sleep apnea should be treated in patients with idiopathic pulmonary fibrosis." *Sleep and Breathing* 19.1 (2015): 385-391.



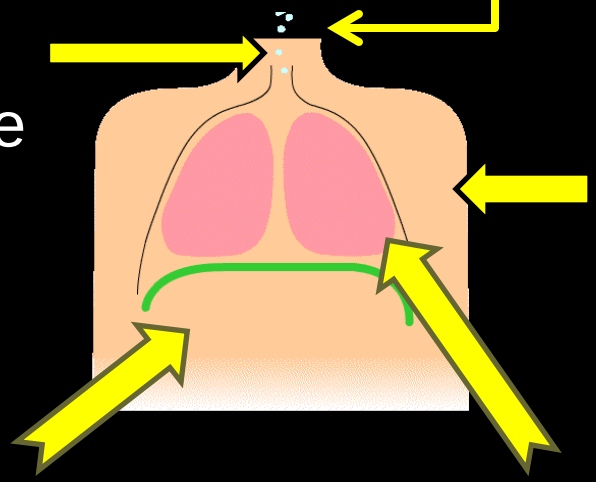


Papadogiannis, George, et al. "Patients with idiopathic pulmonary fibrosis with and without obstructive sleep apnea: differences in clinical characteristics, clinical outcomes, and the effect of PAP treatment." Journal of Clinical Sleep Medicine 17.3 (2021): 533-544.

Physiological Changes during Sleep

Diminshed
Hypoxic
and
Hypercapnic drive

Increased Upper
Airway Resistance

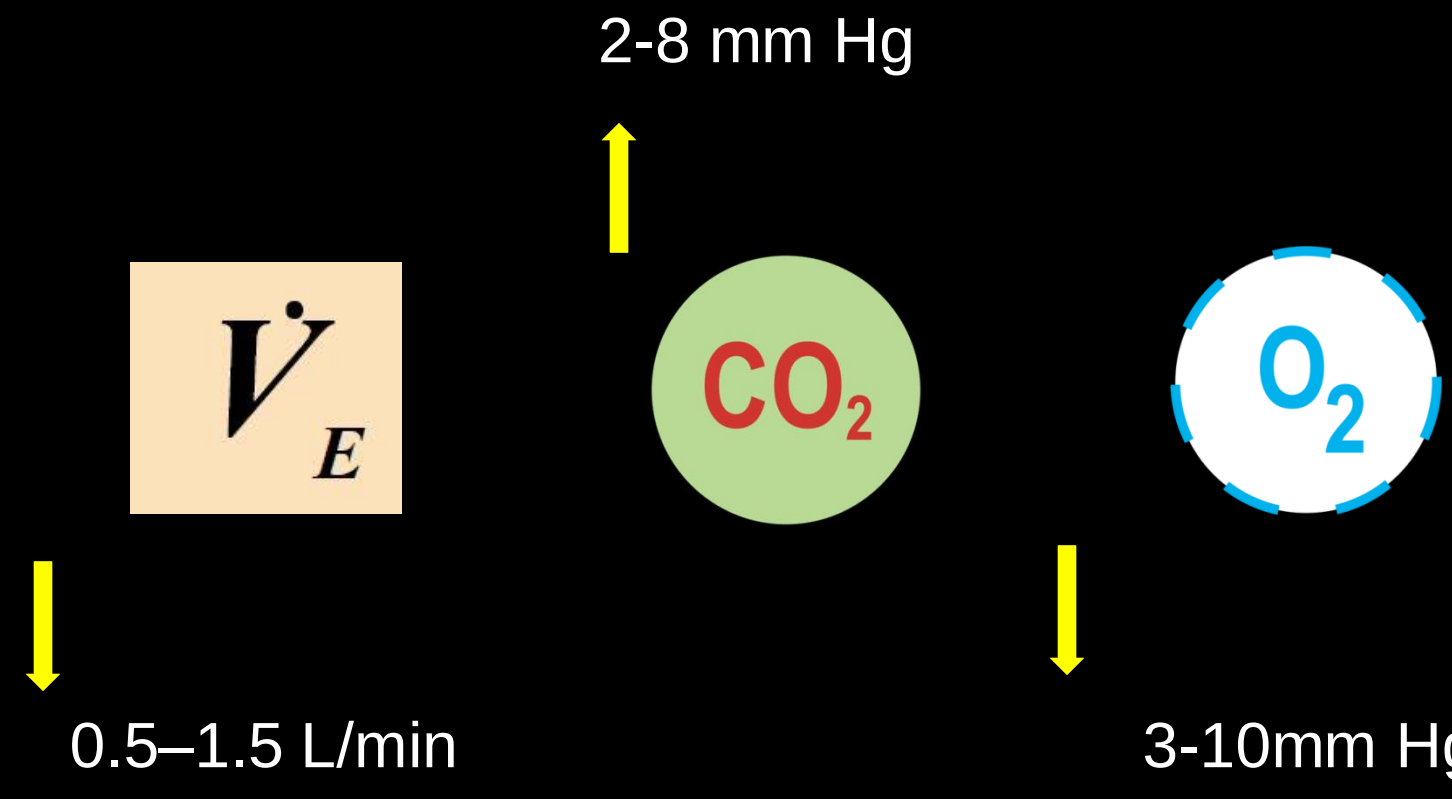


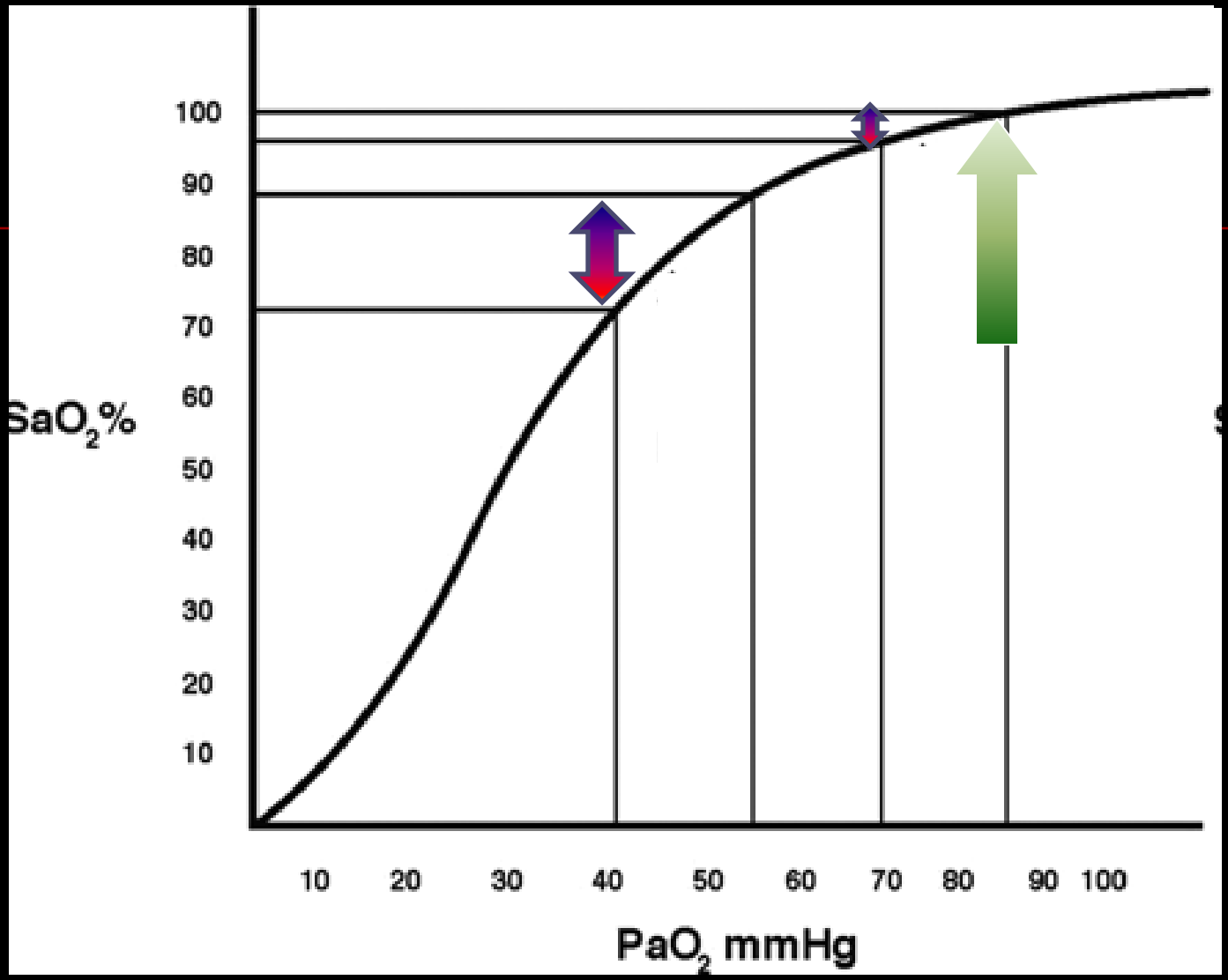
Diminished activity of
accessory muscles
of respiration

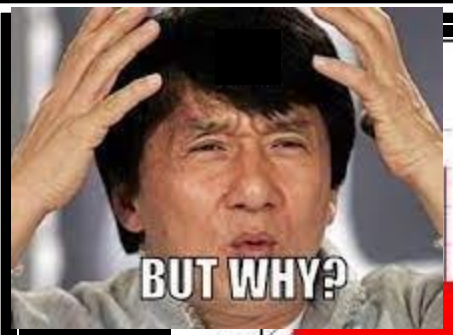
Reduced tidal volume =>
Reduced minute ventilation

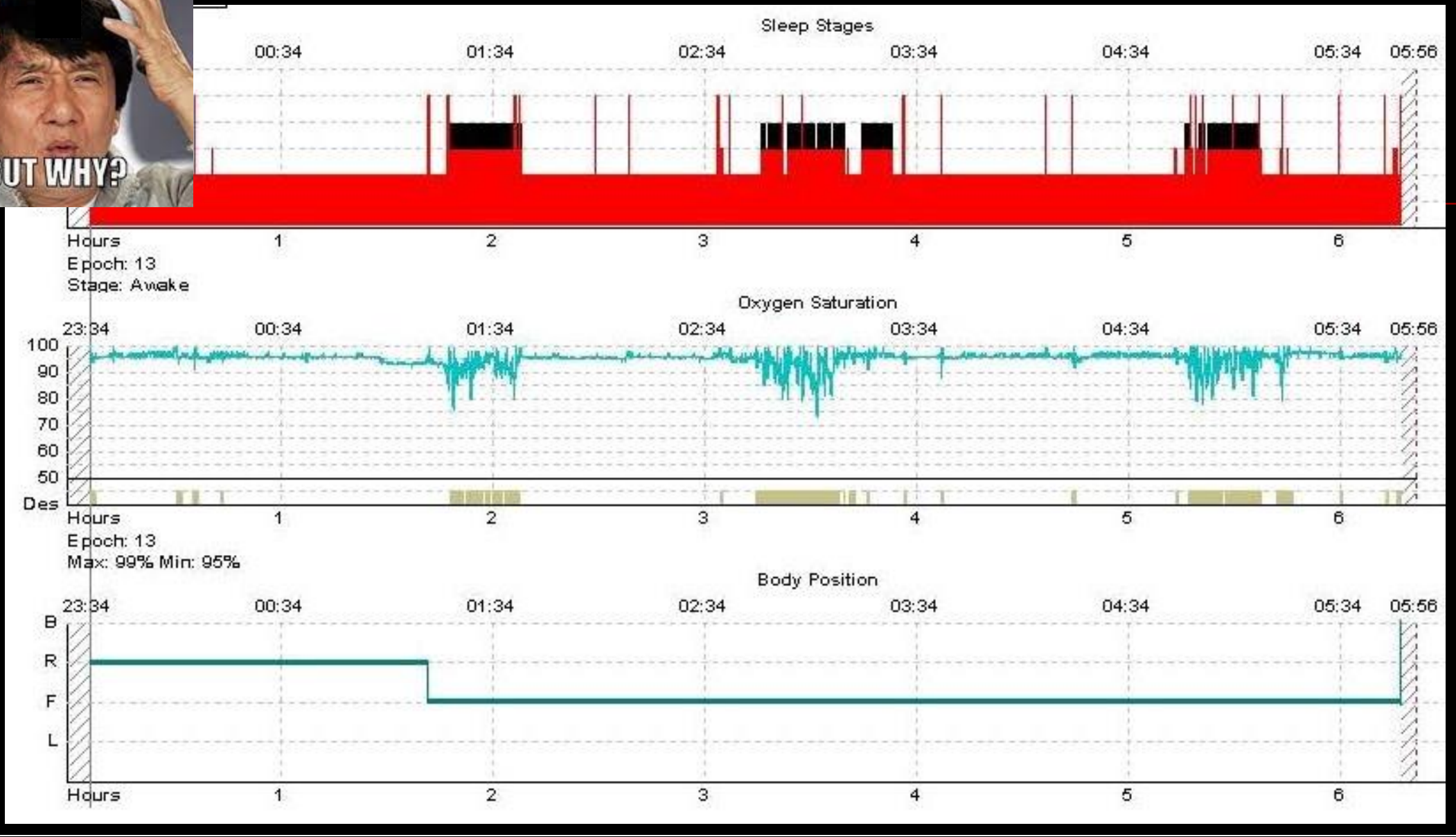
Reduced Functional
Residual Capacity (FRC)

Changes during Sleep

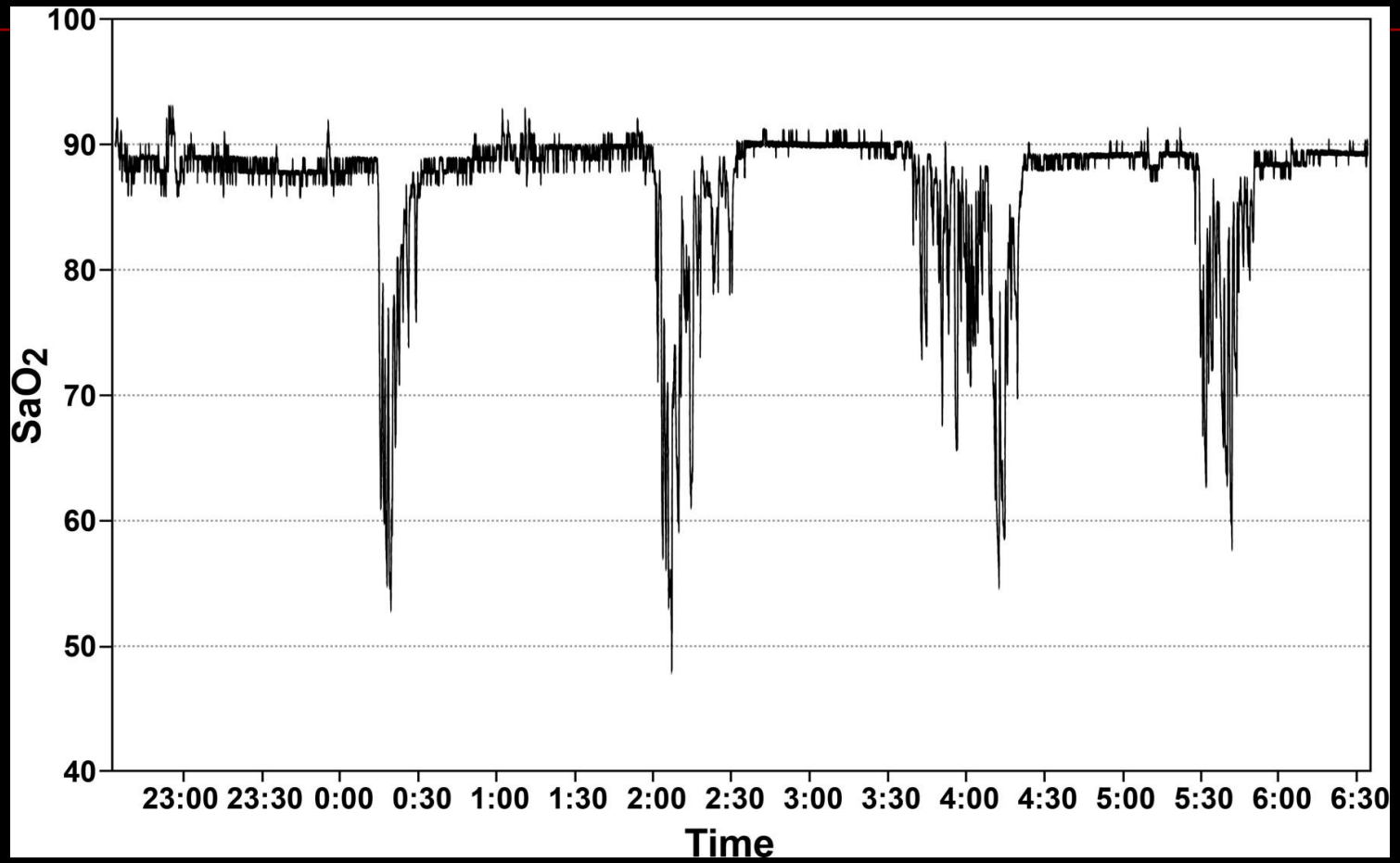



100
90
80
70
60
50
40
30
20
10
SaO2%
10
20
30
40
50
60
70
80
90
100
PaO2 mmHg


BUT WHY?


Sleep Stages
00:34
01:34
02:34
03:34
04:34
05:34
05:56
Hours
1
2
3
4
5
6
Epoch: 13
Stage: Awake
Oxygen Saturation
23:34
100
90
80
70
60
50
Des
Epoch: 13
Max: 99% Min: 95%
Body Position
B
R
F
L

Nocturnal Oximetry in Lung Disease



Parish, CHEST 2009;135(2):563-572

Nocturnal Hypoxemia

Decreased daytime energy levels

Impaired social and physical functioning

Thorax, 56 (2001), pp. 482–486

END OF CHAPTER 1:
Sleep in Pulmonary Disorders

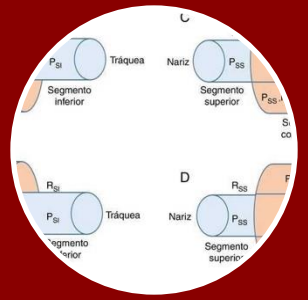
BEGINNING OF CHAPTER 2:
Pathophysiology of sleep apnea

Obesity and OSA

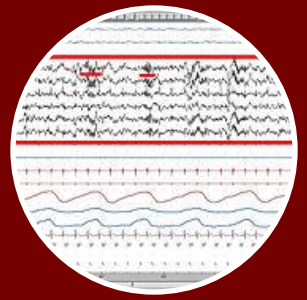
- 10% weight gain: 32% increase in AHI
- 10% weight loss: 26% decrease in AHI
- 20-40% are not obese

Peppard et al, “Longitudinal study of moderate weight change and SDB” JAMA, 284 (23)

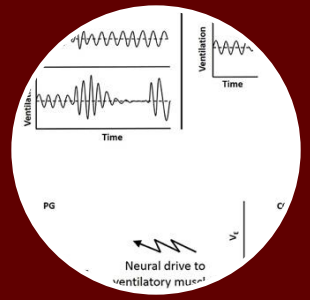
Sleep Apnea Endotypes (PALM)



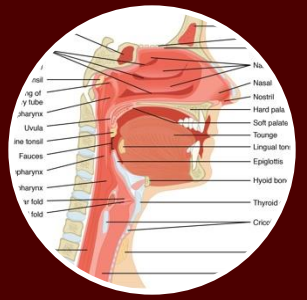
Pharyngeal Critical Closing **P**ressure (Pcrit)



(Low) **A**rousal Threshold

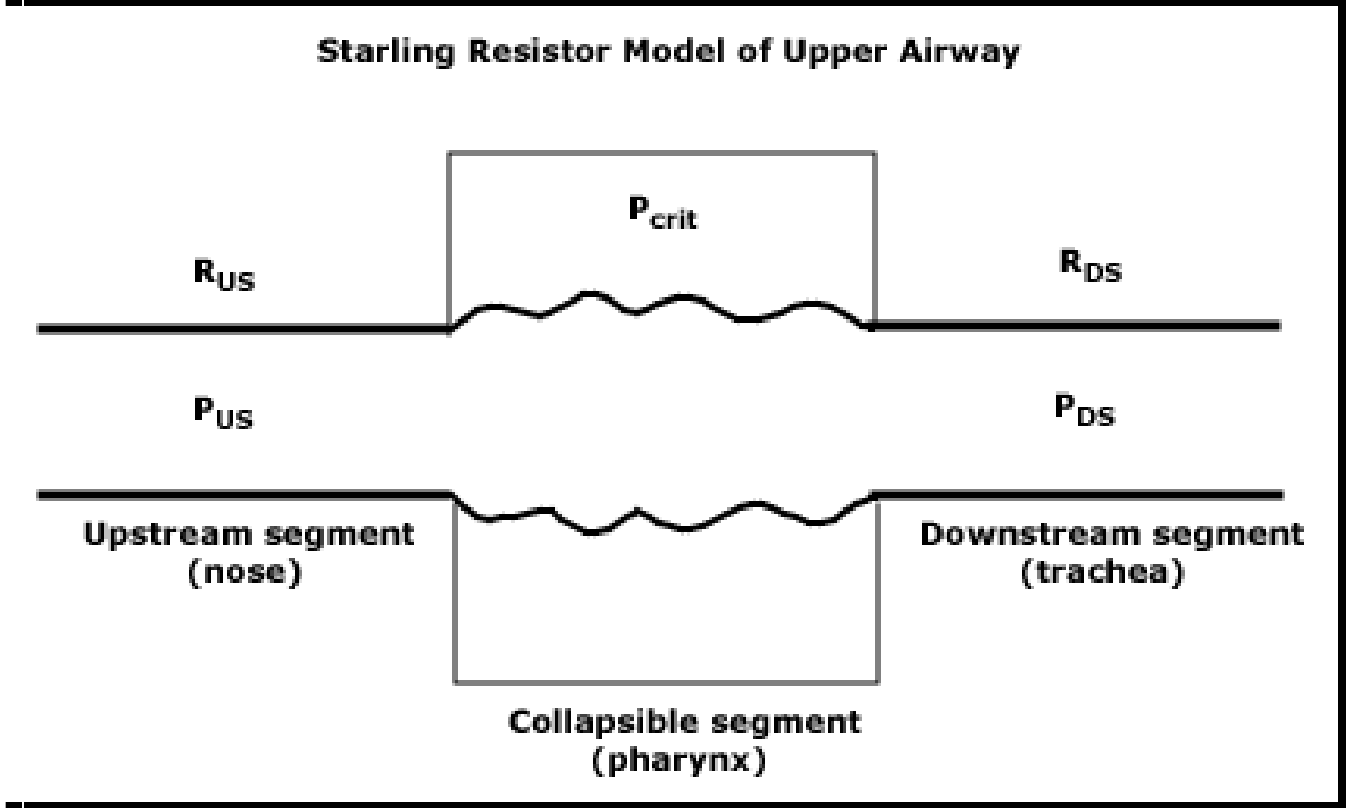


(High) **L**oop Gain



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

Pcrit



- -12 to -2 cm H2O

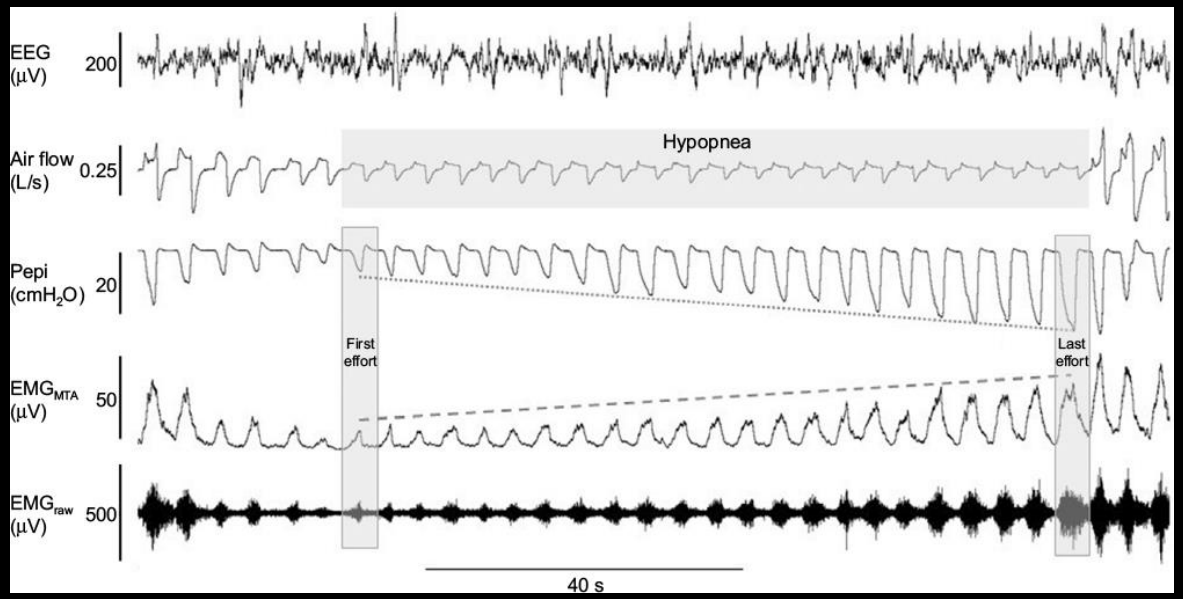
Hypopnea

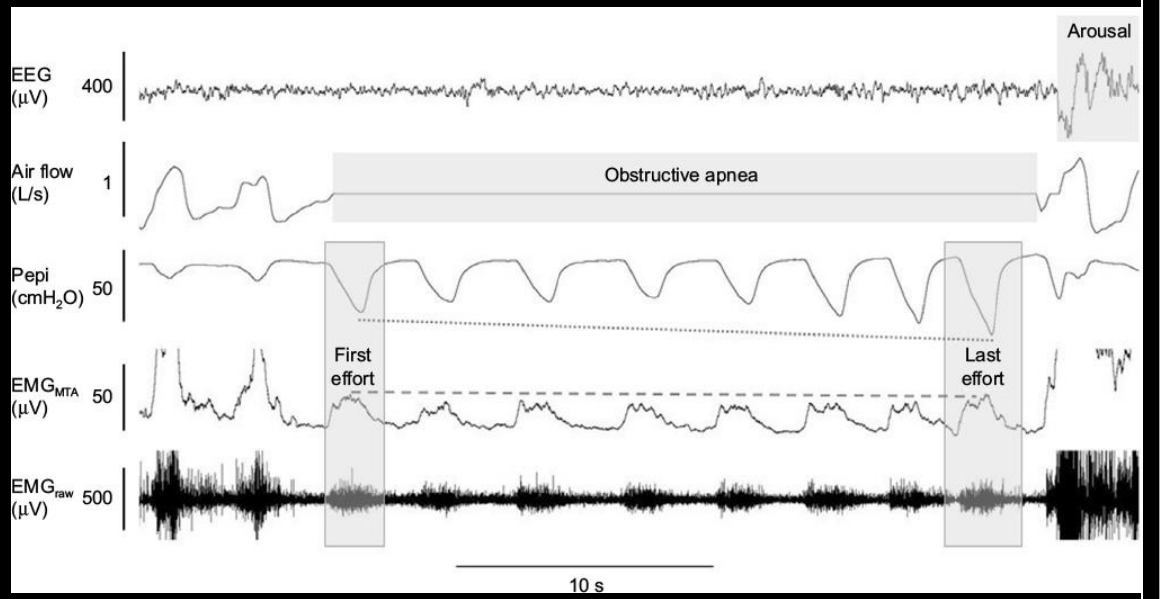
- -4 to +1 cm H2O

Apnea

- -1 to + 5 cm H2O

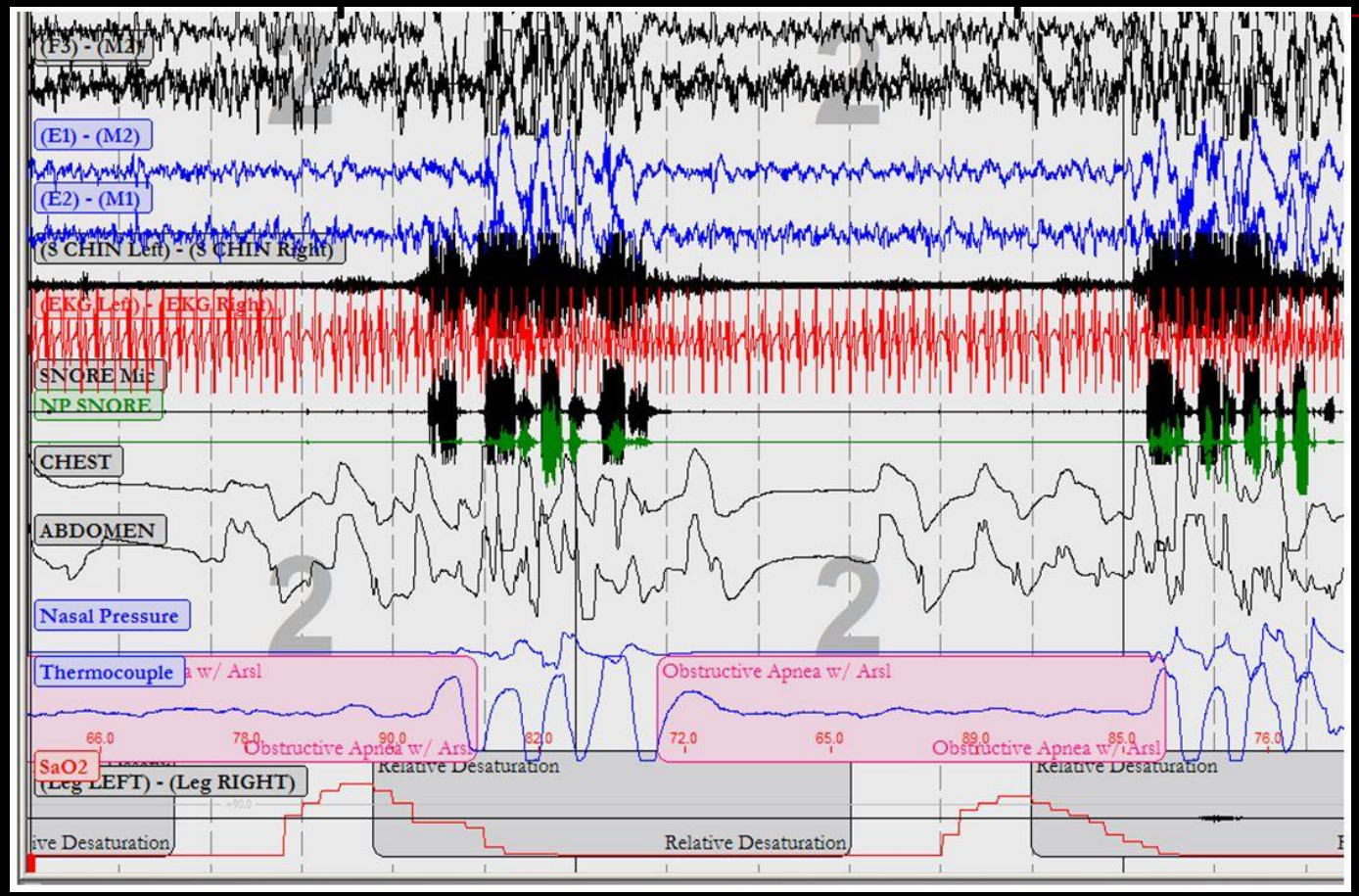
Normal versus diminished genioglossus activation





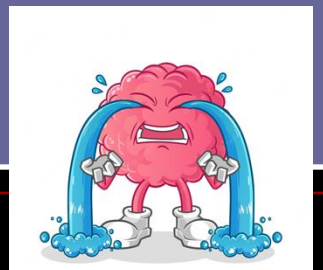
Osman, Amal M., et al. "Obstructive sleep apnea: current perspectives." Nature and science of sleep 10 (2018): 21

Low Arousal Threshold



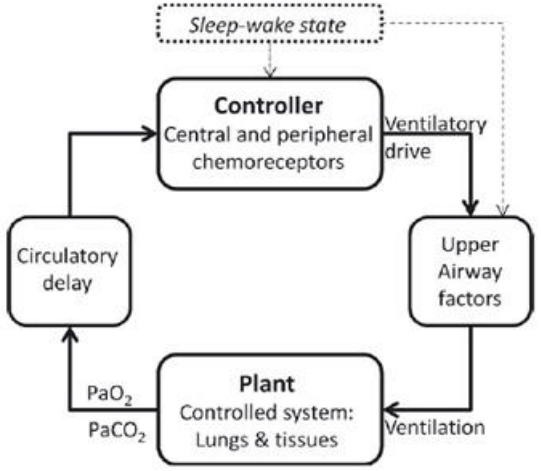
- Prior to GG recruitment
- Prevents deeper, more stable stages
- Destabilizes breathing patterns

Loop Gain

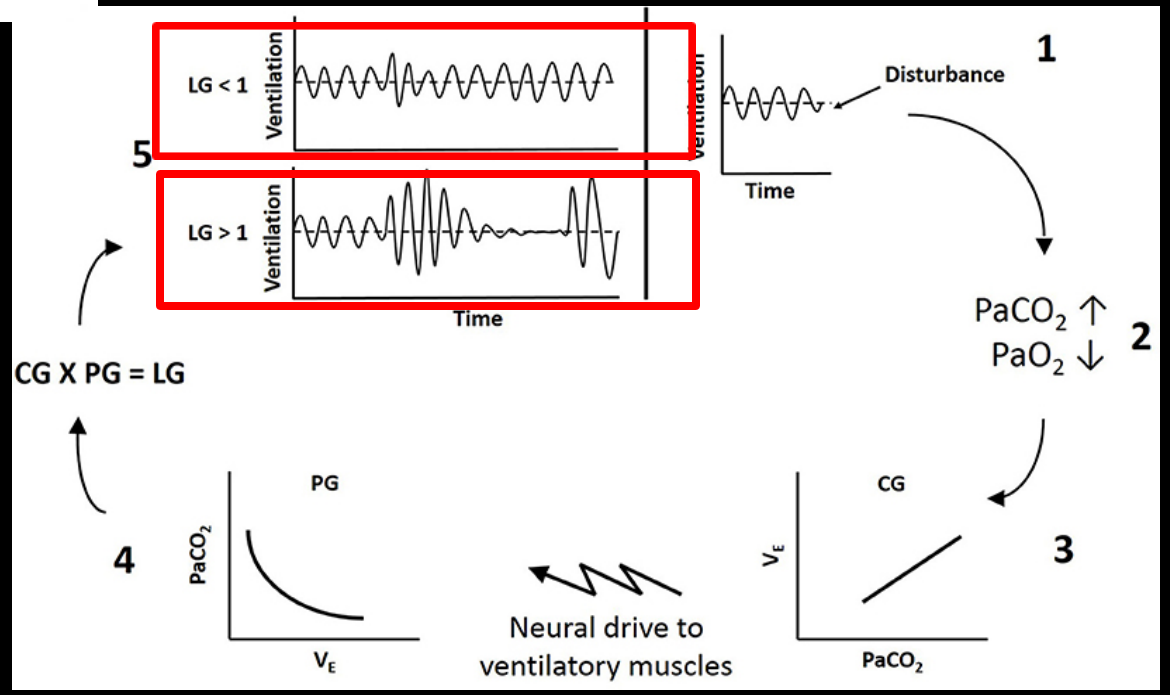


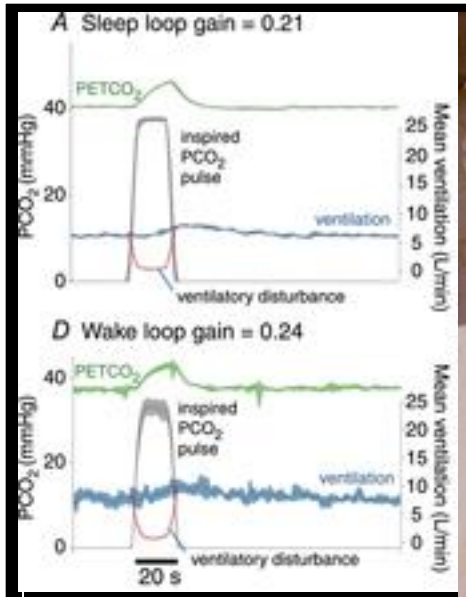
Loop-gain theory:

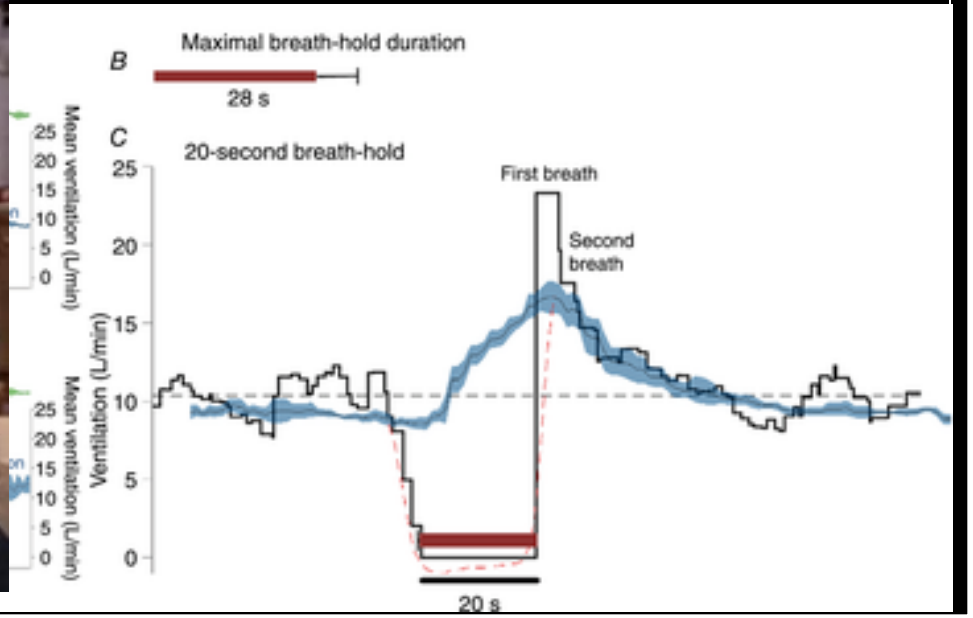
Loop gain = Response to disturbance / Disturbance



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





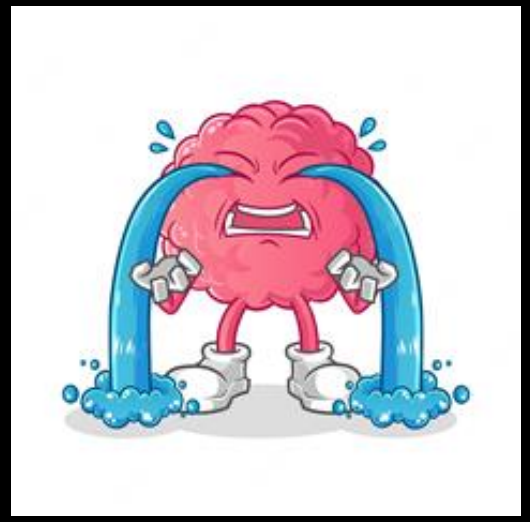


Messineo L, Taranto-Montemurro L, Azarbarzin A, Oliveira Marques MD, Calianese N, White DP, Wellman A, Sands SA. Breath-holding as a means to estimate the loop gain contribution to obstructive sleep apnoea. The Journal of physiology. 2018 Sep;596(17):4043-56.

P

A

L



M

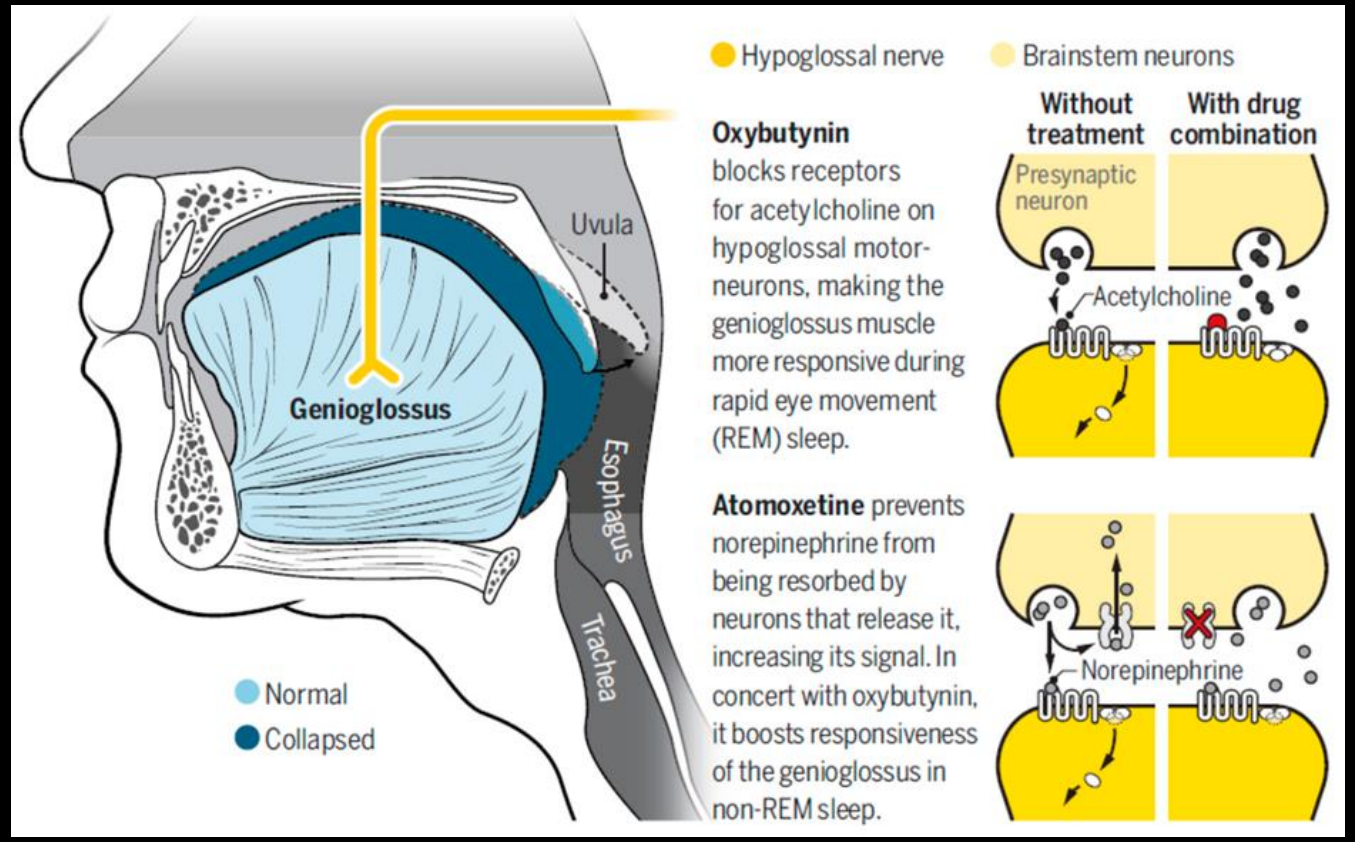
Arousal Threshold

- Hypnotics
- ?Treat underlying anxiety/ depression/PTSD

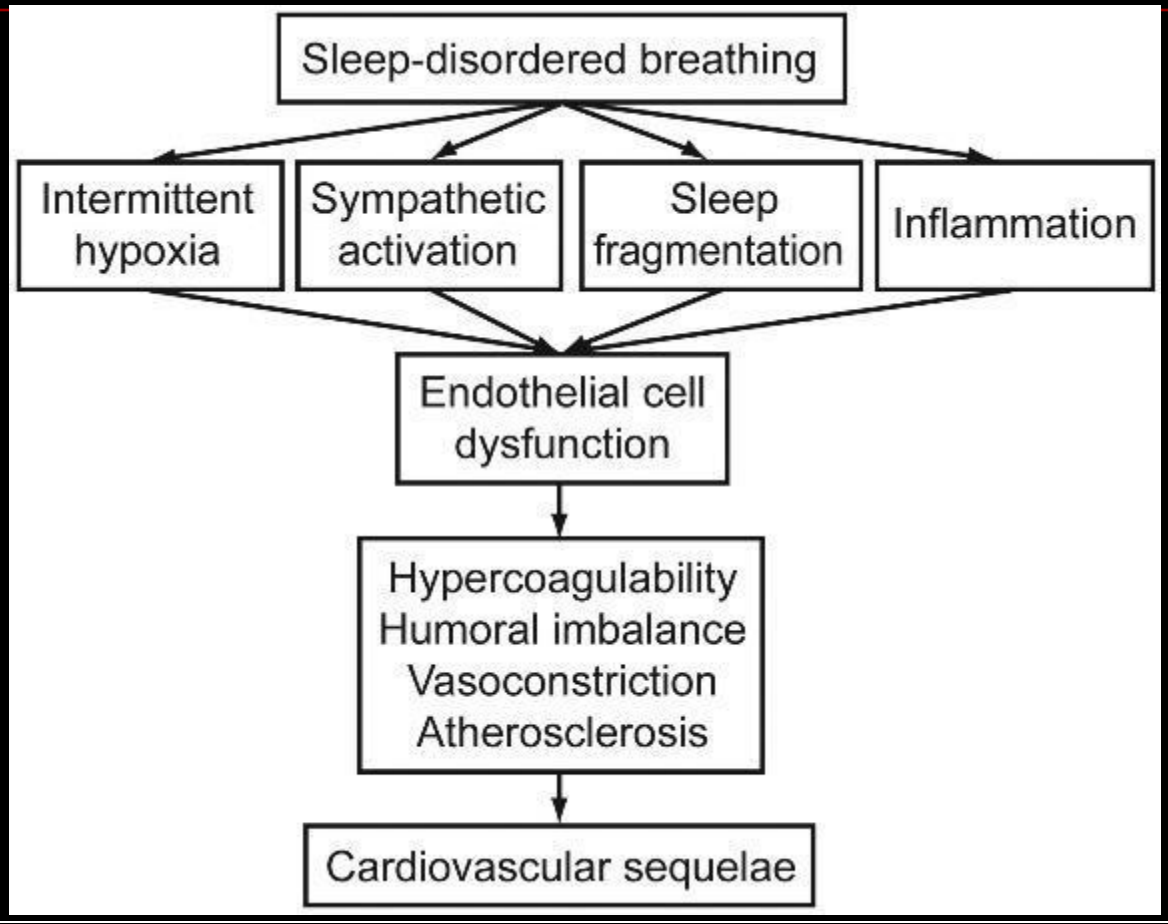
Loop Gain

- 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.

END OF CHAPTER 2:
Pathophysiology of sleep apnea

BEGINNING OF CHAPTER 3:
Diagnosis of sleep apnea

Symptoms of OSA

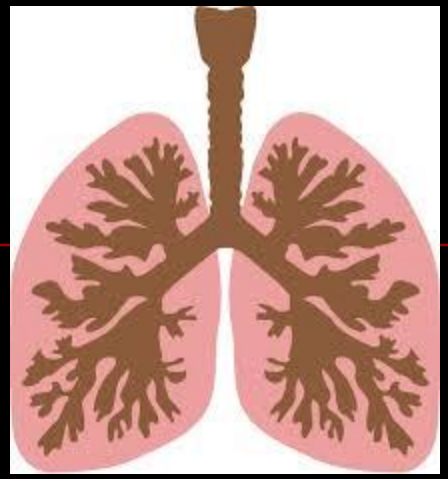

ON
OFF

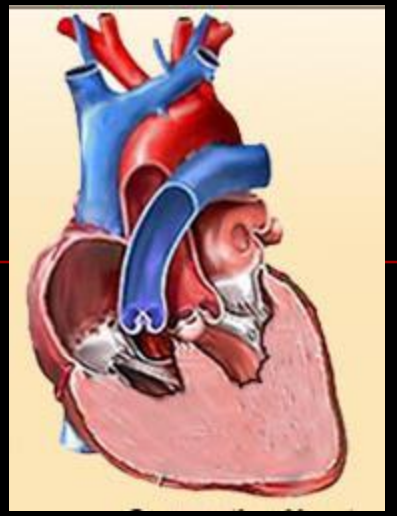
Type 1: full attended PSG (≥ 7 channels) in-lab

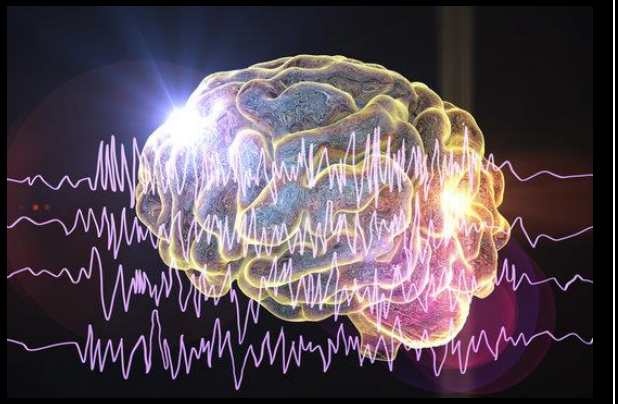
Type 2: full unattended PSG (≥ 7 channels)

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

Type 4: 1 or 2 channels usually using oximetry as 1 of the parameters







Home Study

Non-inferior outcomes in CPAP acceptance and functional improvements

Apnea-Hypopnea index (AHI)

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

END OF CHAPTER 3:

Diagnosis of sleep apnea- Symptoms and sleep Studies

BEGINNING OF CHAPTER 4:

Management of sleep apnea

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

CPAP

5-15

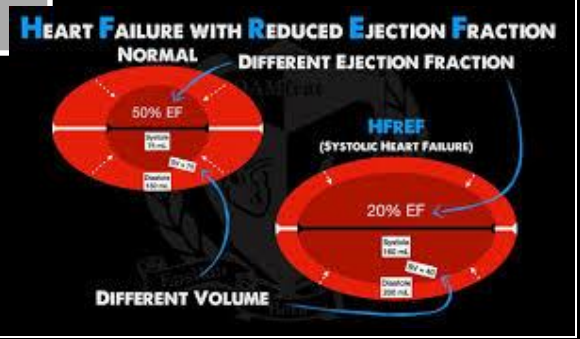
APAP

12/8

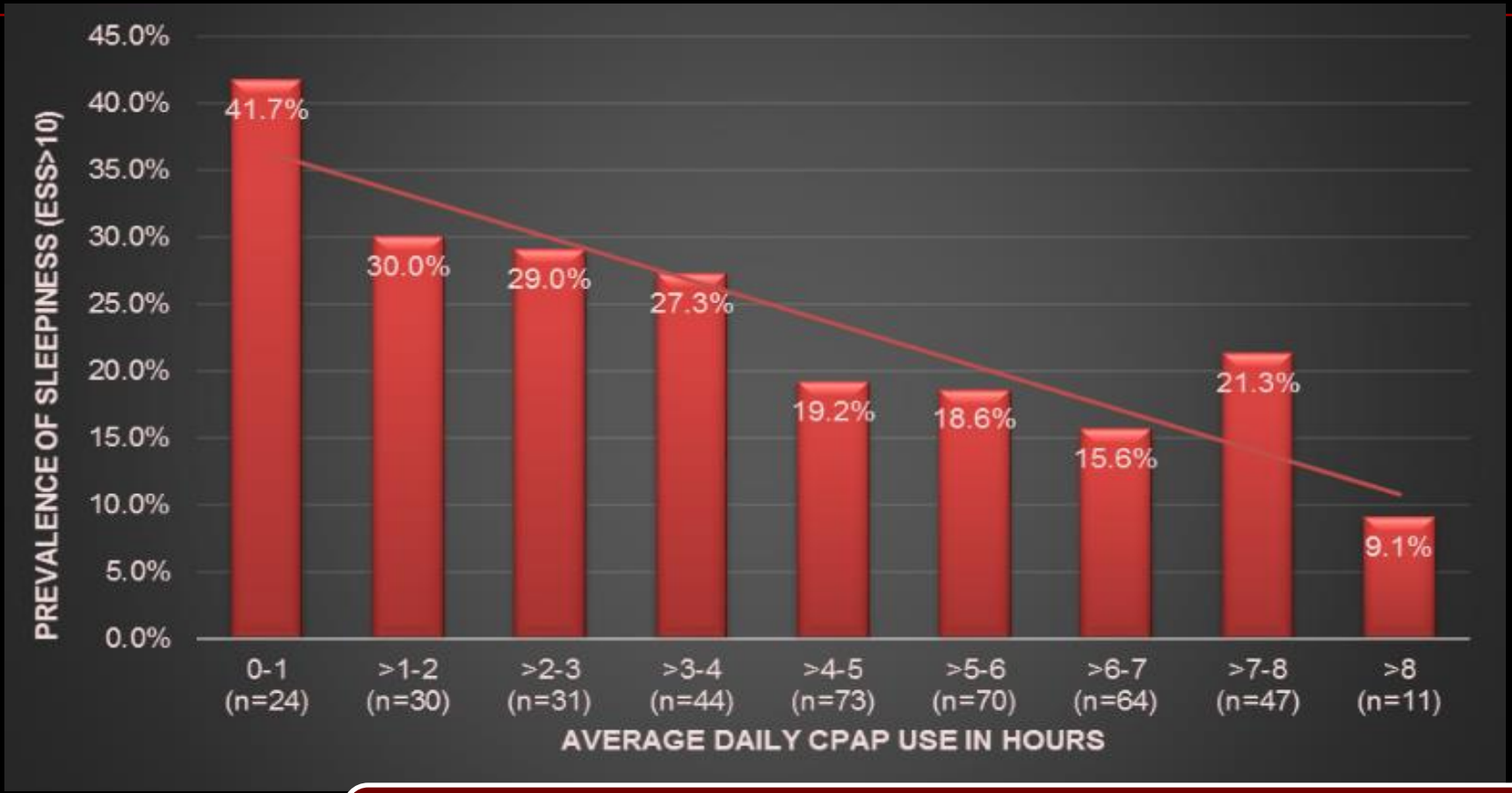
BPAP

ASV
AutoSV

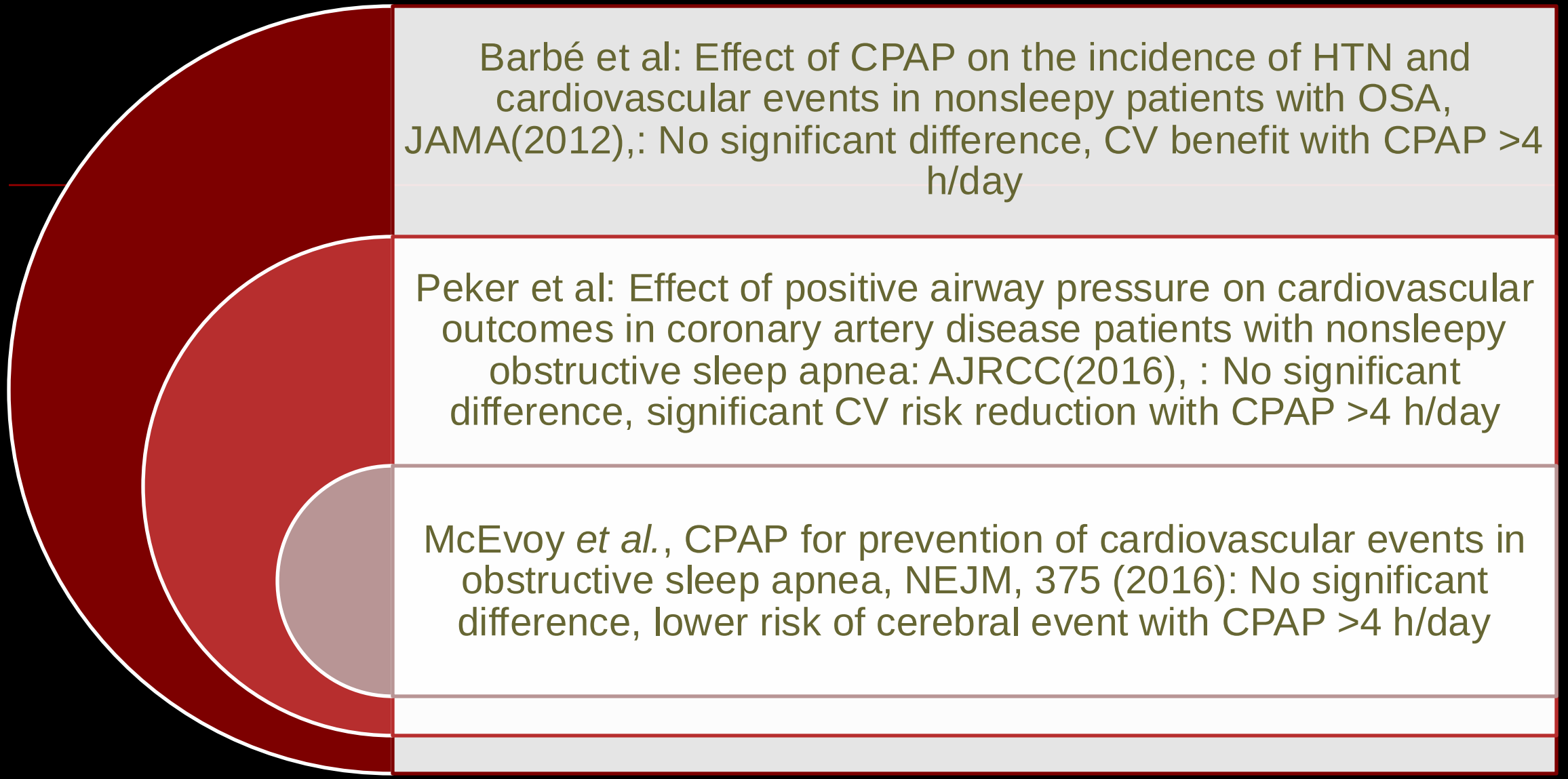
EPAP 4–15
PS: 0–20
Rate: Auto



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.



Javaheri, Shahrokh, et al. "Sleep apnea: types, mechanisms, and clinical cardiovascular consequences." *Journal of the American College of Cardiology* 69.7 (2017): 841-858.

Effect of CPAP on CV outcomes

Adherence Analysis

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

Javaheri, Shahrokh, et al. "Sleep apnea: types, mechanisms, and clinical cardiovascular consequences." *Journal of the American College of Cardiology* 69.7 (2017): 841-858.

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

AHI ≥ 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 ≥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).

Peker, Yüksel, et al. "Effect of OSA and CPAP treatment on cardiovascular outcomes in acute coronary syndrome in the RICCADSA trial." Journal of clinical medicine 9.12 (2020): 4051.

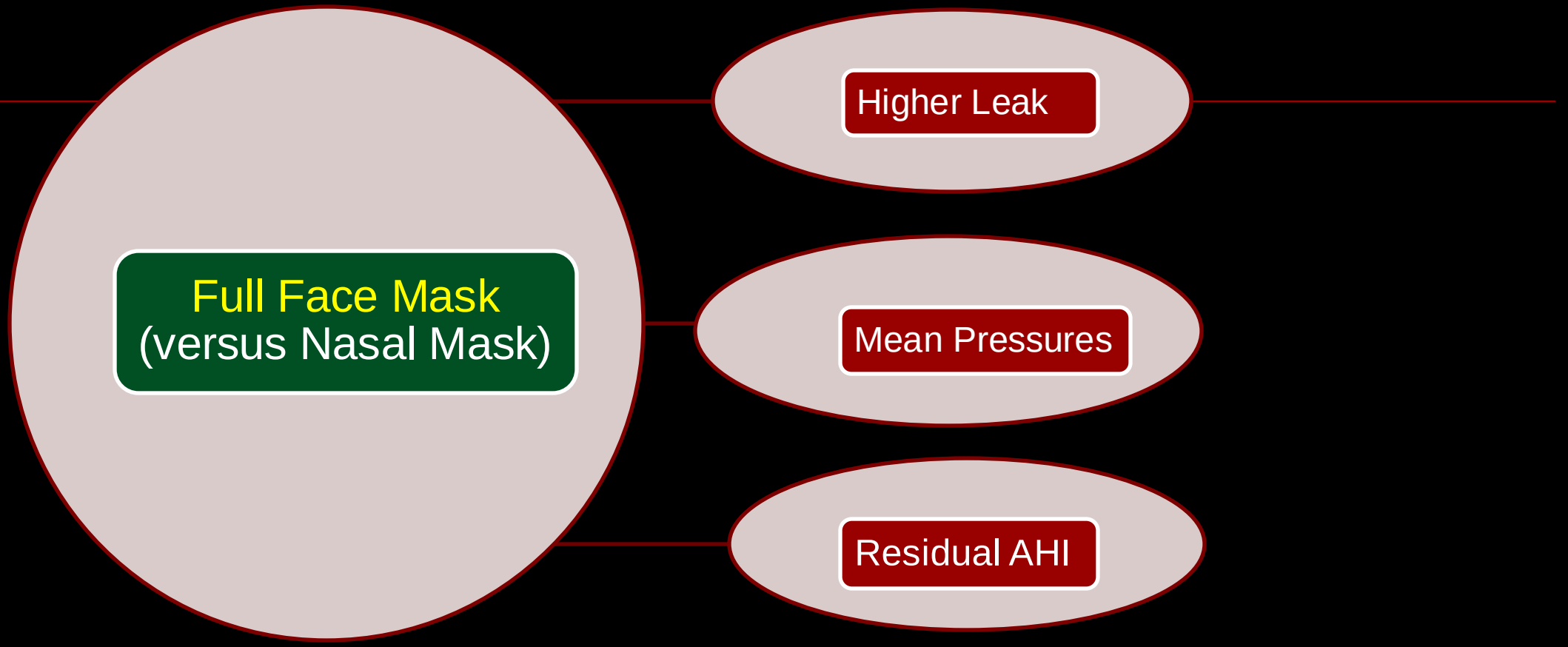
Objective Adherence

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

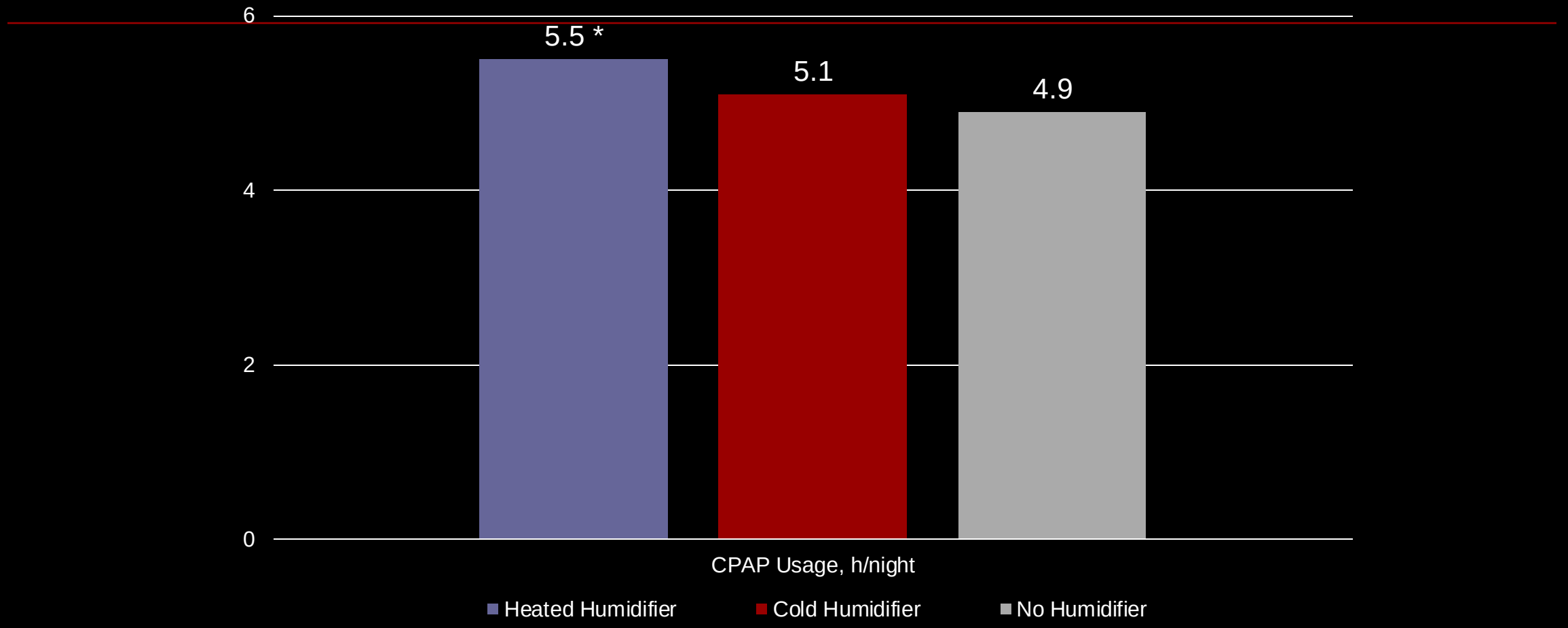
CPAP is uncomfortable

It's the most effective therapy


Full Face Mask
(versus Nasal Mask)
Higher Leak
Mean Pressures
Residual AHI

“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.

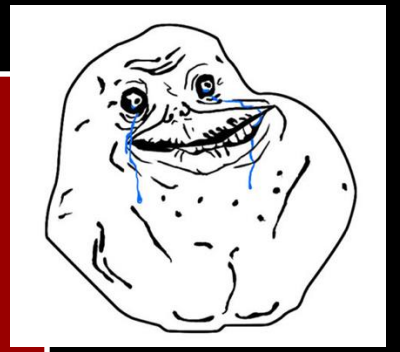
More common in those with GERD

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

- Nasal Masks
- Wear the CPAP while awake
- PATIENT EDUCATION
- Cognitive behavior therapy
- Anxiety medications

Participants with Good Adherence

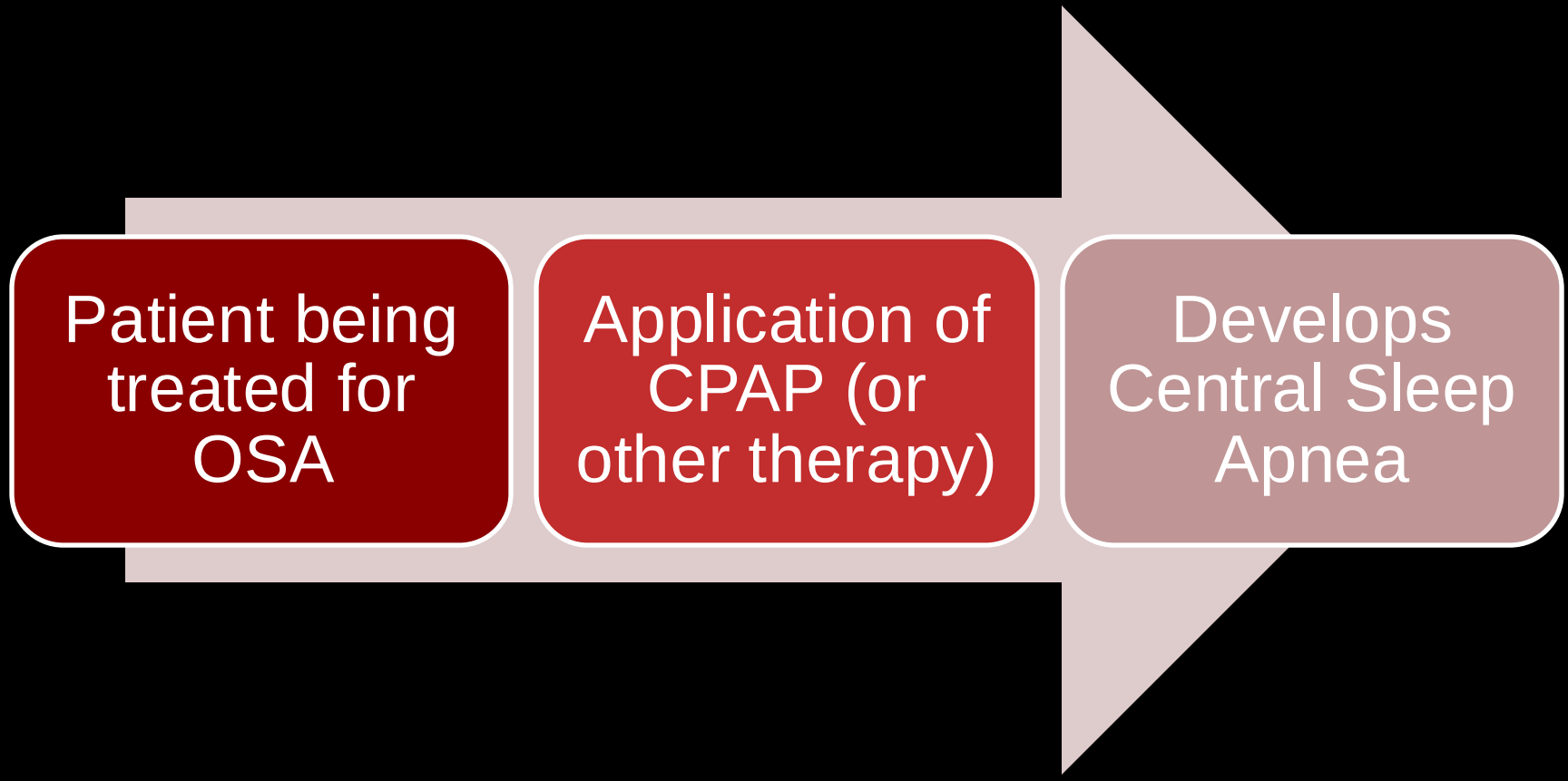
The prevalence of ESS >10 after 6m of CPAP 18.1%

Higher in those with baseline excessive sleepiness

No other variables were significantly associated with odds of sleepiness

Budhiraja, Rohit, et al. "Predictors of sleepiness in OSA at baseline and after 6 months of CPAP therapy." *European Respiratory Journal* 50.5 (2017): 1700348.

Treatment-Emergent Central (Complex) 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 pCO2 levels increase the risk

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

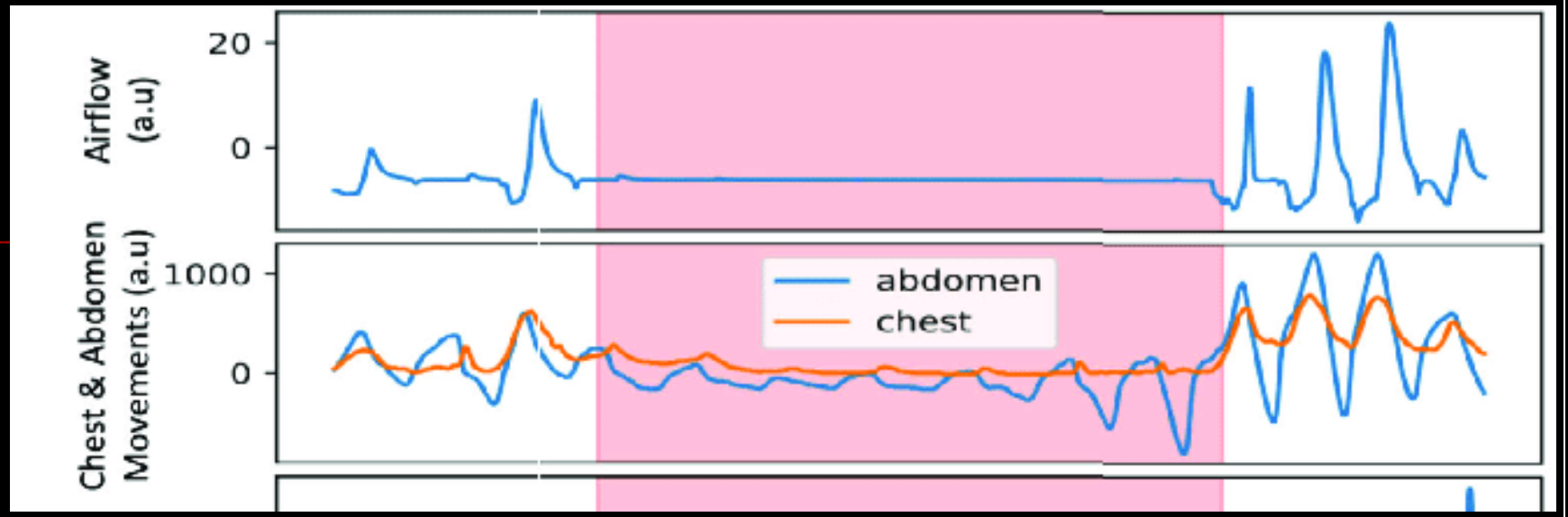
ASV appears superior to BPAP-ST for the long-term treatment of persistent CSA.

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

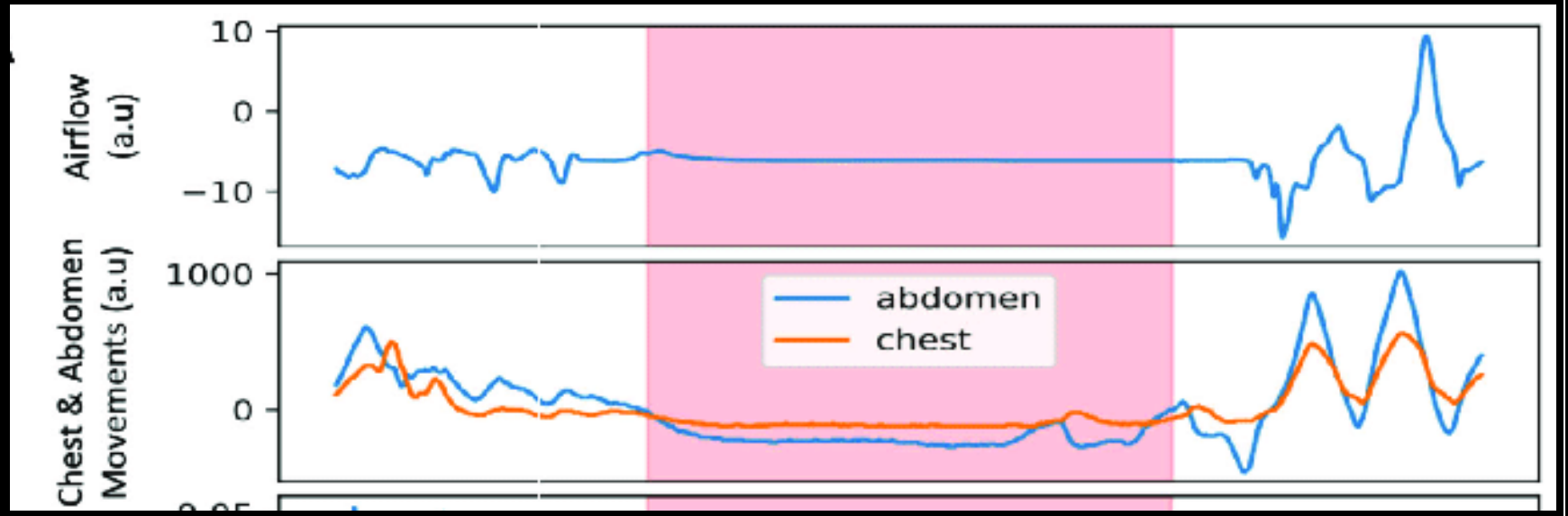
Moro, Marilyn, et al. "Clinical predictors of central sleep apnea evoked by positive airway pressure titration." *Nature and science of sleep* 8 (2016): 259.

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

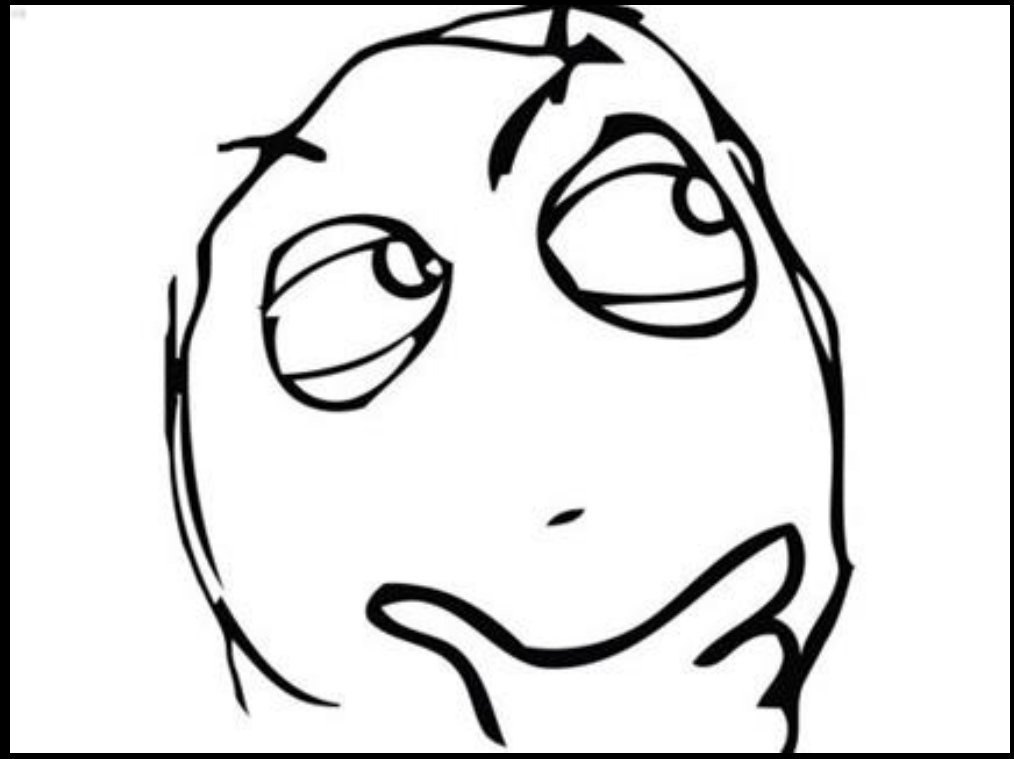
Obstructive



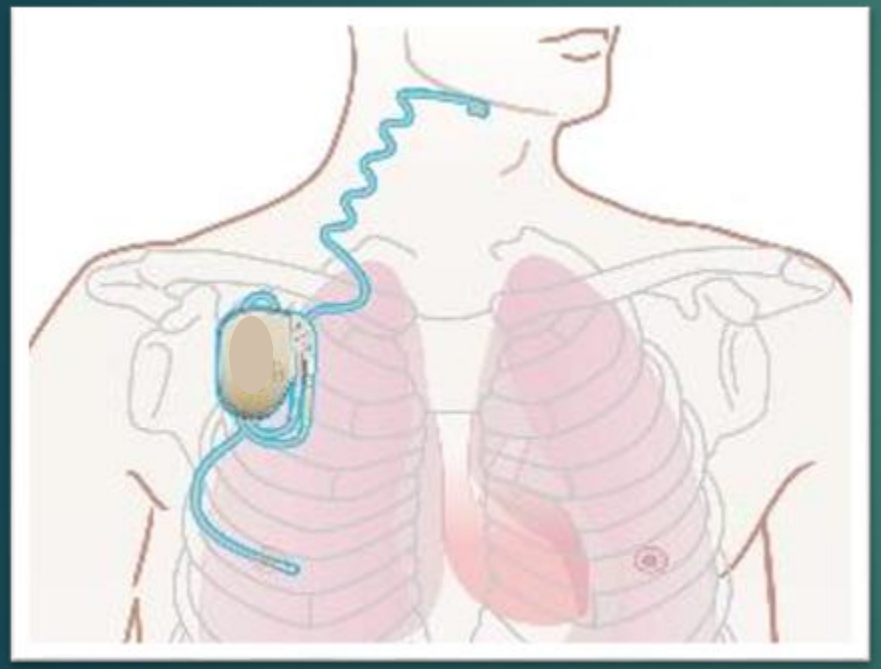
Central/ Mixed

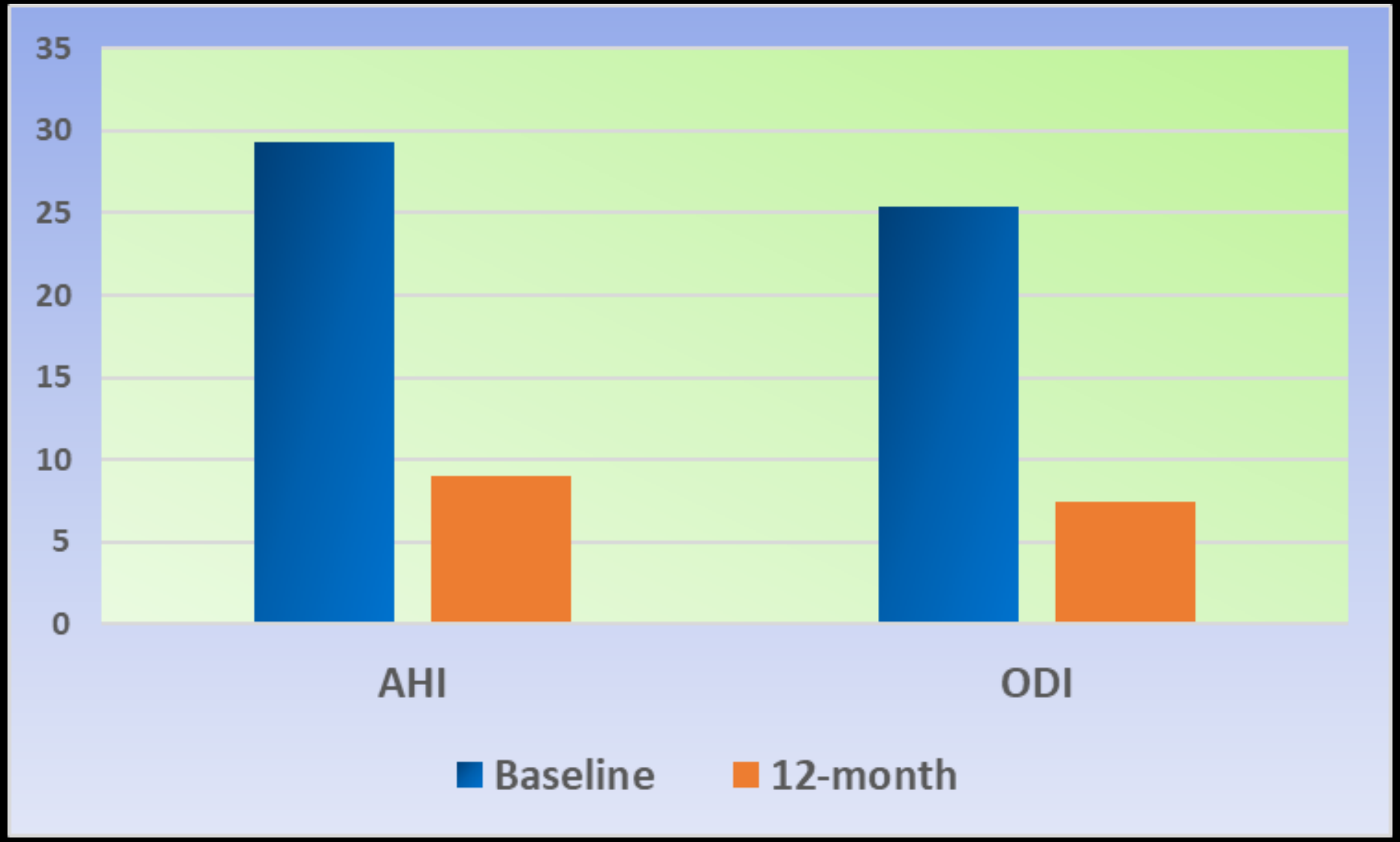


What else do you got?



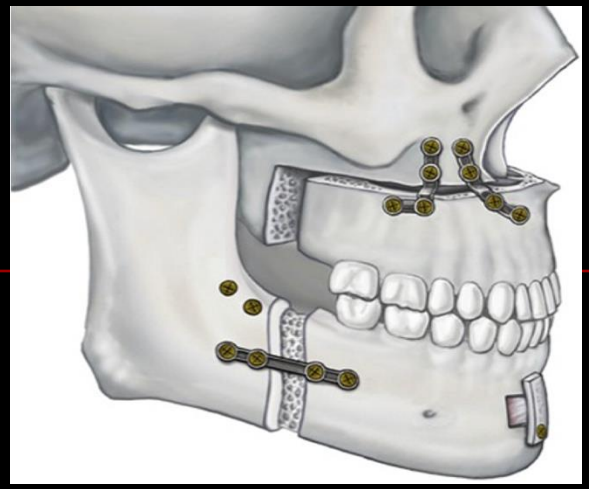
Hypoglossal Nerve Stimulation

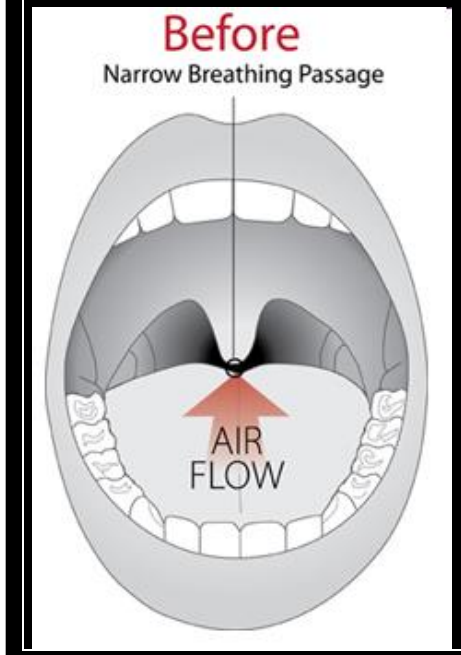


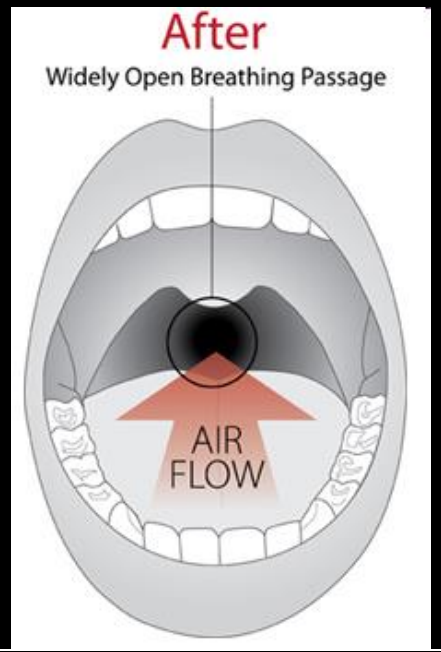


Strollo Jr, Patrick J., et al. "Upper-airway stimulation for OSA." NEJM 370.2 (2014): 139-149.

Surgery







Didgeridoo

Gaps in OSA Knowledge

Endotypes

Consequences of OSA & benefits of therapy

CPAP adherence & Alternative treatments

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

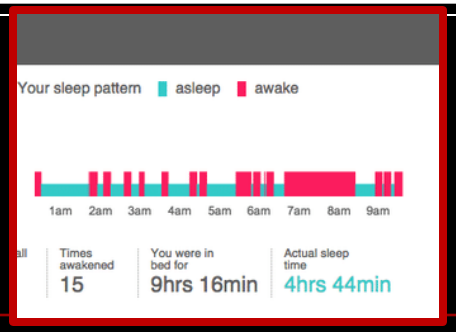
Budhiraja et al, Sleep Medicine Clinics, Available online 16 March 2016

Big Data Sources

Electronic health records (EHR)

Mobile phones, wearable health devices

Large clinical trials


Your sleep pattern
asleep
awake
1am
2am
3am
4am
5am
6am
7am
8am
9am
Times awakened
15
You were in bed for
9hrs 16min
Actual sleep time
4hrs 44min

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

Anatomy AND Physiology

‘Other’ Symptoms

Monitor and Improve CPAP Adherence

Other treatments

MAD, HNS, Positional, Surgical

Treat Overall Sleep

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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