



AMERICAN
COLLEGE of
CARDIOLOGY

Sleep Apnea: Types, Mechanisms and Clinical Cardiovascular Consequences A Frequent Condition, but Easily Missed

Shahrokh Javaheri, MD

Sleep Physician, Bethesda North Hospital
Professor Emeritus, University of Cincinnati,
Cincinnati, Ohio

New York Cardiovascular Symposium
December 11-13, 2015

Definitions

Apnea

Cessation of airflow
 ≥ 10 seconds
(missing 2 breaths)

Hypopnea

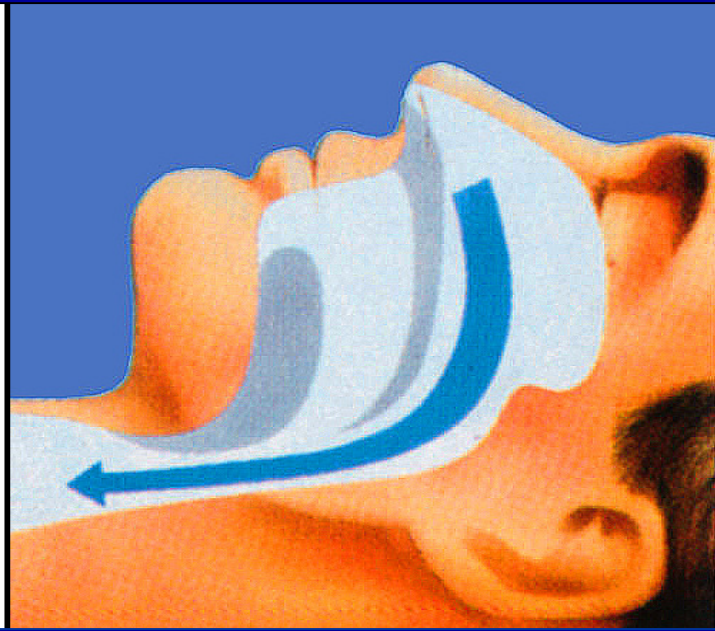
Decrease in airflow
 ≥ 10 seconds

Definitions

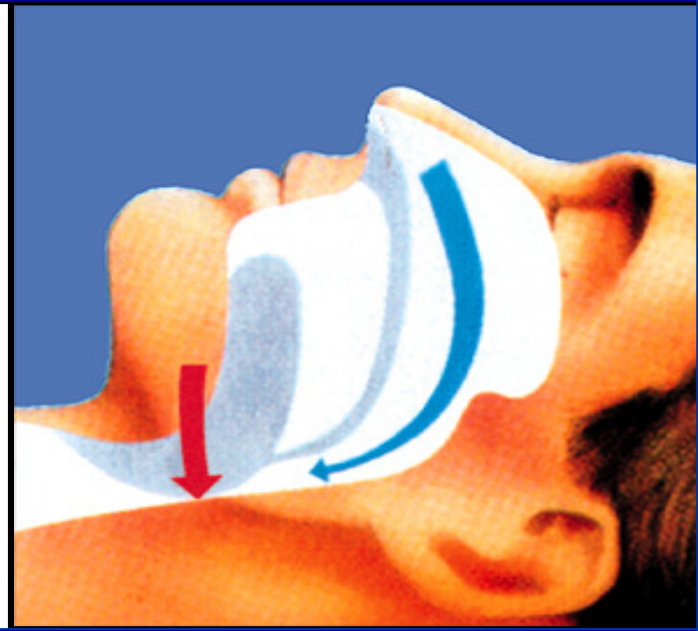
Apnea: Cessation of airflow
 ≥ 10 seconds

2 phenotypes:
OSA and CSA

Sleep and Genioglossus Muscle OA, Hypopnea and Snoring



Normal Airway



Obstructed Airway

AHI is the metric to define the presence and the severity of sleep apnea as a disorder

- **AHI:** number of events per hour of sleep
- **NI :** less than 5
- **Mild sleep apnea :** 5, <15
- **Moderate sleep apnea :** 15, < 30
- **Severe sleep apnea :** ≥ 30
(**HSAT**)

Risk Factors for OSA

1. Obesity : Most important risk factor for OSA

Neck fat (within the throat)

**Neck size 17 in males
16 in females**

35% of US population are obese

Current Prevalence of OSA in USA population

(Age, years)	2007-2010 Peppard/Young Am J Epidemiol, 2013	2015
Men (%)		
AHI > 5/hr (30-70)	34	?
AHI > 15/hr (30-70)	13	
Women (%)		
AHI > 5/hr (30-70)	17	?
AHI > 15/hr (30-70)	6	

OSA a Major Public Health Issue

34% in males and 17% in females

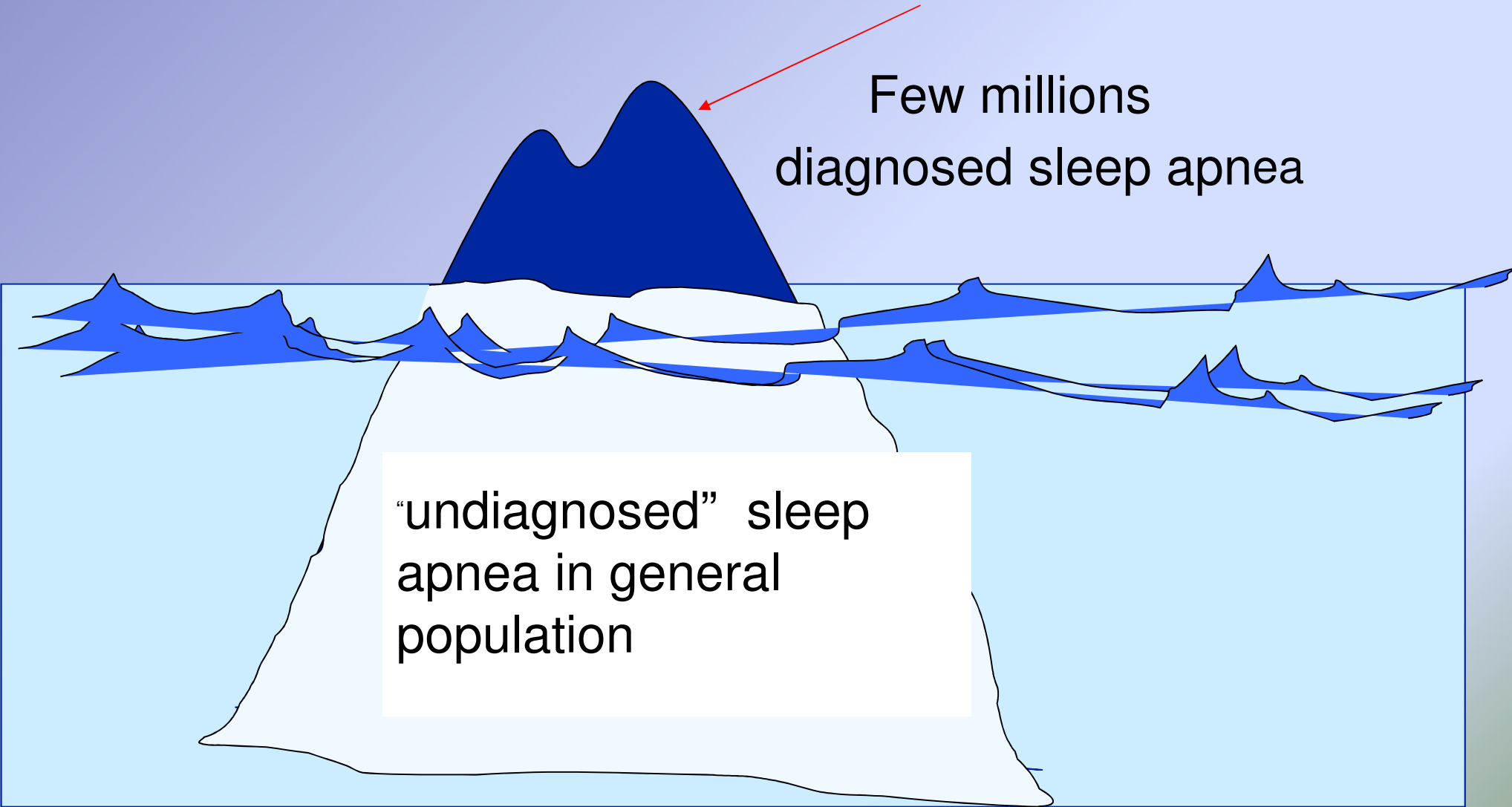
$$34\% + 17\% = 51 / 2 = 25\%$$

$$25\% \text{ of } 300,000,000 = 75,000,000$$

.....Only the “tip” has received medical attention

Few millions
diagnosed sleep apnea

“undiagnosed” sleep
apnea in general
population

An iceberg floating in a light blue sea. The visible tip of the iceberg is dark blue and jagged, representing diagnosed sleep apnea. A red arrow points from the text 'Few millions diagnosed sleep apnea' to this tip. The much larger, submerged part of the iceberg is light blue and represents undiagnosed sleep apnea. A white rectangular box is placed on the submerged part, containing the text '“undiagnosed” sleep apnea in general population'. The background is a solid light purple.

OSA a Major Public Health Issue

Cardio-metabolic consequences of OSA

HTN

Resistant HTN

Pulmonary HTN

CAD

CHF, HFrEF and HFpEF

A. Fib

TIA

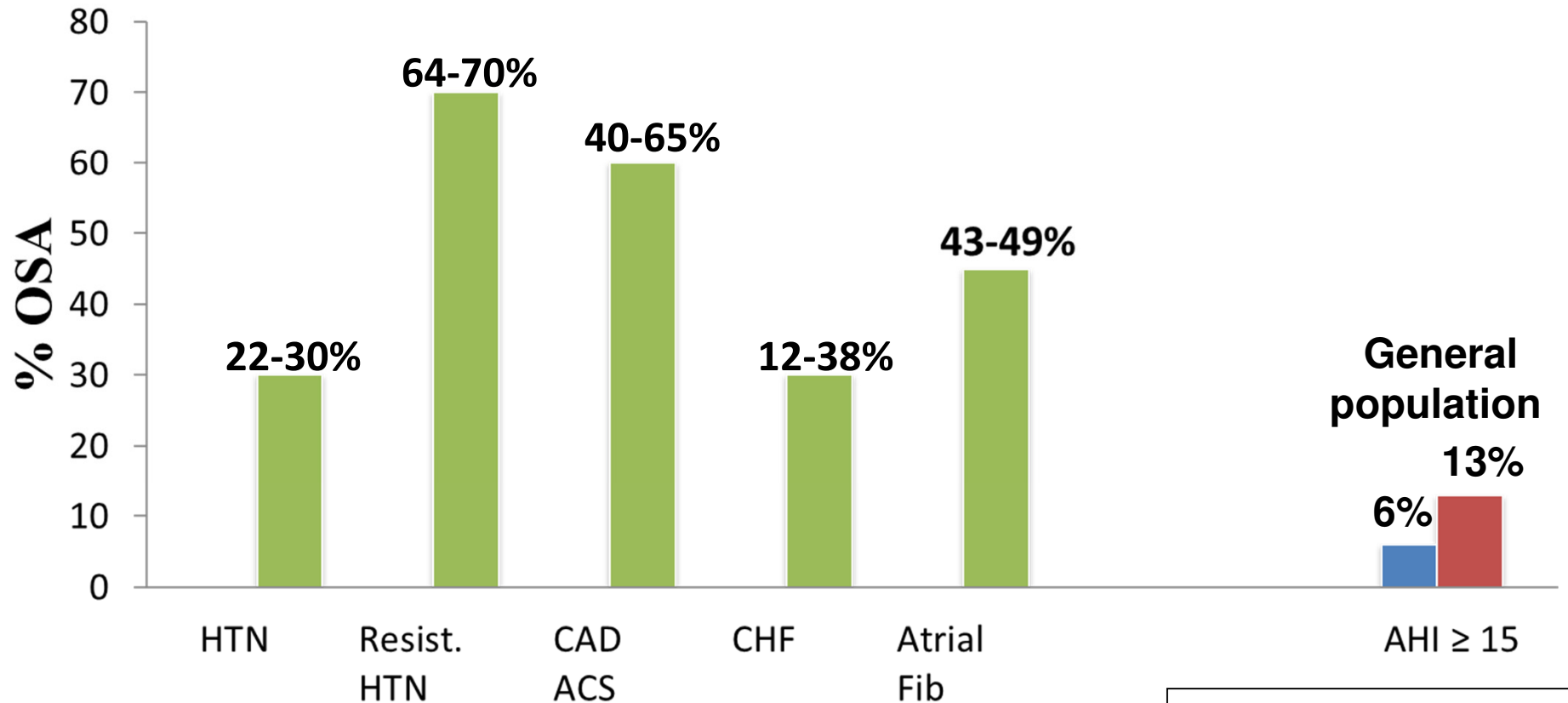
Stroke

Sudden death

Metabolic dysregulation-Insulin Resist/DM

Huge Health Cost

Prevalence of OSA in CV Population vs. Community Based



**Wisconsin Sleep Study
2013**

Drager, L. Am J Cardiol. 2010

Pedrosa, RP. Hypertension. 2011

Zhao LP. J Clin Sleep Med. 2014

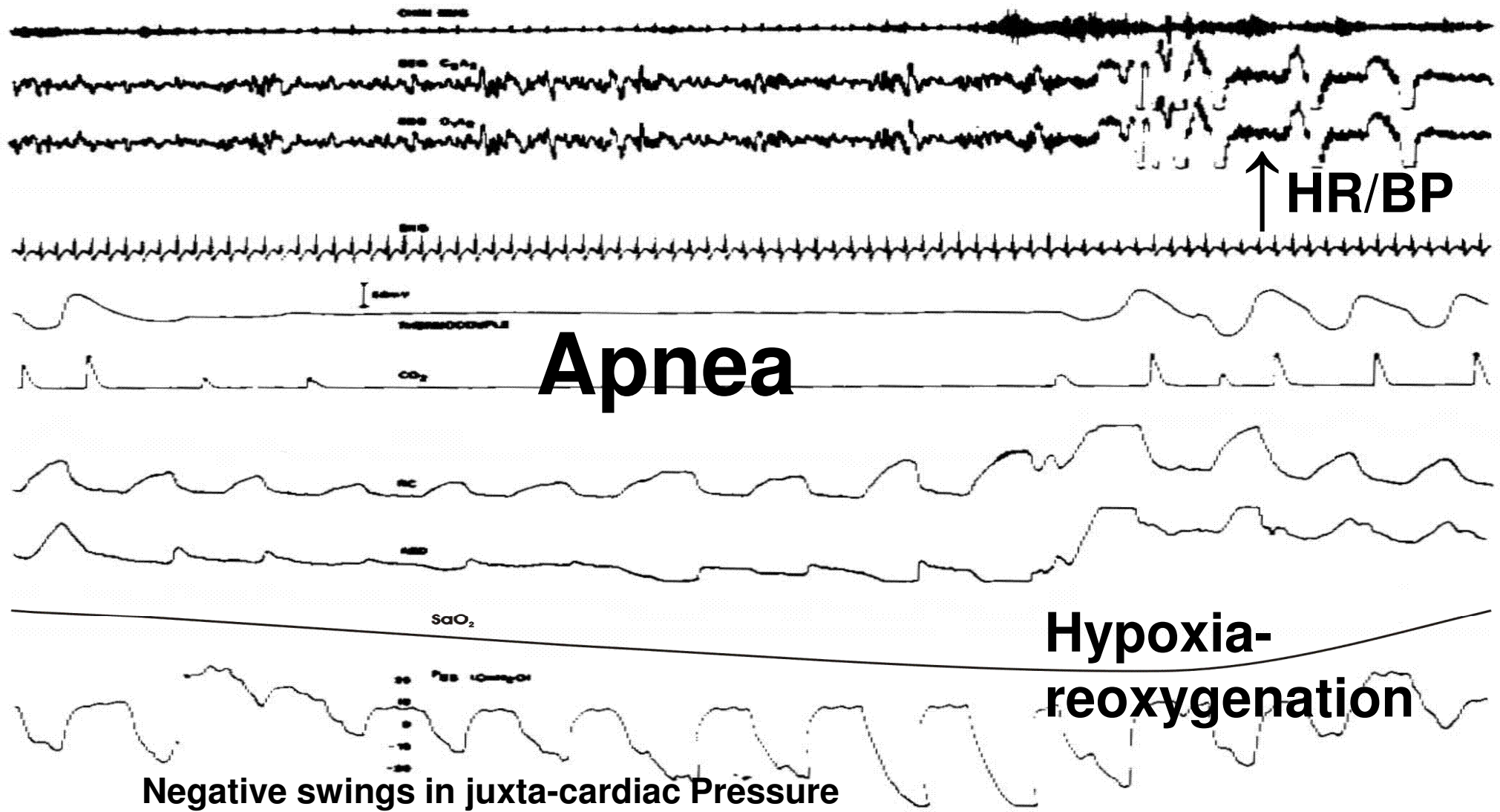
Gami AS. Circulation. 2004

Bitter, T. . Dtsch Arztebl Int. 2009

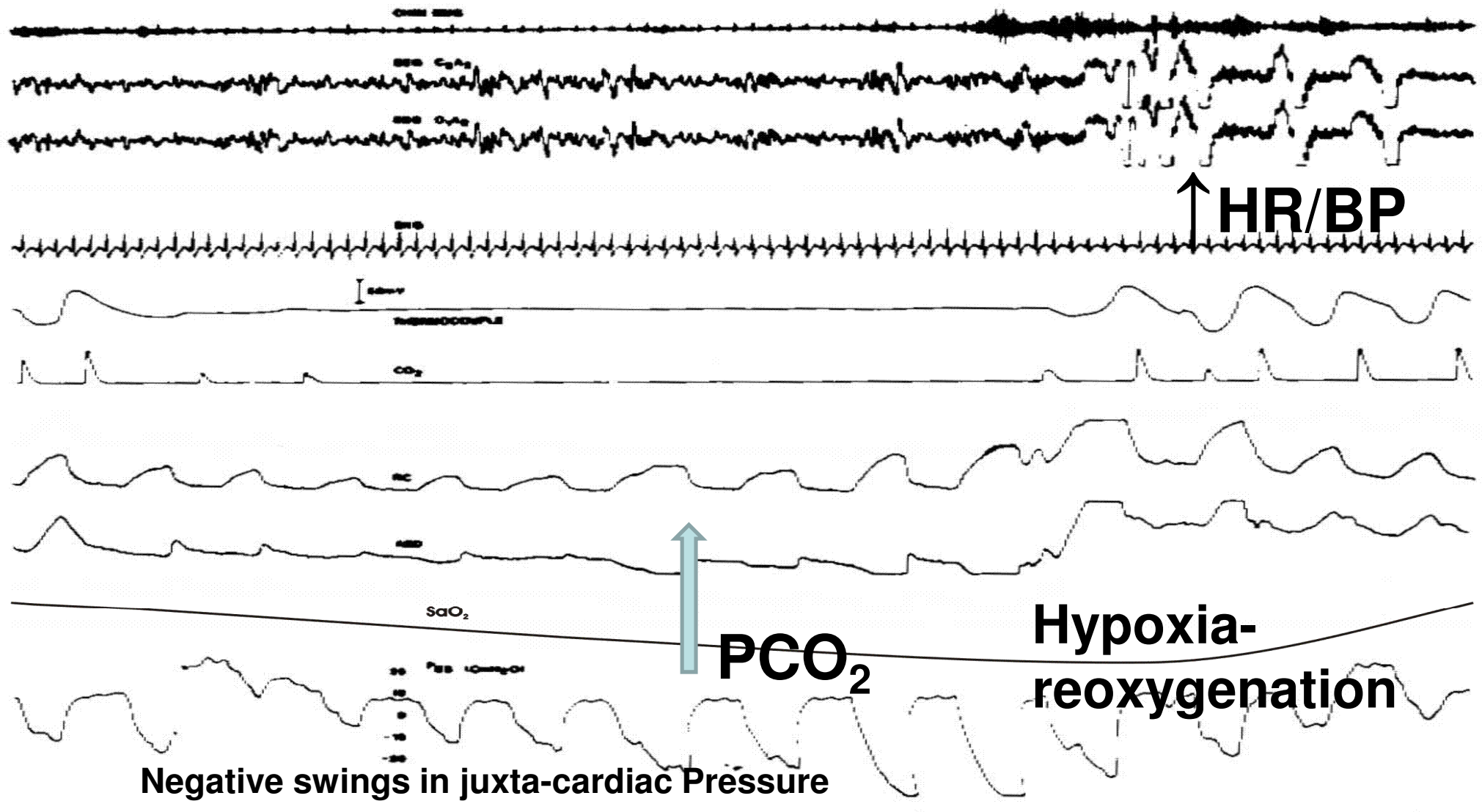
Javaheri, S.. Int J Cardiol. 2006

Oldenburg, O. Eur J Heart Fail. 2007

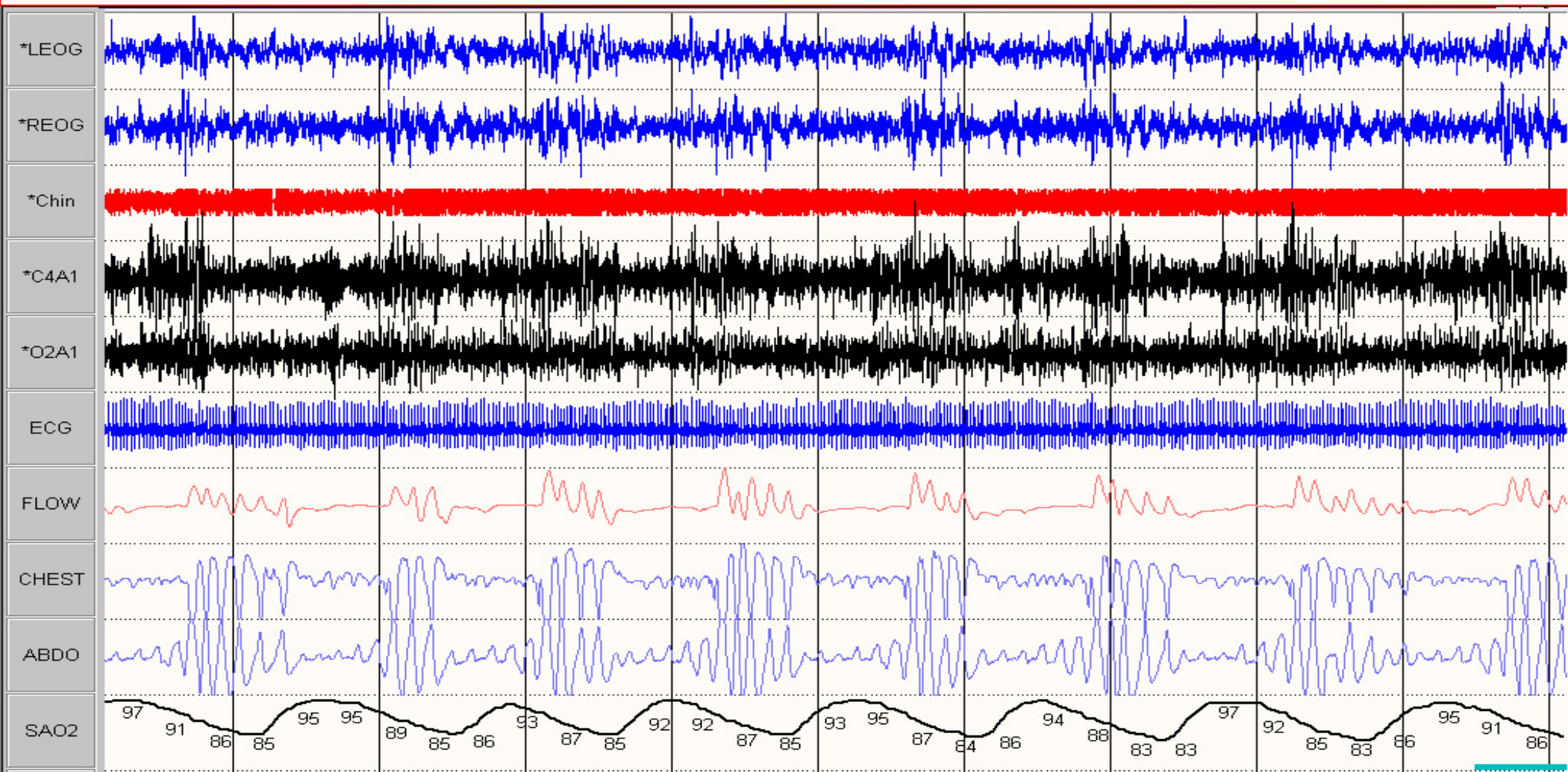
Overnight pathophysiological consequences of OSA Arousal:



OSA



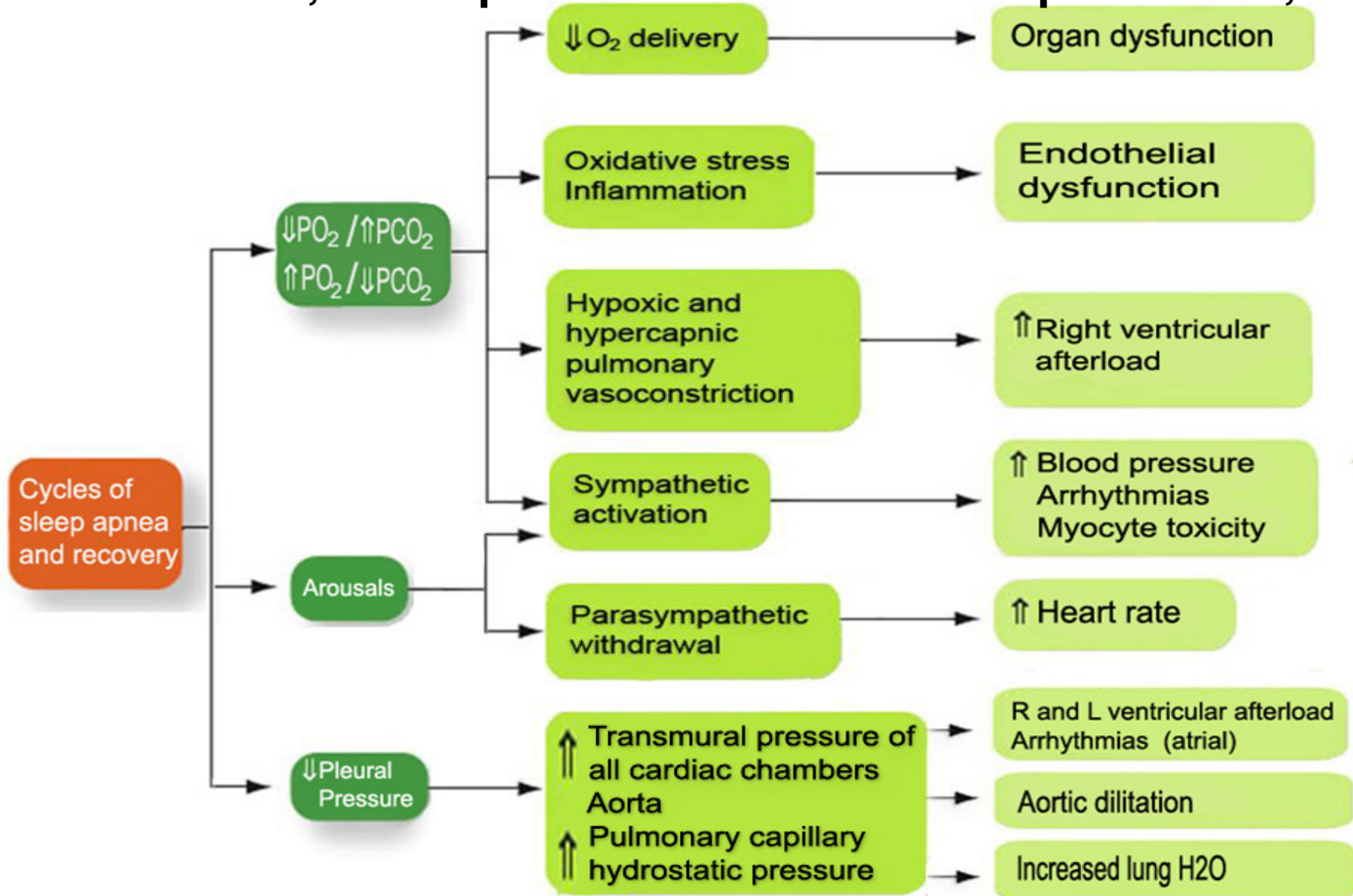
Recurrent episodes OSA(AHI=80/hr)



Polysomnography - 5 minutes page

Biological pathways mediating CV complications of sleep apnea

Javaheri, Principles and Practice of Sleep Medicine, 2016



CVD Comorbidities with OSA and Impact of Therapy with CPAP

-
- **Resistant HTN**

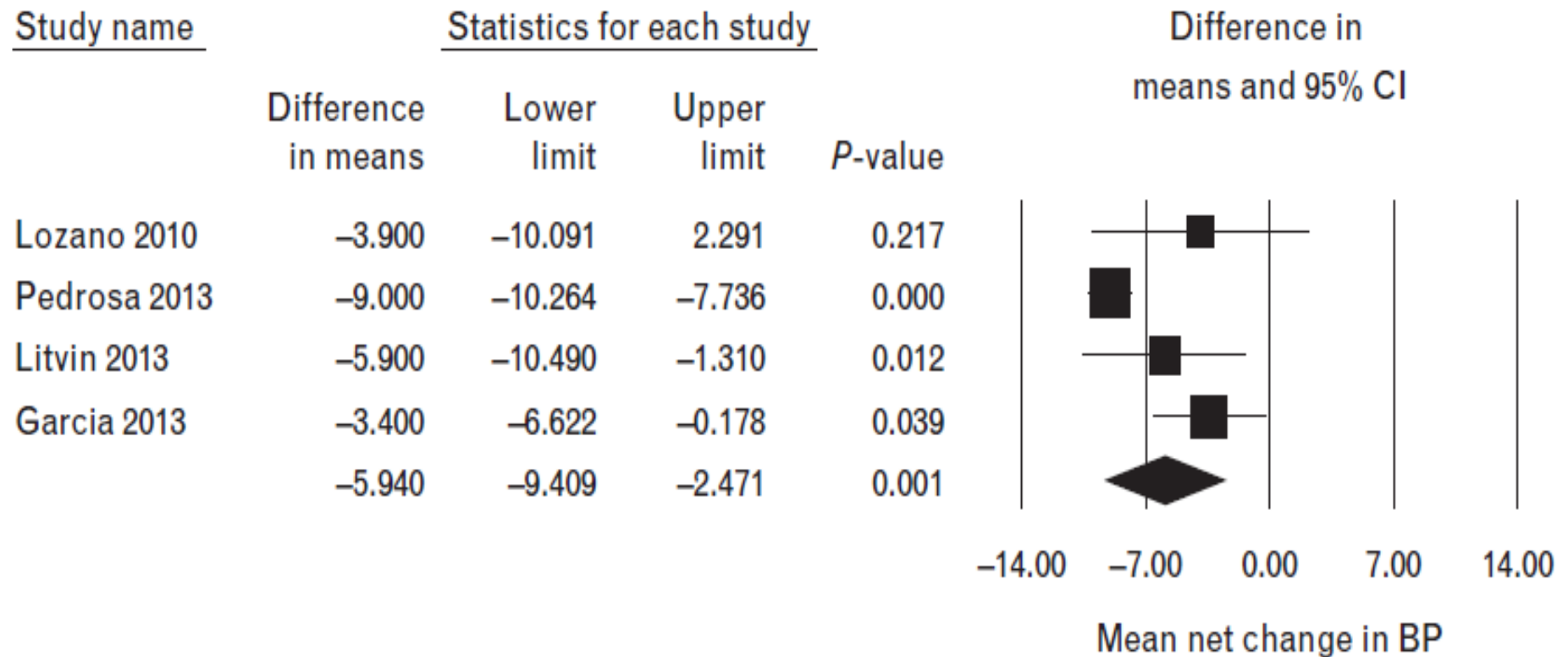
- **A. Fib**

- **HF**

-
-
- **Mortality and SCD**

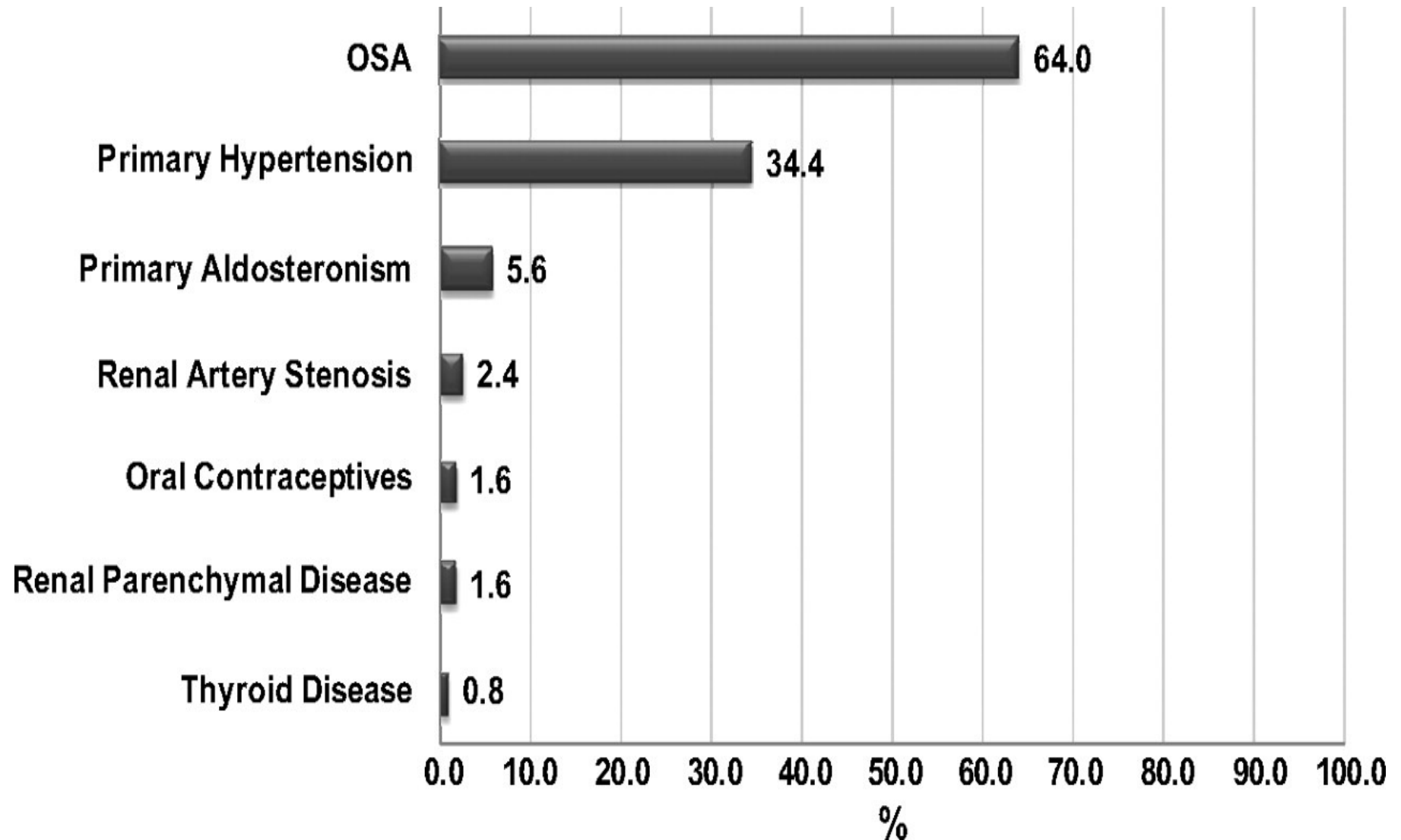


Mean change in 24-h BP from 4 RCTs in Resistant HTN



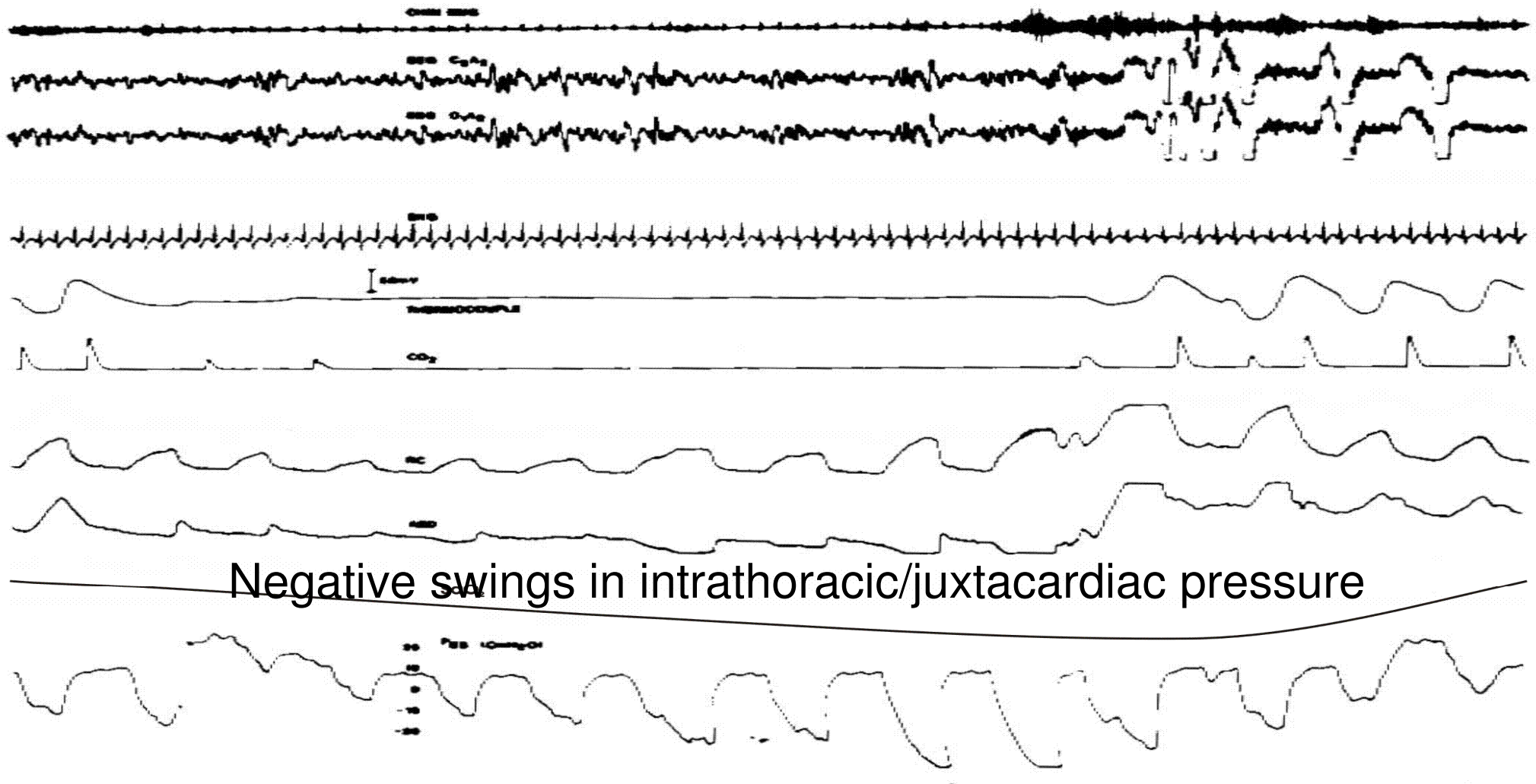
- The pooled estimate shows a favorable reduction of BP with CPAP treatment in patients with resistant hypertension and OSA.
 - The effect sizes are larger than those previously reported in patients with OSA without resistant hypertension
- J Hypertens 2014 32:2341–2350

Prevalence of secondary causes associated with resistant hypertension.

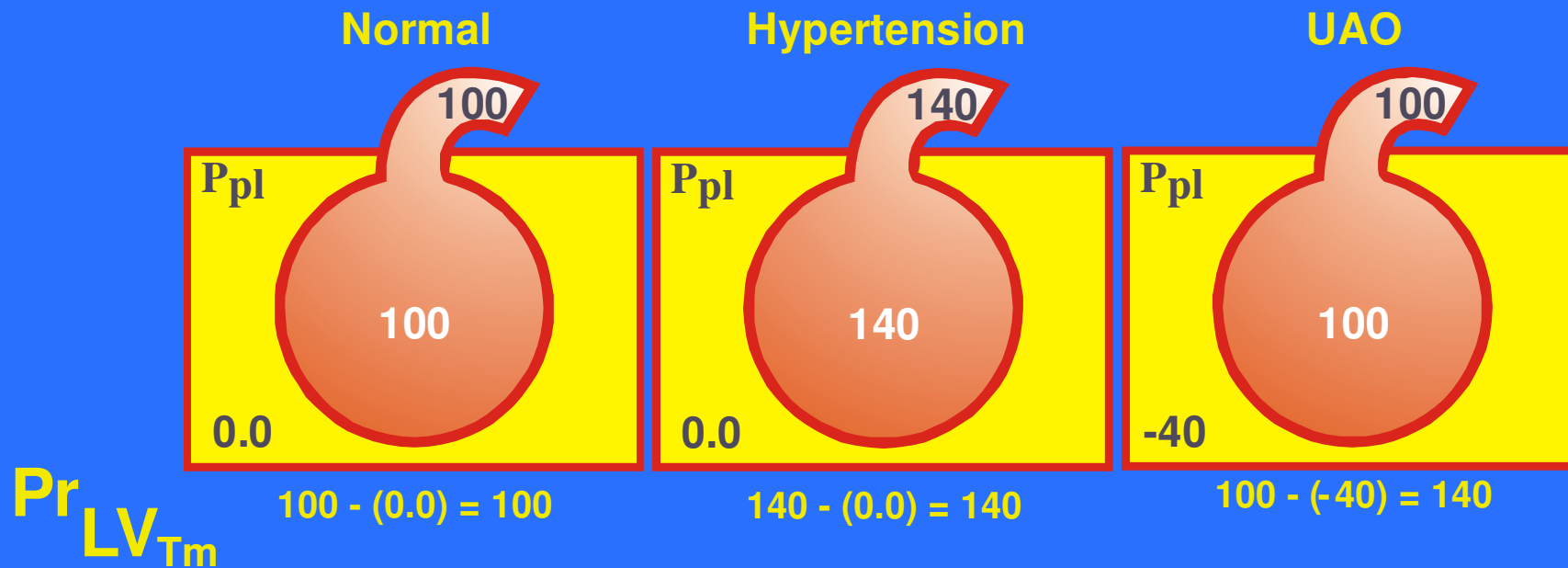


Pedrosa et al. Hypertension. 2011

OSA as a cause and recurrence of A Fib



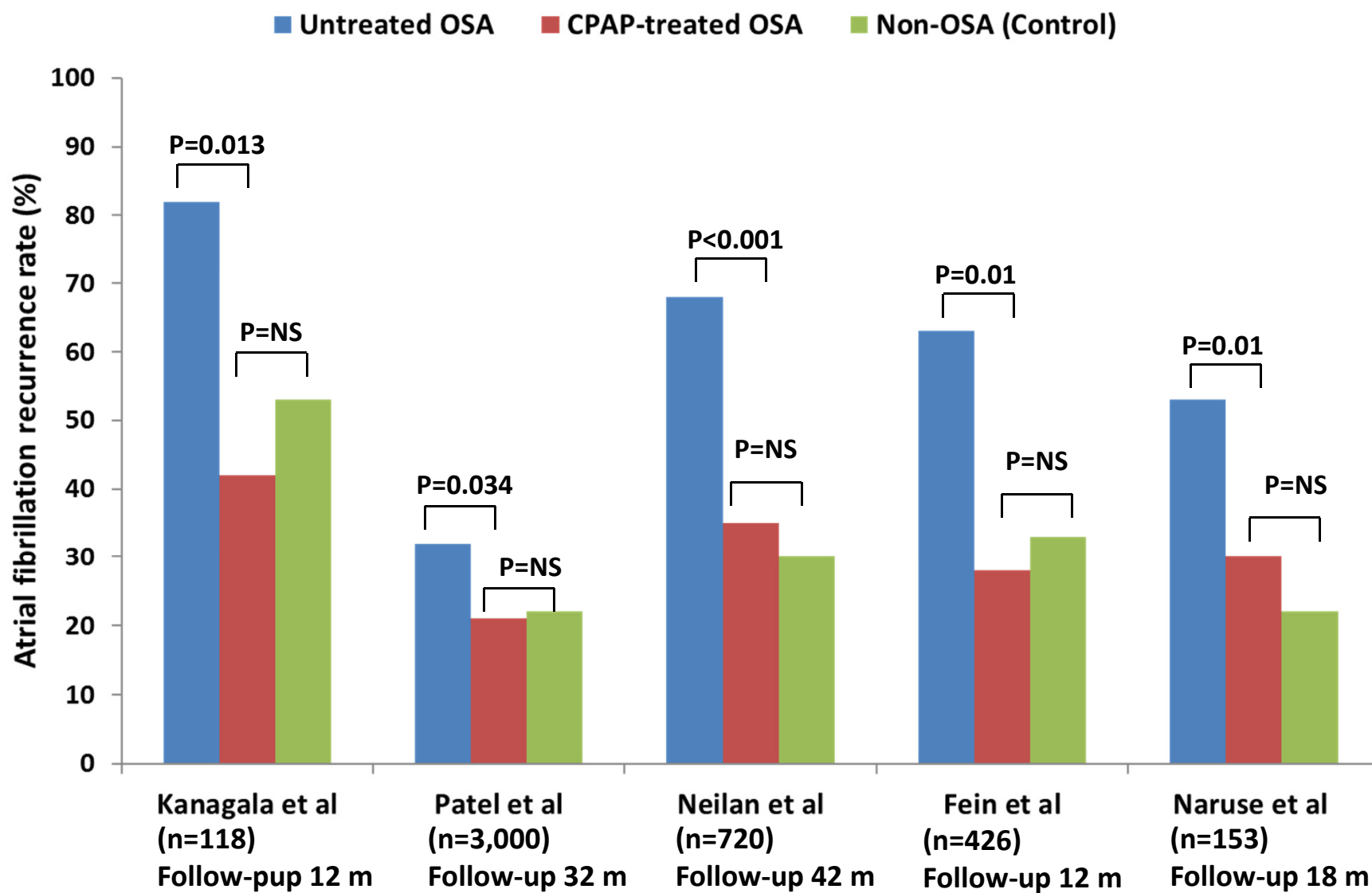
UAO \uparrow transmural Pr of all cardiac chambers



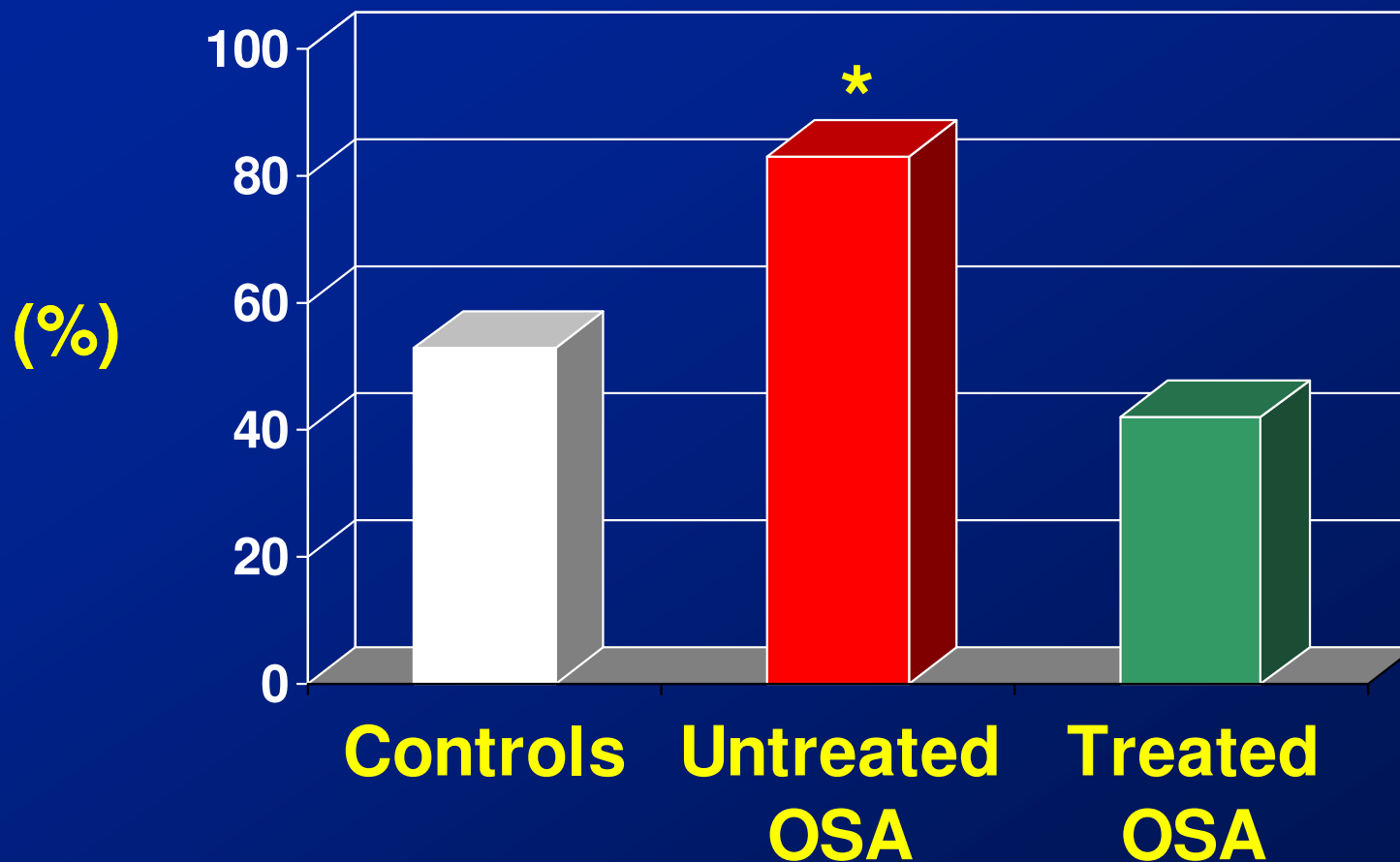
Implications for A. fib and increased ventricular afterload

OSA is arrhythmogenic

- 1. Hypoxia**
- 2. Acidosis**
- 3. Increased sympathetic activity**
- 4. Increased negative intrathoracic pressure
resulting in activation of mechano receptors
and ion channels**
- 5. Upregulation of oxidative stress and
inflammatory cascades**

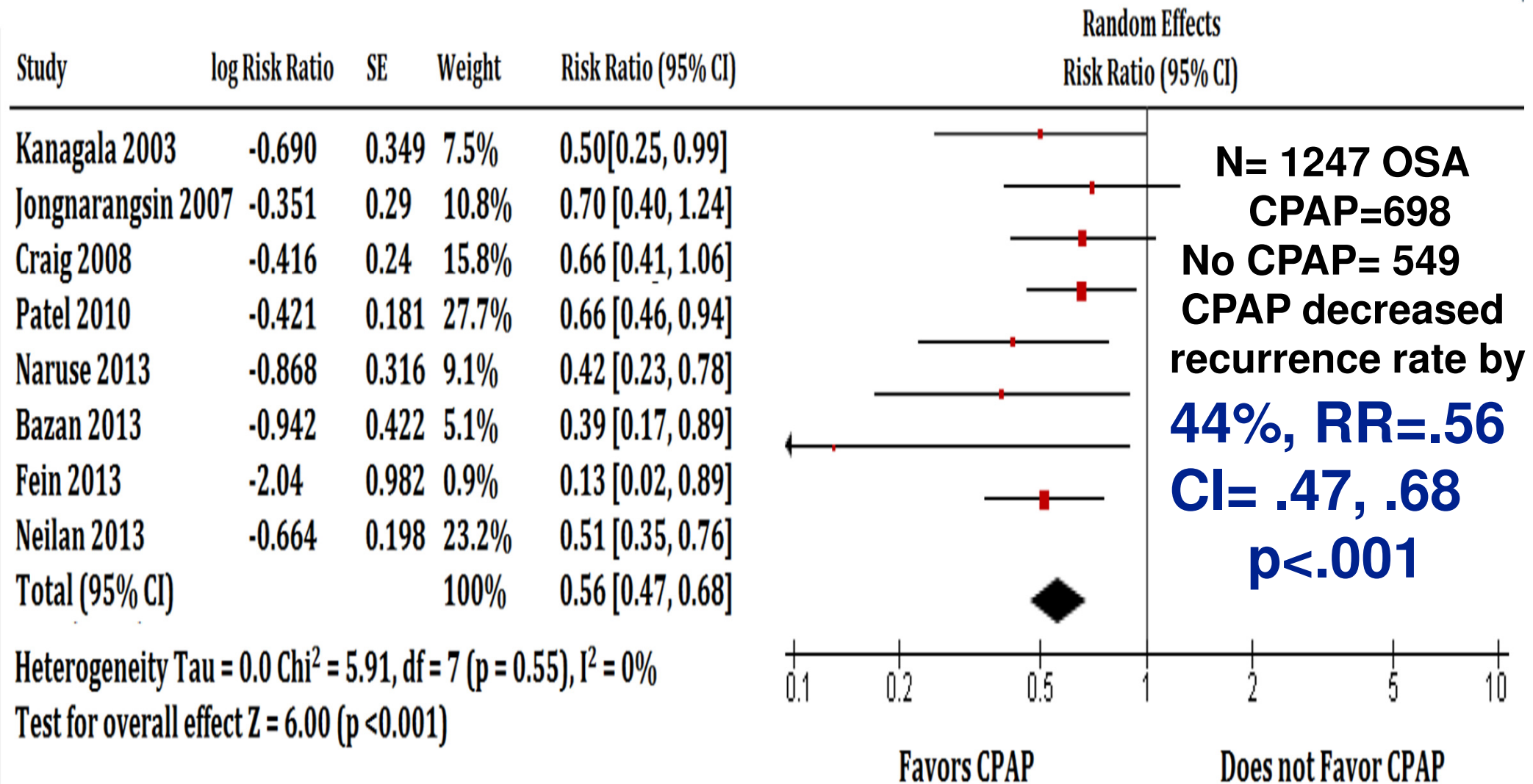


OSA and Recurrent Atrial Fibrillation



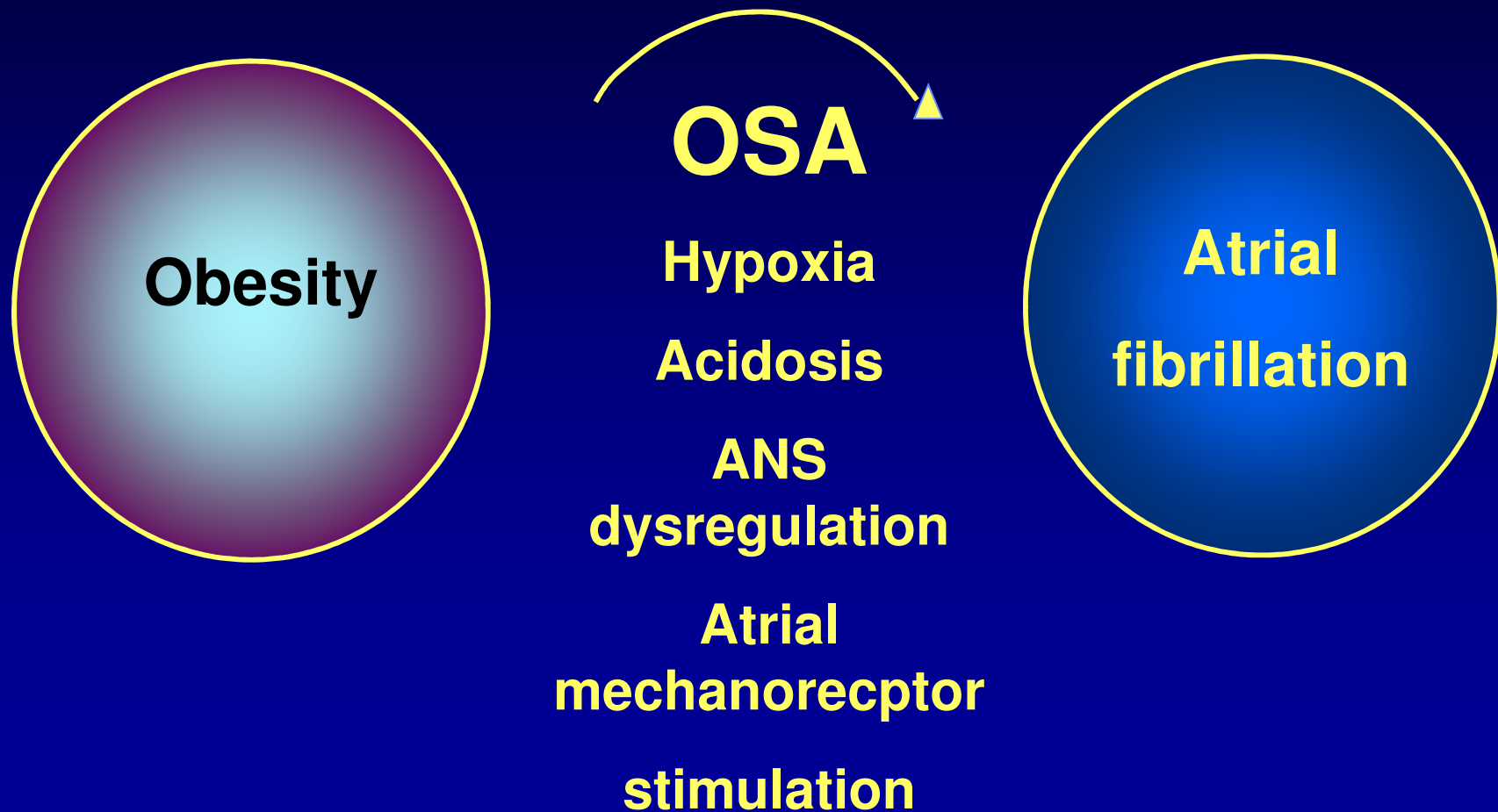
Kanagala et al., Circulation, 2003

CPAP decreases recurrence of post-ablation A Fib in OSA (Qureshi et al, Am J Cardiol, 2015)



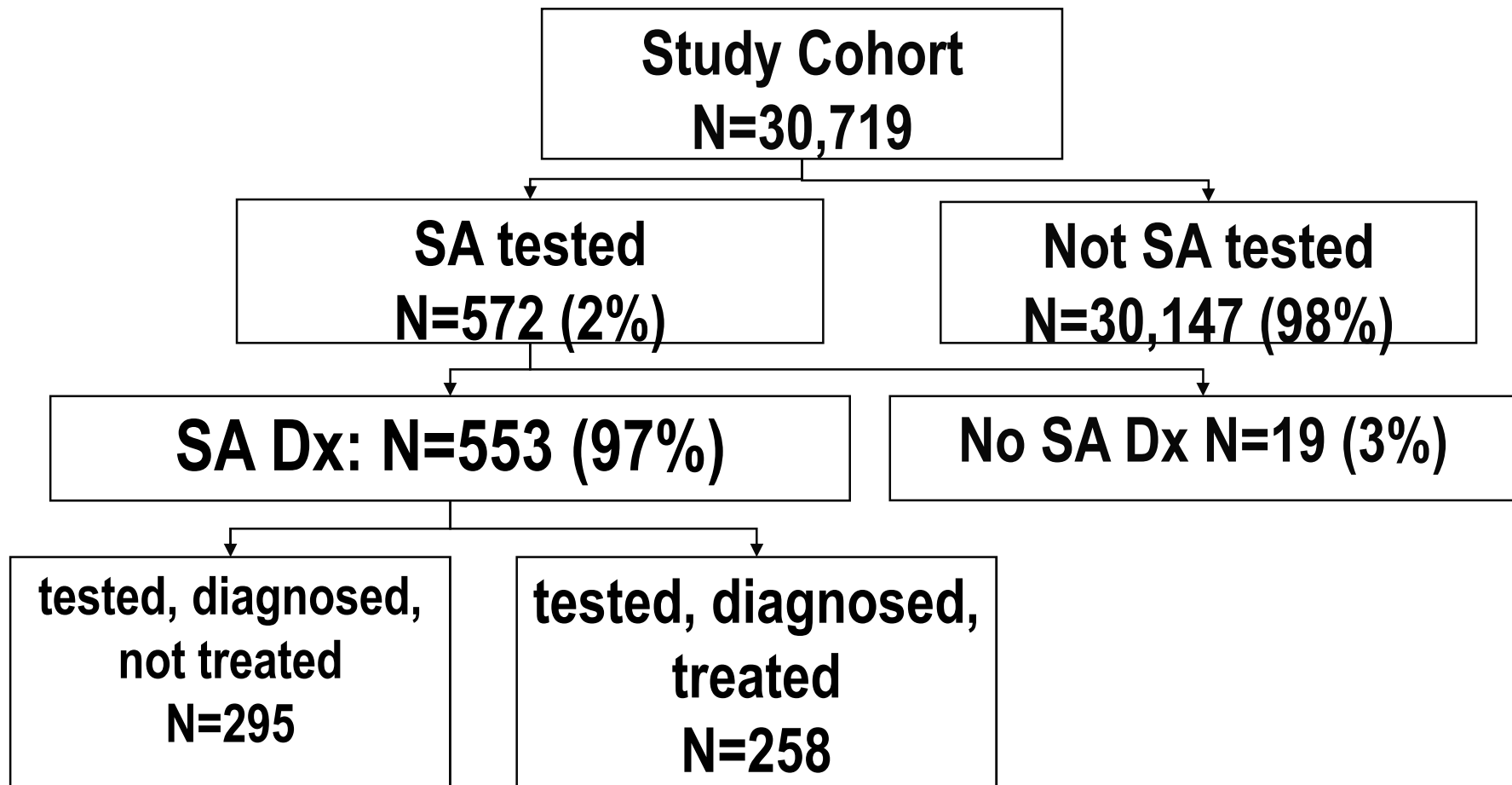
Obesity begets A Fib

The link between OSA and AF



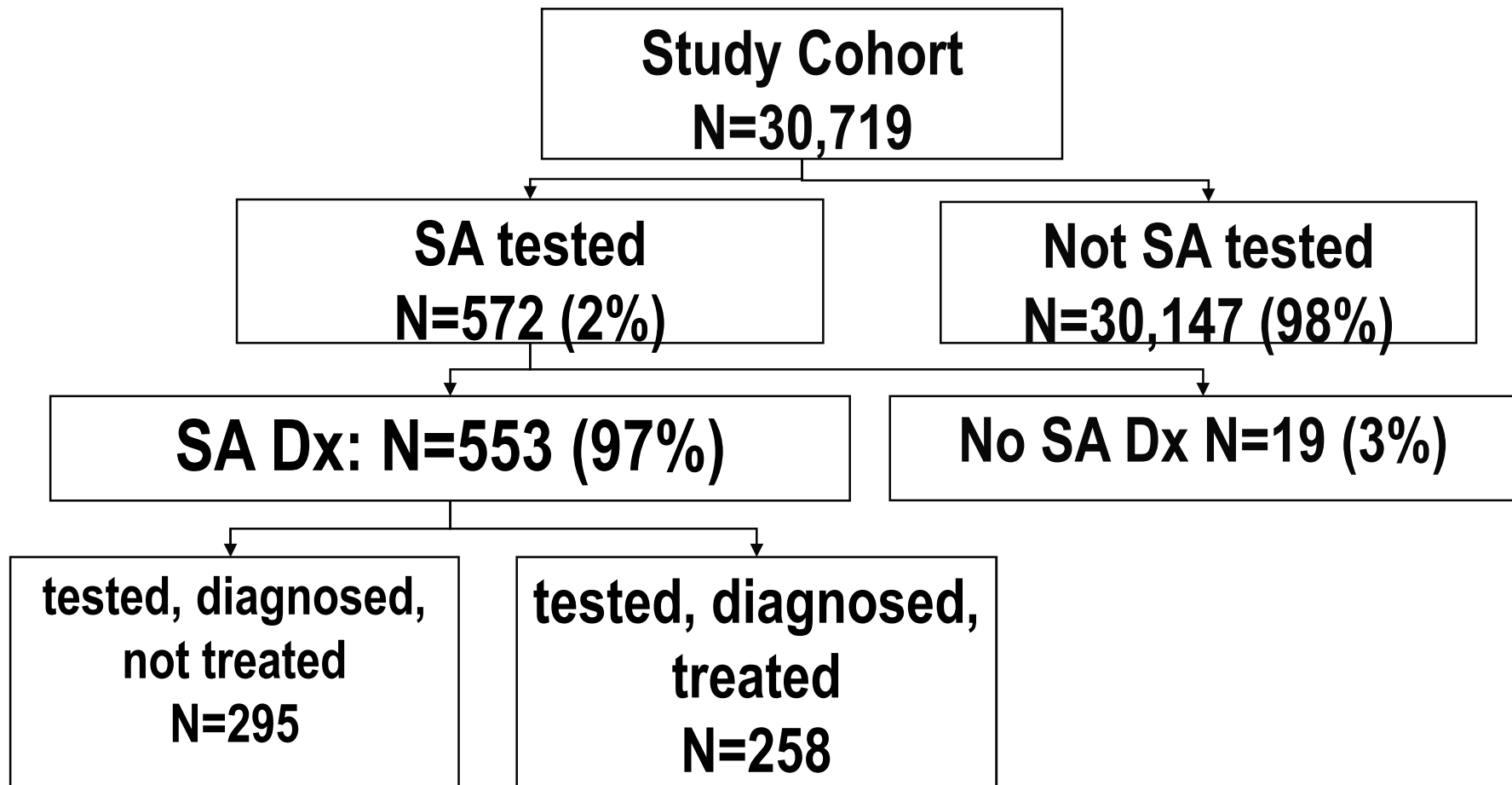


Heart failure comorbid with OSA



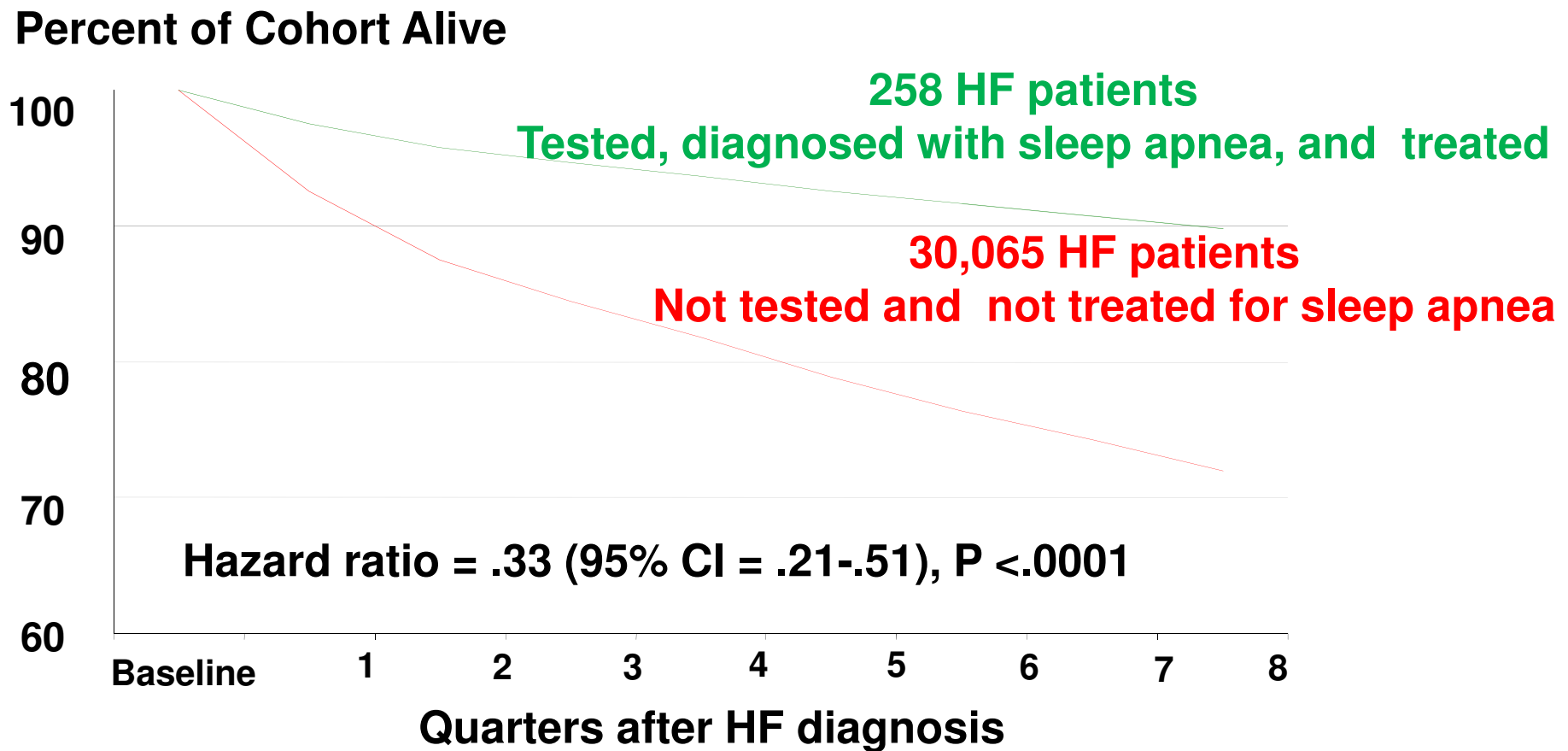
Javaheri et al. Am J Respir Crit Care Med 2011

Heart failure comorbid with OSA



Javaheri et al. Am J Respir Crit Care Med 2011

Kaplan-Meier Survival Curves, Adjusted by Age, Gender, and Charlson Comorbidity Index, 2004-2005



2 y hospitalizations, all cause mortality and mortality

**Clinically
suspected
tested, diagnosed
treated**

**Clinically
suspected
not tested
not treated**

Patients, No (%)	258 (100)	630 (100)
Mortality, No (%)	20 (7.8)	185 (29.4)
Patients hospitalized, No (%)	192 (74)	570 (91)
Medicare payment per patient	42859 \$	63747 \$
Difference per patient		21000 \$

Medicare savings

If 630 patients were all tested, diagnosed
and treated with CPAP :

Cost of 2 sleep studies 1300 \$

Cost of CPAP device 1200 \$

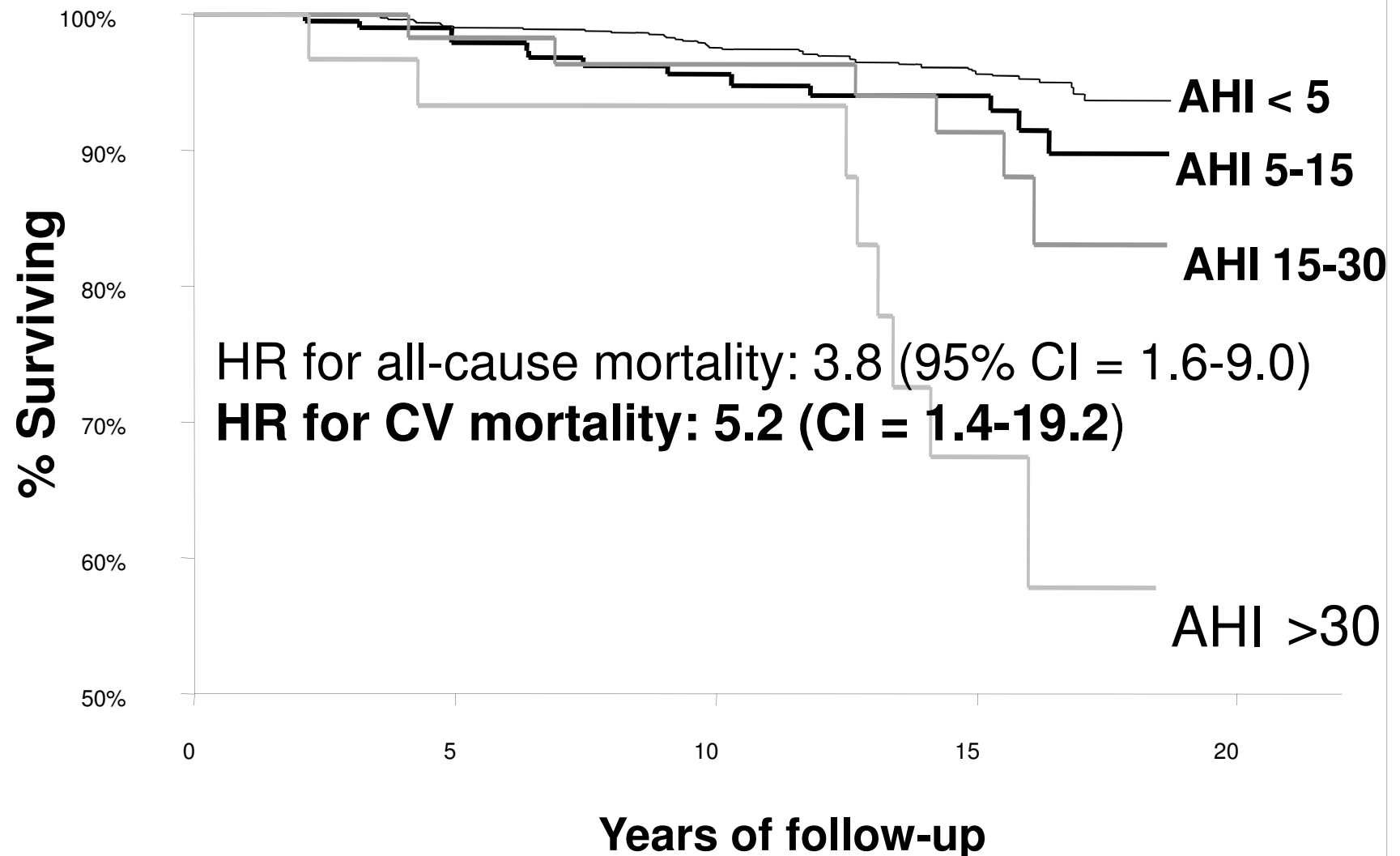
Cost per patient 2500 \$

Cost for 630 patients 1,6 million \$

Actual cost difference for 630 patients 13,200000 \$

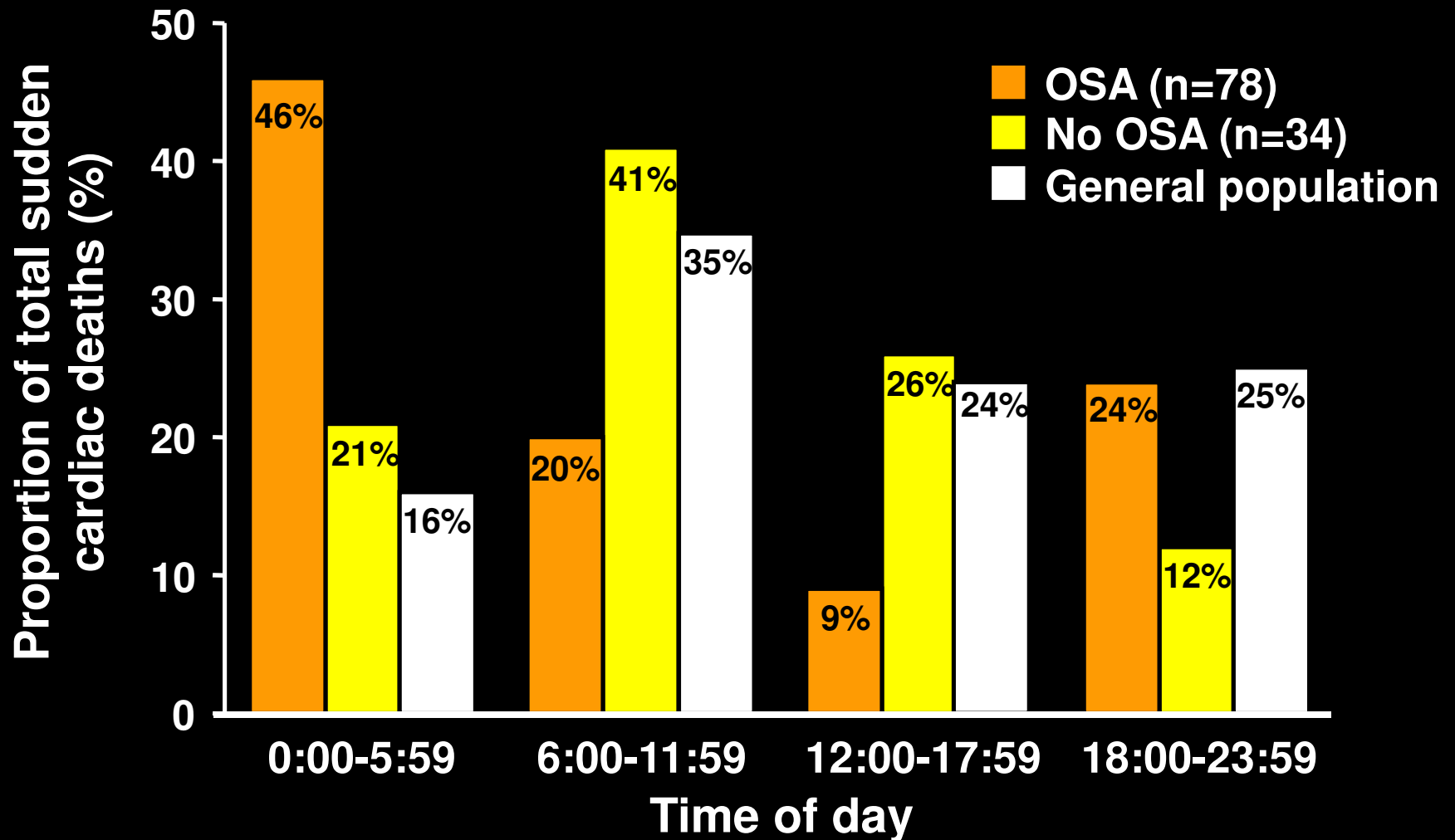
2 y Medicare savings for 630 patients 12 million \$

Probability of survival over 18 year f/u period (n=1522)

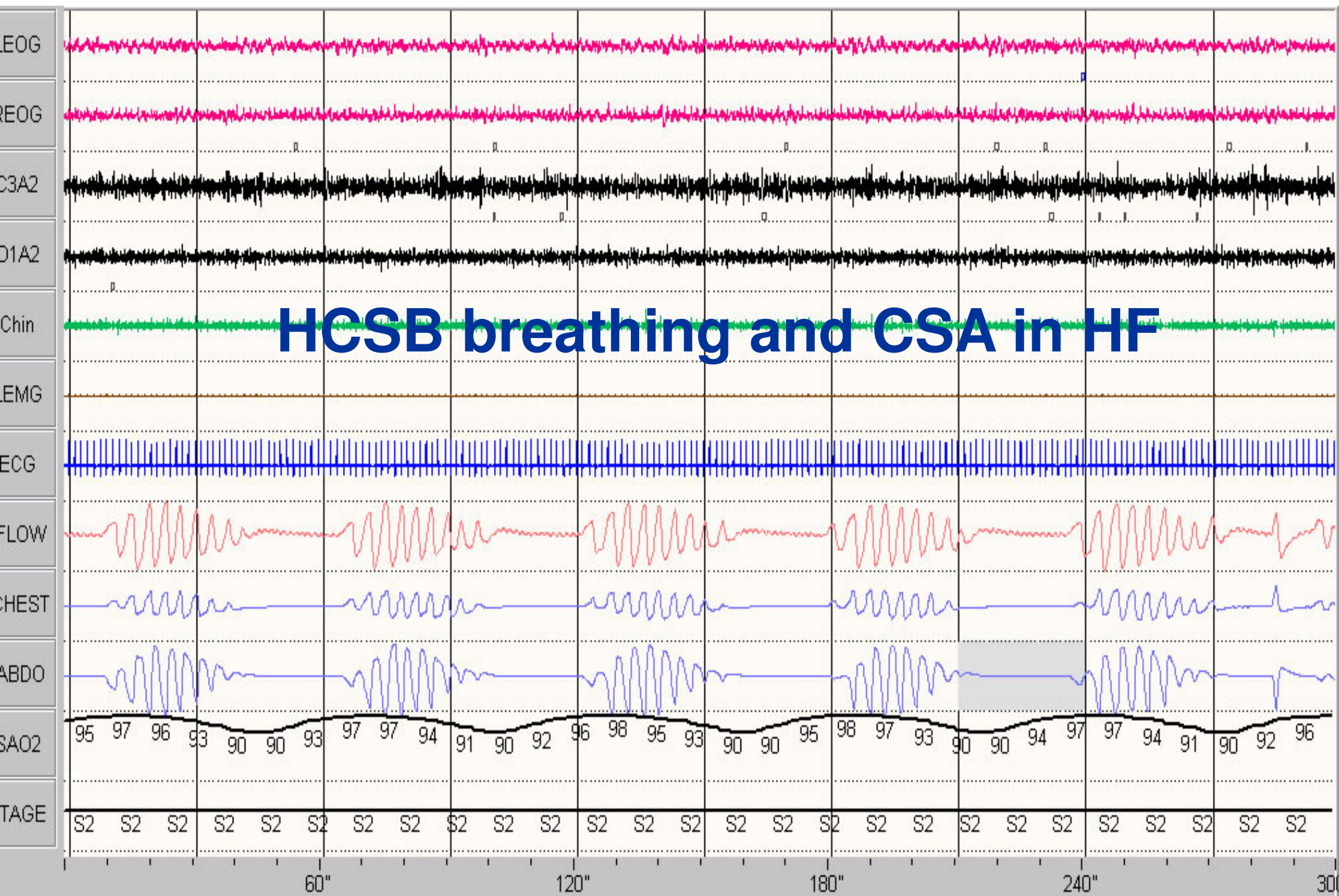


**All-cause mortality with untreated SDB,
(sample excludes 126 CPAP users)(Young,Sleep,2008)**

Day-Night Pattern of SCD

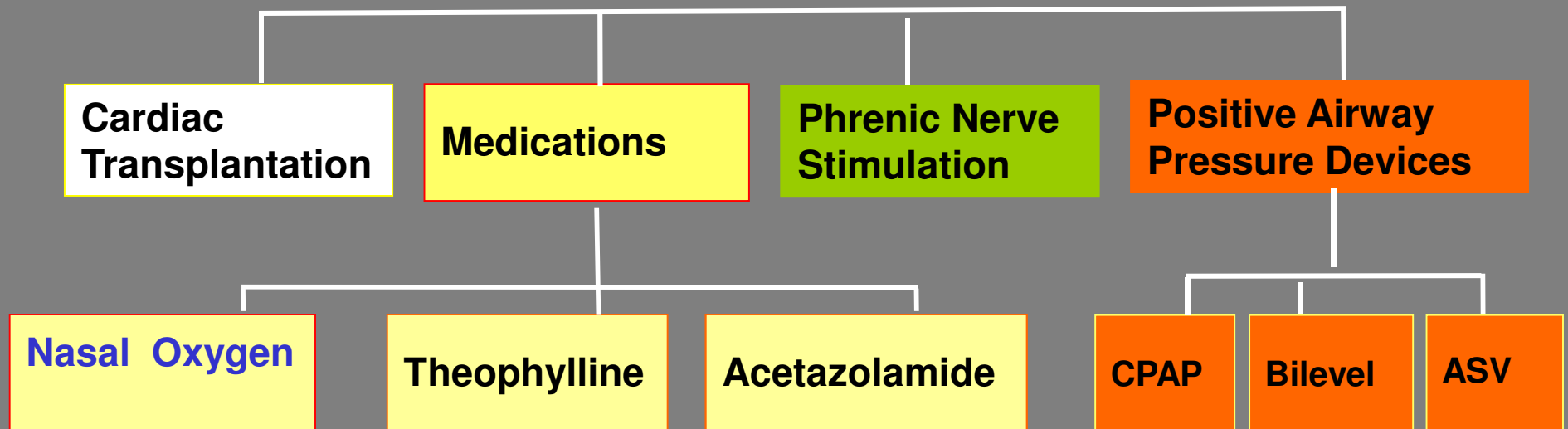


Gami, Howard, Olson, Somers NEJM 2005

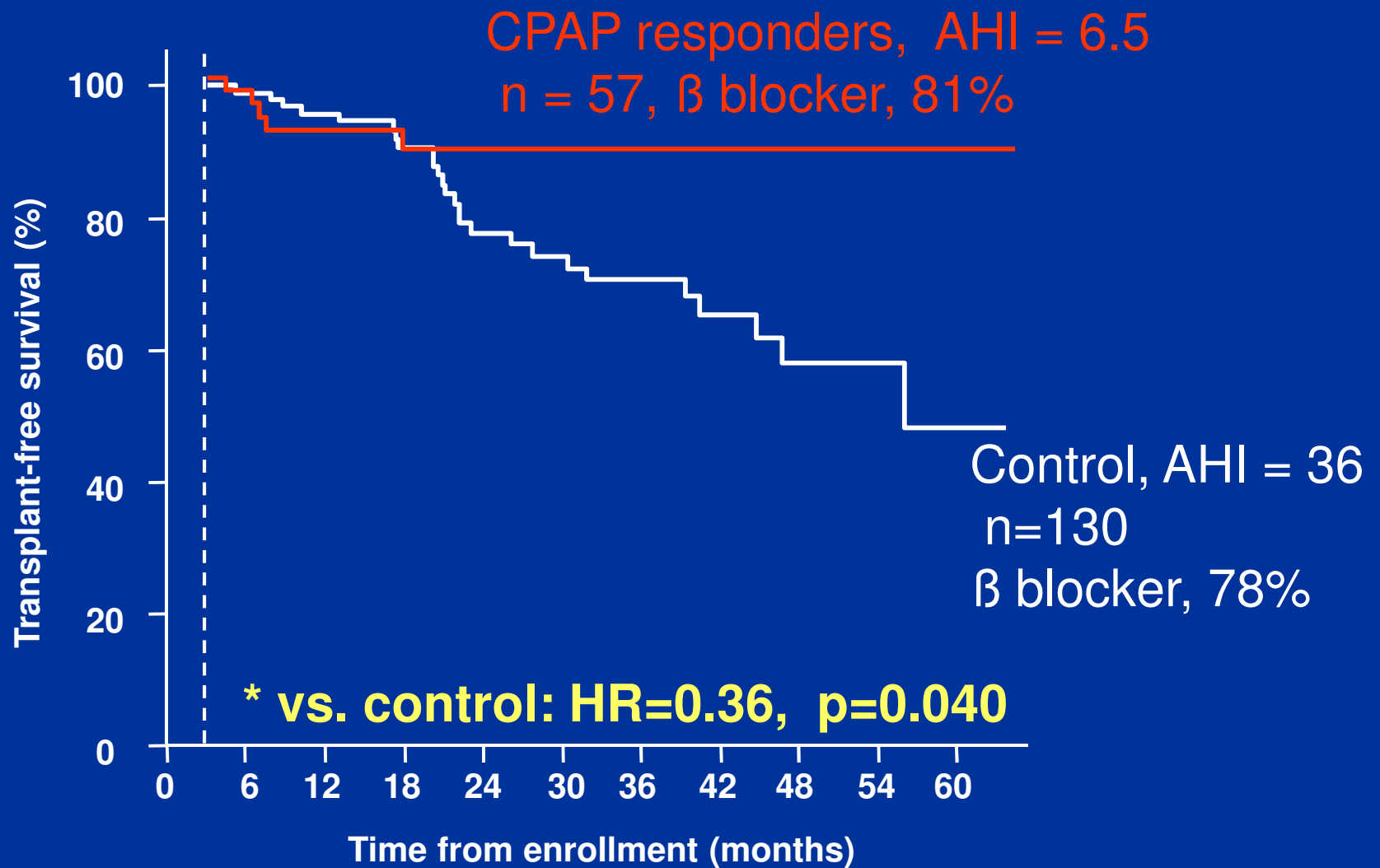


Treatment of CSA

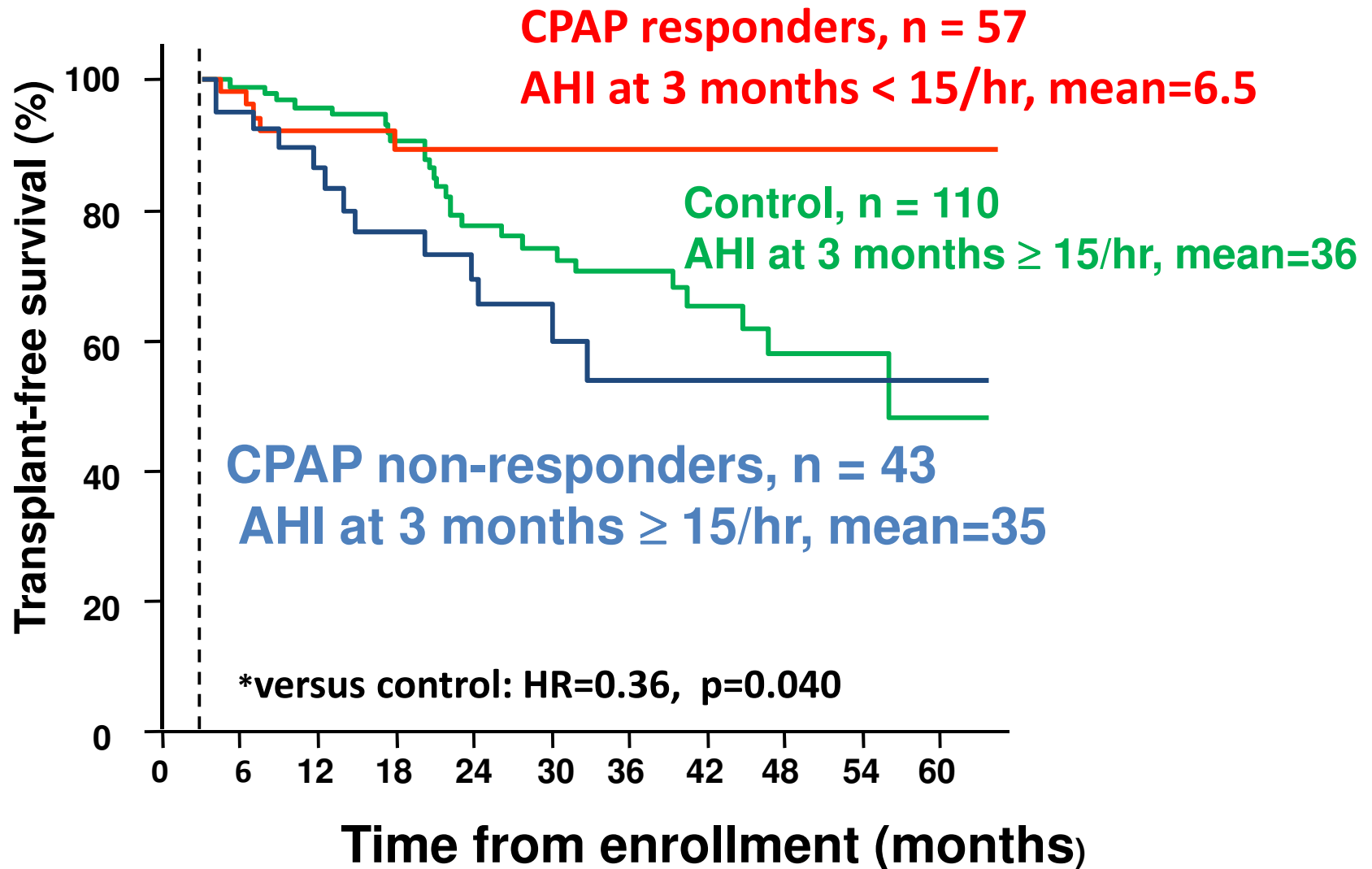
Optimization of cardiac dysfunction



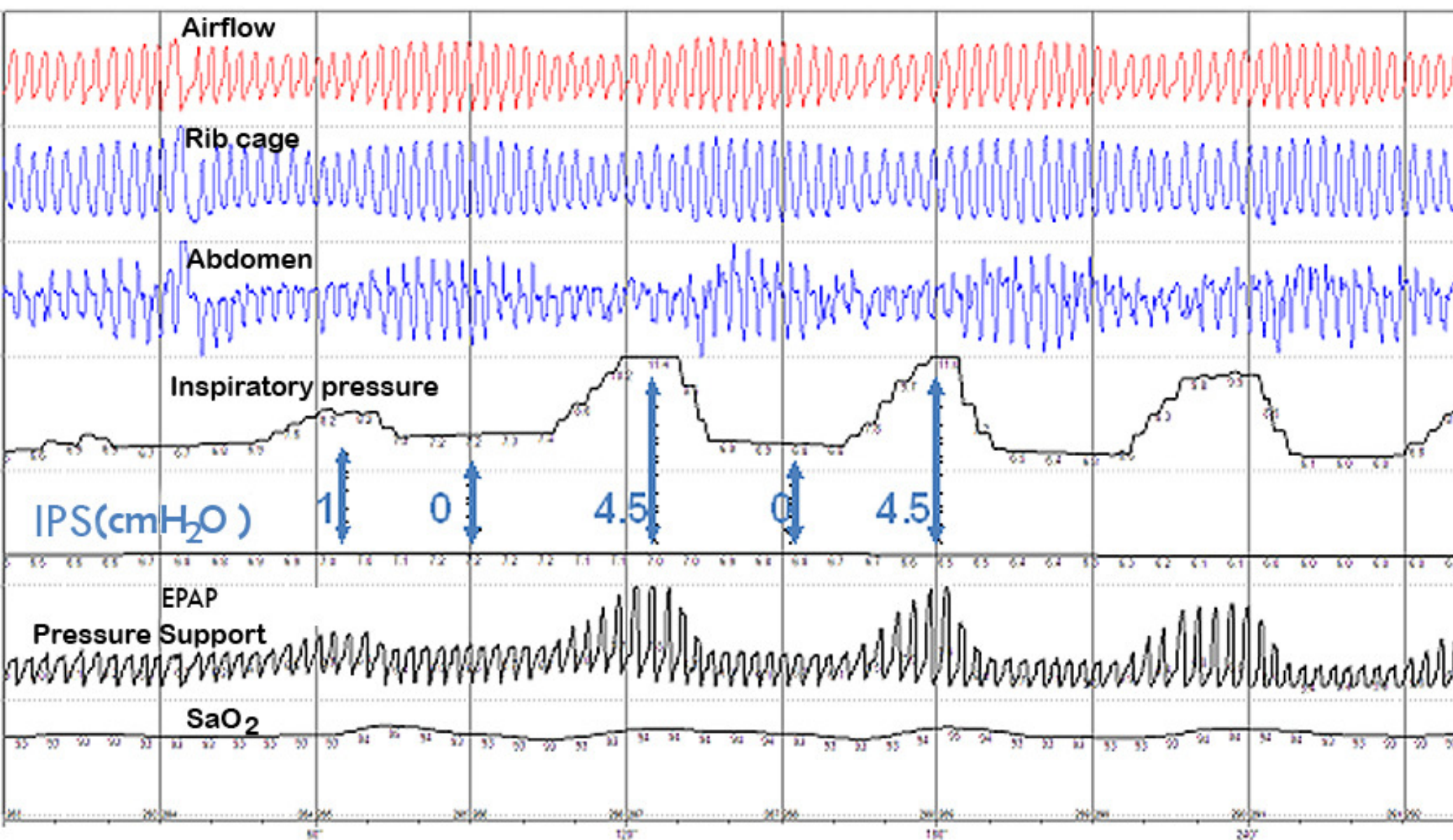
Transplant-free survival in SHF patients
according to effect of CPAP on CSA (Artz, Circ, 2007)



Transplant-free survival
in the control group and according to effect of CPAP on CSA



Changes in inspiratory pressure support during Hunter-Cheyne-Stokes breathing



3 RCT in Sleep Apnea Comorbid with HFrEF

Study Name	Sleep Apnea	Sites	NO	Intervention	Primary Endpoints
SERVE-HF	CSA	Europe	1325	ASV vs conservative treatment	Morbidity and Mortality
ADVENT-HF	CSA OSA	Multi-national	860	ASV vs conservative treatment	Morbidity and Mortality
Remede system	CSA	multinational	173	PNS vs. optimal therapy	AHI reduction of 50% with PNS ⁴⁰

Stimulation Location

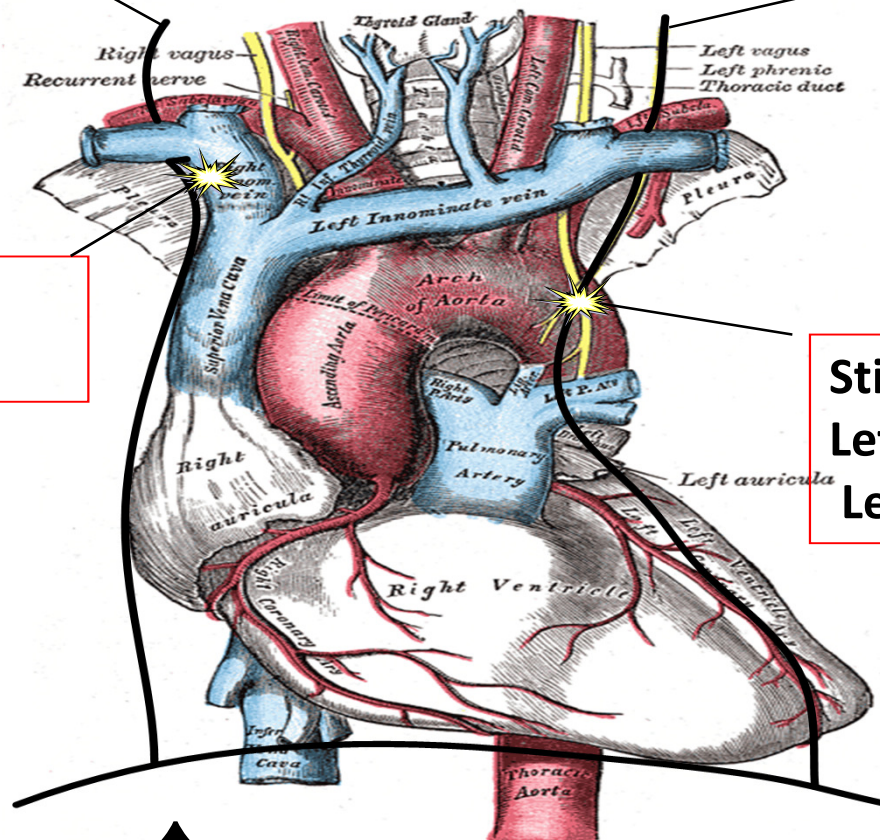
Right Phrenic Nerve

Left Phrenic Nerve

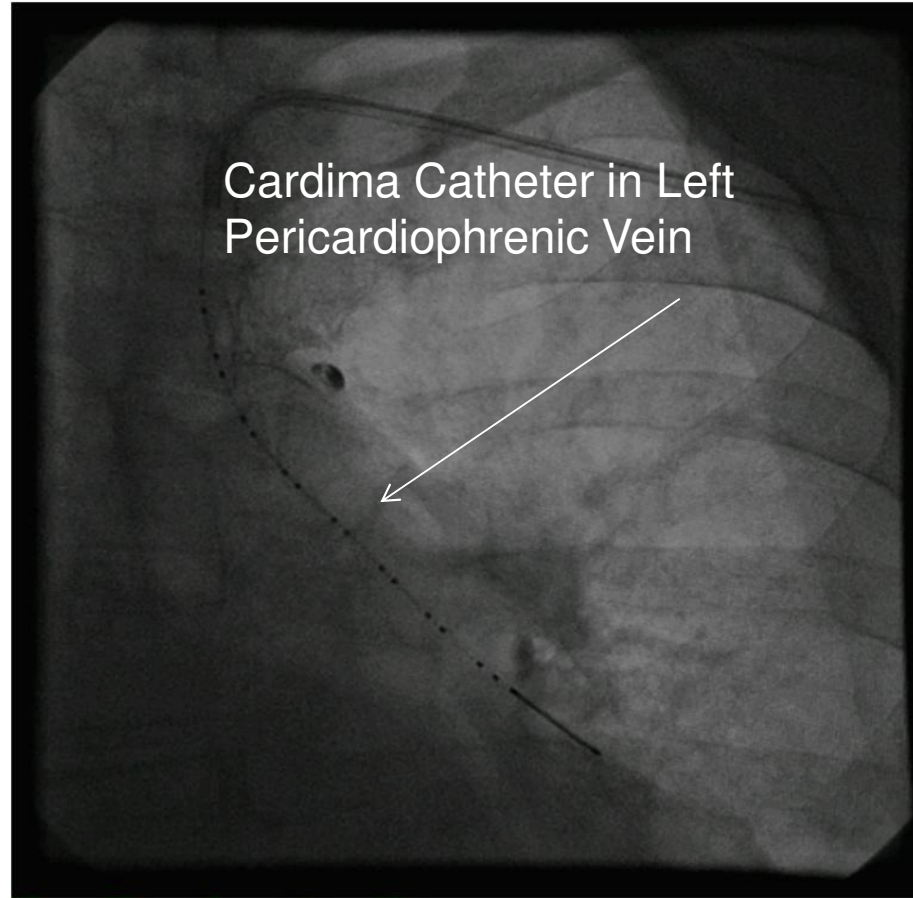
Stimulation Site
Right Brachiocephalic Vein

Stimulation Site
Left Pericardiophrenic or
Left Brachiocephalic Vein

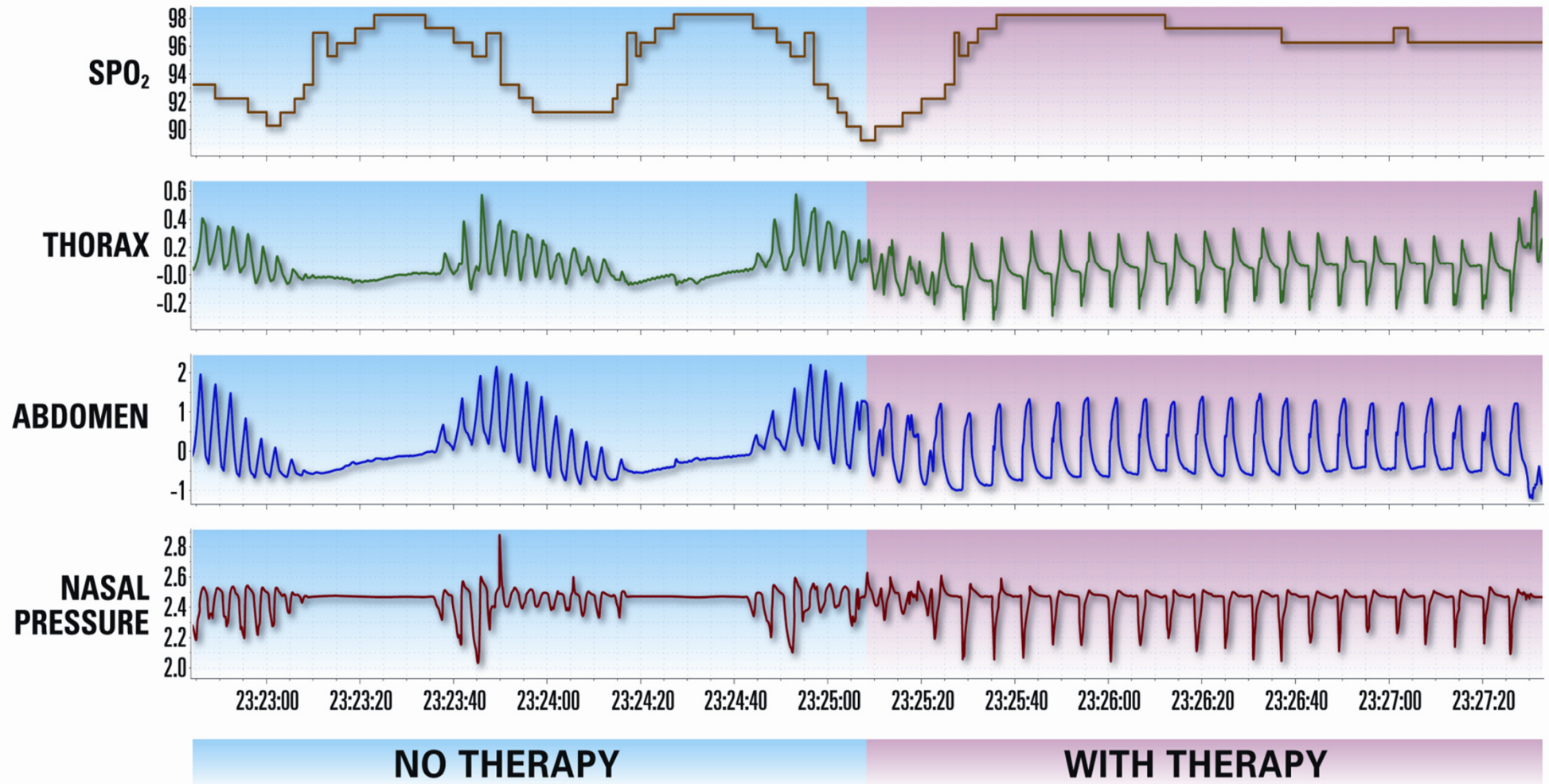
Diaphragm



Left Pericardiophrenic Vein



Therapy Terminates CSA



**“Don’t ever go to sleep.
Too many people die there.”**



— Mark Twain