

# **Sleep and the Heart**

**Rami N. Khayat, MD**  
Professor of Internal Medicine  
Medical Director, Department of Respiratory Therapy  
Division of Pulmonary, Critical Care  
and Sleep Medicine  
The Ohio State University Wexner Medical Center

## **Impact of Heart Disease**

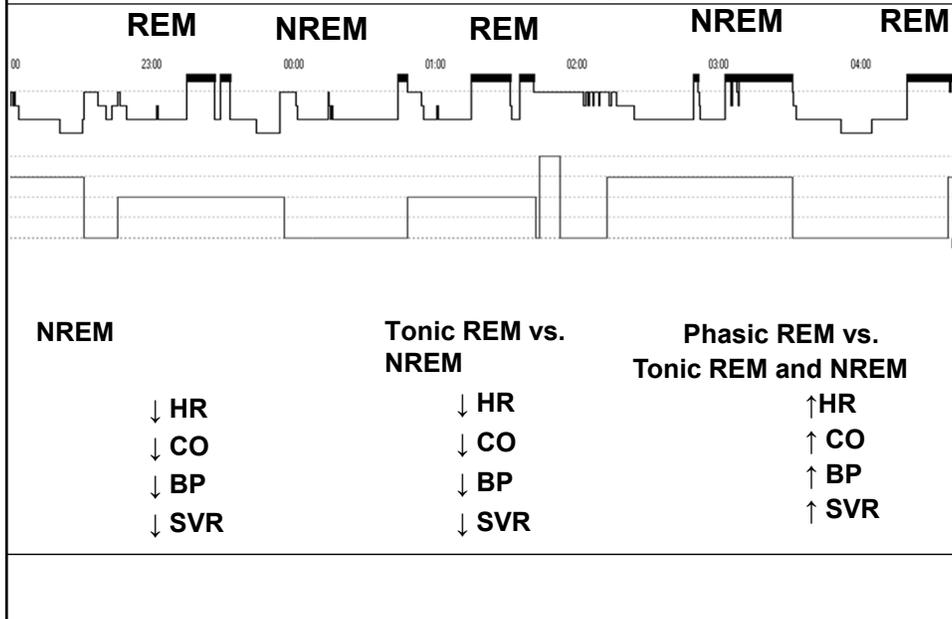
- **Cardiovascular disease (CVD) accounts for nearly 801,000 deaths in the US (1/3 of all deaths)**
- **2,200 Americans die of CVD each day (1 death every 40 seconds)**
- **CVD claims more lives each year than all forms of cancer and Chronic Lower Respiratory Disease combined.**
- **About 92.1 million American adults are living with some form of CVD or the after-effects of stroke.**
- **Direct and indirect costs of CVD and stroke are estimated to total more than \$316 billion.**
- **By 2030, total direct medical costs of CVD are projected to increase to about \$920 billion.**

Heart and Stroke Statistics-2017; Circulation 2017

# OUTLINE

- Overview of physiology of the cardiovascular system during sleep
- Mechanism of cardiovascular disease in Sleep Disordered Breathing (SDB)
- Management of SDB in heart disease

## Physiologic Changes in Cardiovascular Parameters during Sleep

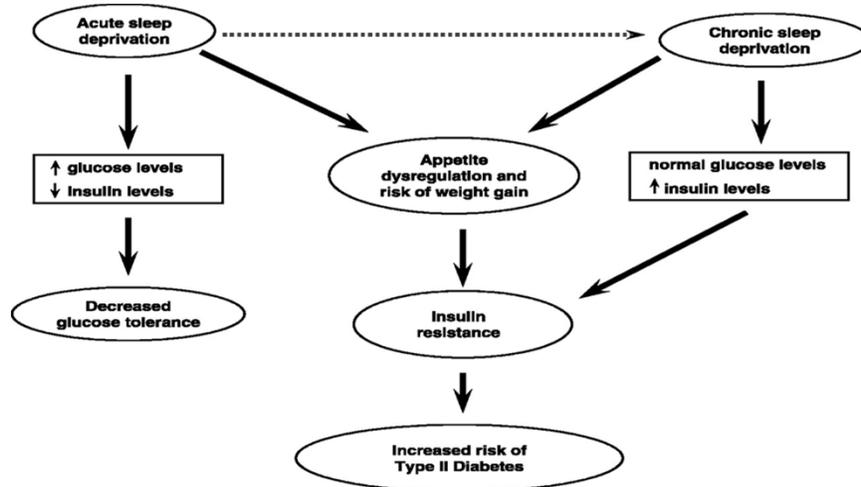


## National Sleep Foundation 2011 Sleep in America Poll

- 43% of Americans (ages 13-64) say they rarely or never get a good night's sleep on weeknights.
- 60% experience a sleep problem every night (snoring, waking in the night, waking up too early, or non-refreshed sleep).
- 63% say their sleep needs are not being met during the week (Most need about 7 1/2 hours of sleep to feel their best, but get 6:55 sleep on weeknights).
- 15% of adults say they sleep less than 6 hours on weeknights.



## Voluntary Sleep Loss: a risk factor for insulin resistance and Type 2 DM



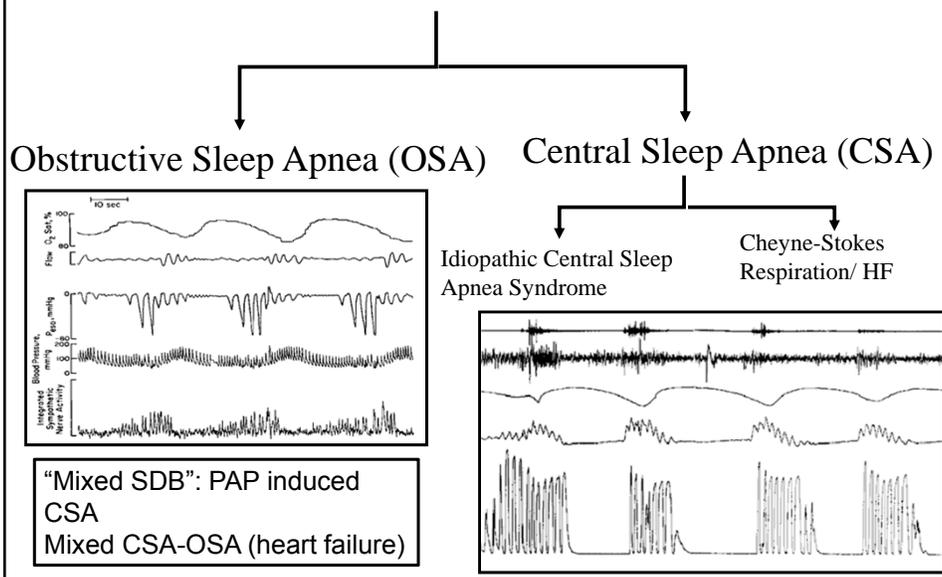
Halson, S.L. Sports Med (2014) 44(Suppl 1): 13.

## Sleep Duration and Quality: Impact on Lifestyle Behaviors and Cardiometabolic Health

A Scientific Statement From the American Heart Association

- **ABSTRACT:** Sleep is increasingly recognized as an important lifestyle contributor to health. However, this has not always been the case, and an increasing number of Americans choose to curtail sleep in favor of other social, leisure, or work-related activities. This has resulted in a decline in average sleep duration over time. Sleep duration, mostly short sleep, and sleep disorders have emerged as being related to adverse cardiometabolic risk, including obesity, hypertension, type 2 diabetes mellitus, and cardiovascular disease. Here, we review the evidence relating sleep duration and sleep disorders to cardiometabolic risk and call for health organizations to include evidence-based sleep recommendations in their guidelines for optimal health.

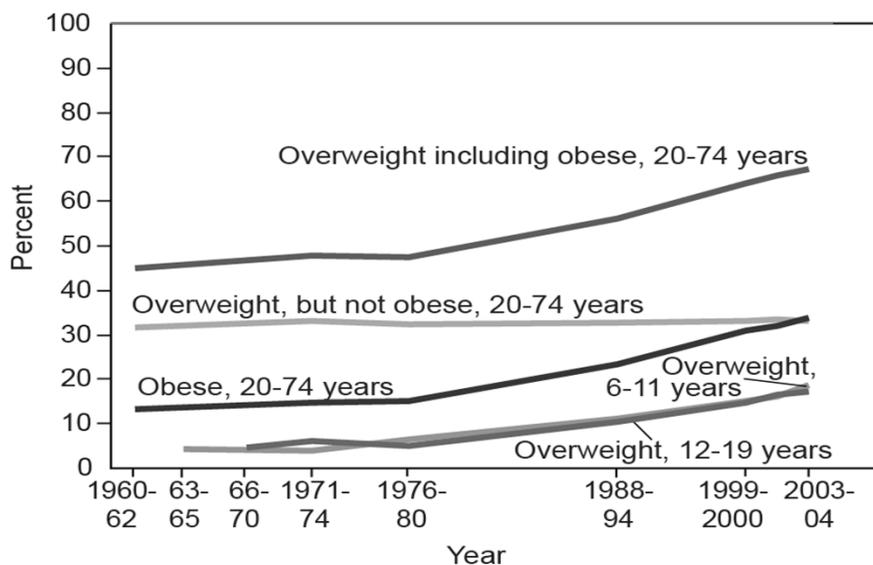
## Sleep Disordered Breathing (SDB)



# Prevalence of OSA

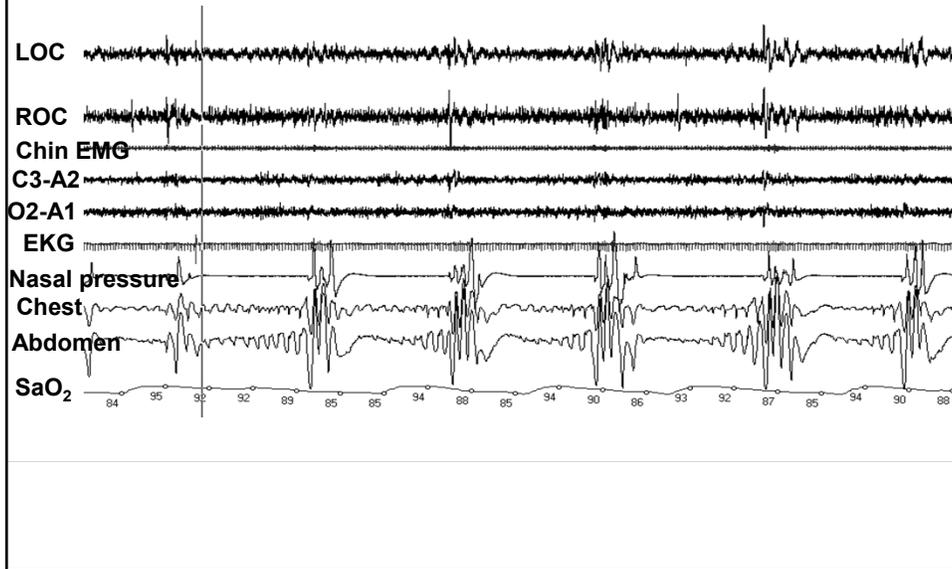
- In 1993, OSA (defined as AHI > 5 events/hour of sleep) is present in:
  - 24% men and 9% women 30-60 years
  - 31% men and 16% women 50-60 years
    - » Wisconsin Sleep Cohort NEJM 1993
- Increased age and weight are the most important risk factors for OSA
- In individuals with CVD, the prevalence of OSA exceeds 50%

## Overweight and obesity

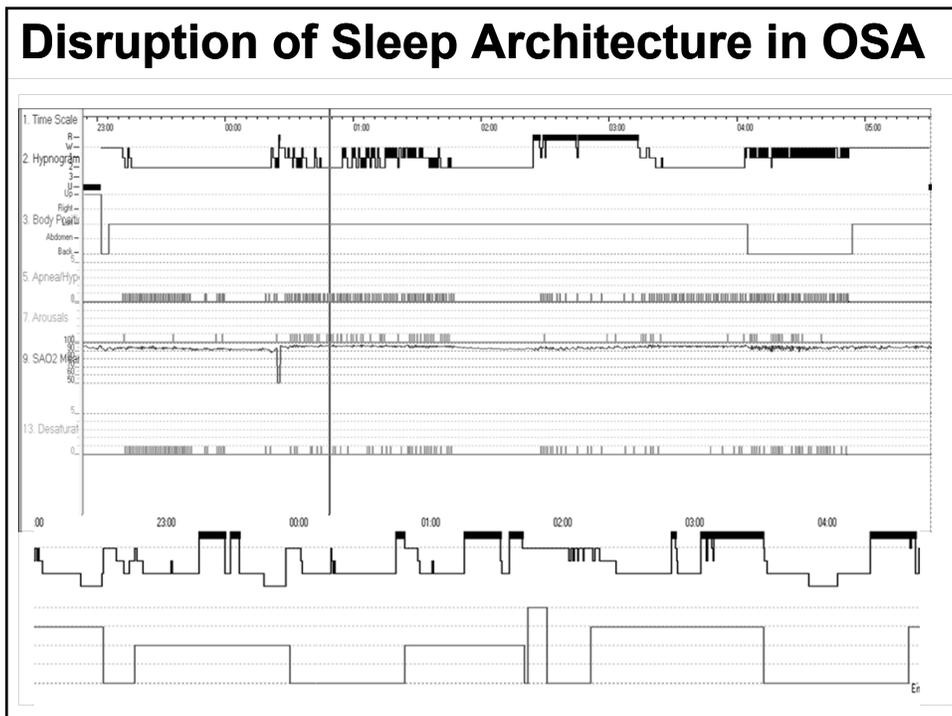


SOURCES: Centers for Disease Control and Prevention, National Center for Health Statistics, *Health, United States, 2006*, Figure 13. Data from the National Health and Nutrition Examination Survey.

# Obstructive Sleep Apnea on Nocturnal Polysomnography



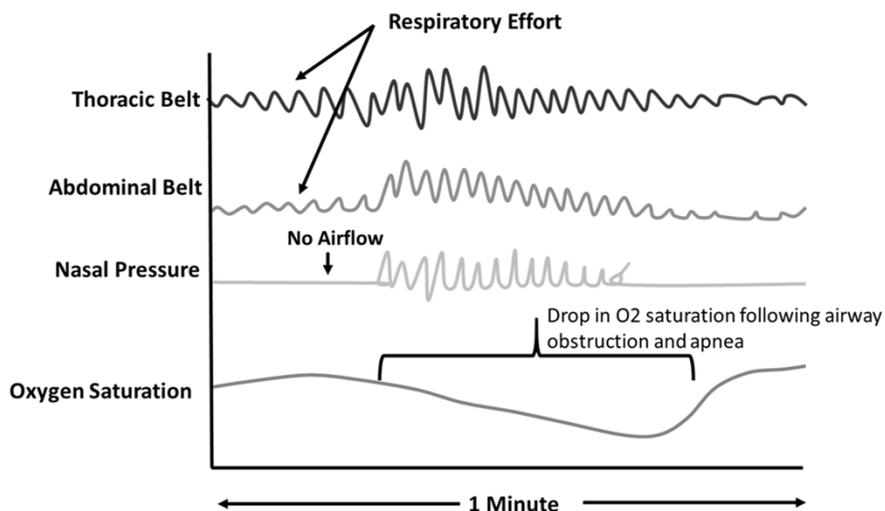
# Disruption of Sleep Architecture in OSA



# OSA and Metabolic Dysfunction

- OSA is an independent risk factor for the metabolic syndrome (Coughlin et al. *Eur Heart J.* 2004)
- OSA is associated with increased peroxidation of lipids, endothelial dysfunction and atherosclerosis
- Treatment of OSA reverses the metabolic syndrome in OSA
- CPAP improves insulin sensitivity in some patients with OSA
- (Harsch I, et al *Am J Respir Crit Care Med* 2004)

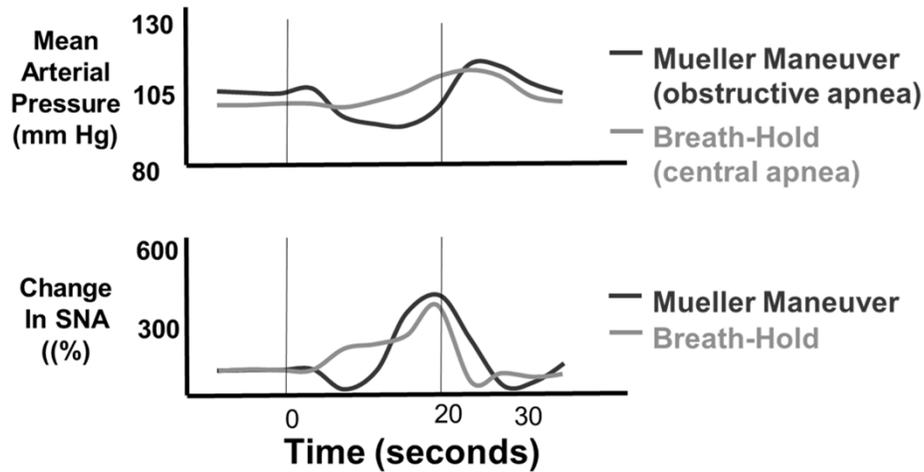
## Obstructive sleep apnea (OSA)



Apnea represents a complete cessation of air flow > 10 seconds  
Hypopnea occurs when there is a significant decrease in air flow with a drop in oxygen saturation

Khayat et al. *J Cardiac Fail* 2013;19:431e444

## Hypoxia is the Critical Stimulus BP and Sympathetic Surge in Both Central and Obstructive Apneas

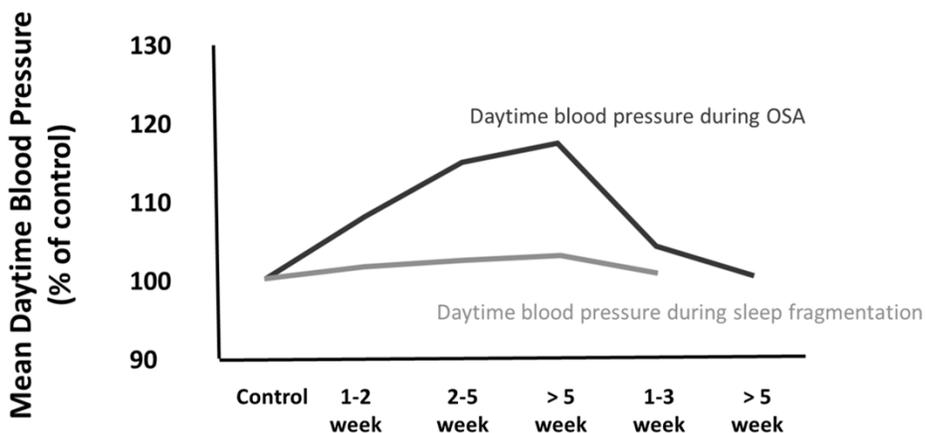


Xie et al JAP 1996

## Immediate Consequences of an apnea

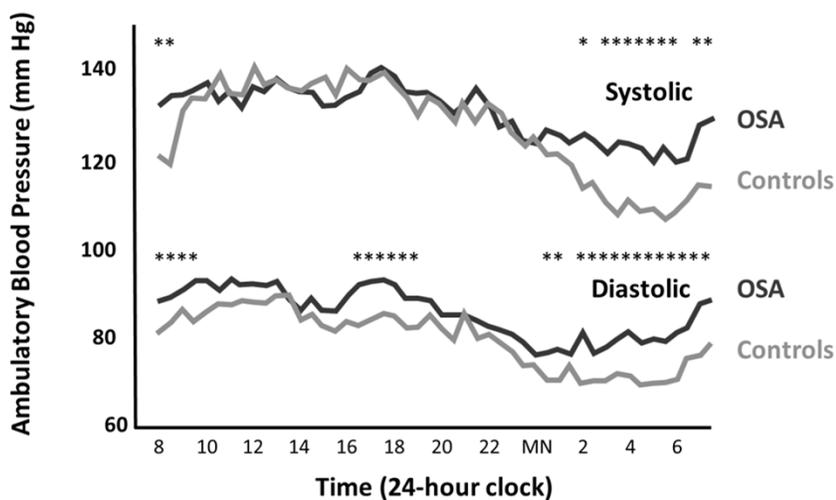
- Hypoxia
- Arousal
- Increased sympathetic activity
- Surge in blood pressure

## OSA- Induced Hypertension- Dog Model of Airway Occlusion



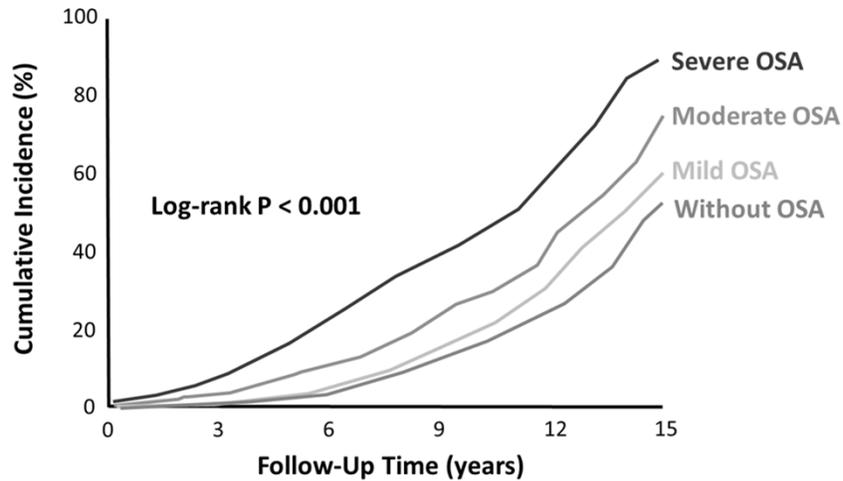
Brooks, et al. J Clin Invest 99:106, 1997

## Nocturnal Blood Pressure Response to SDB



Davies CWH, Crosby JH, Mullins RL, et al  
 Case-control study of 24 hour ambulatory blood pressure in patients with obstructive sleep apnoea and normal matched control subjects  
 Thorax 2000;55:736-740.

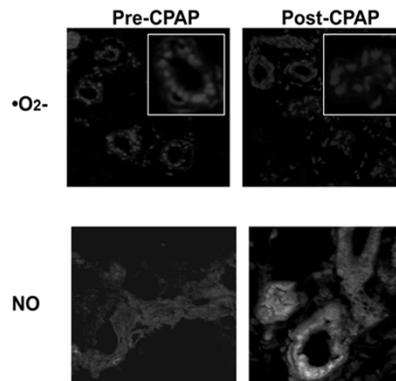
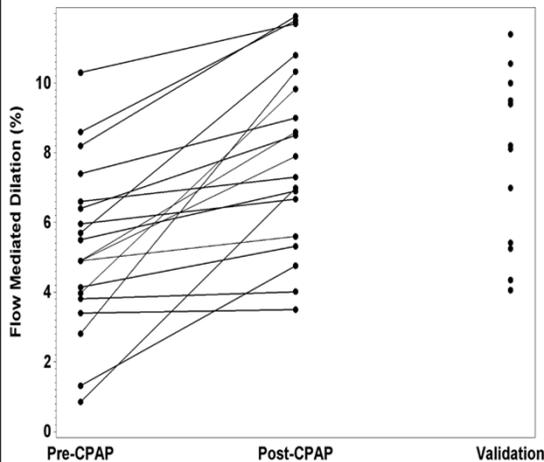
## Association Between Treated and Untreated Obstructive Sleep Apnea and Risk of Hypertension



Mild OSA (AHI, 5.0-14.9), moderate OSA (AHI, 15.0-29.9), and severe OSA (AHI,  $\geq 30.0$ ). P value reflects an overall log-rank test, providing an overall survival difference among the 4 study groups.

JAMA. 2012;307(20):2169-2176.

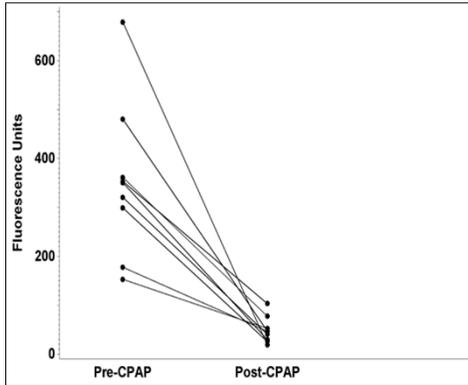
## OSA is associated with Oxidant Mediated Vascular Endothelial Dysfunction



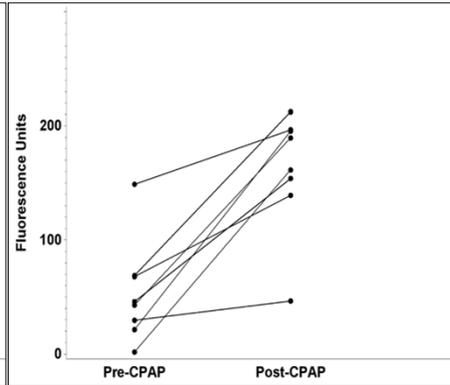
Varadharaj et al Respir Physiol Neurobiol 2015

# Cardiovascular Disease Risk in OSA Patients

**Arteriolar superoxide  
production**



**Arteriolar nitric  
oxide availability**



Varadharaj et al Respir Physiol Neurobiol 2015

# OSA and CVD

- **OSA is a cause of hypertension**
- **OSA patients have endothelial dysfunction and oxidative stress even in the absence of measurable CVD**
- **OSA is associated with CAD, stroke, and heart failure**

## **OSA and Arrhythmia**

- **Increased atrial and ventricular ectopy during the night in patients with OSA**
  - Mehra et al 2006
- **Increased firing of defibrillators in patients with heart failure and both OSA and CSA**
  - Oldenburg Eu Heart J 2015

## **OSA and Atrial Fibrillation**

- **Increased prevalence of OSA in patients with AF**
- **Increased rate of recurrence of AF in patients with untreated OSA**
- **Increased rate of failure of anti-arrhythmic medication in AF patients who have untreated OSA**
- **Increased likelihood of failure of first and second ablation procedure if OSA is untreated**

Gami, et al. *JACC* 2007;49:565-71

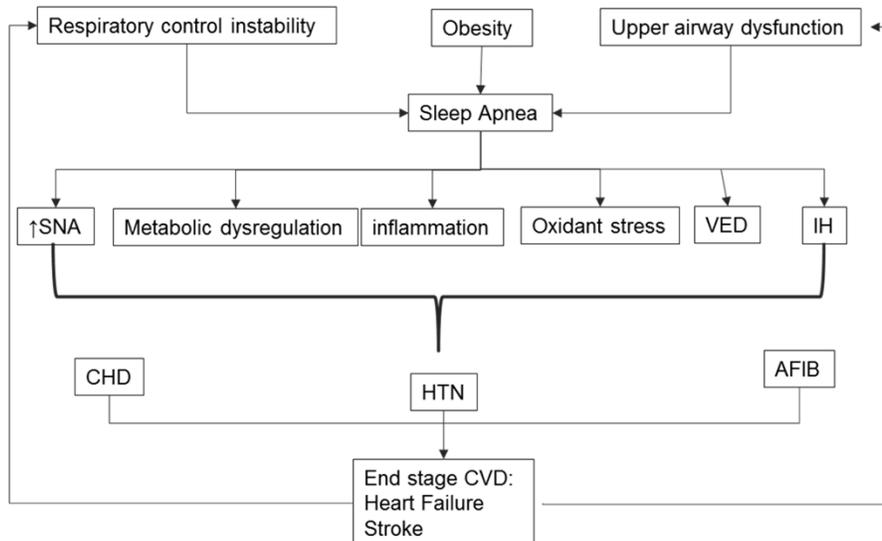
Fein et al. *J Am Coll Cardiol* 2013;62:300-5

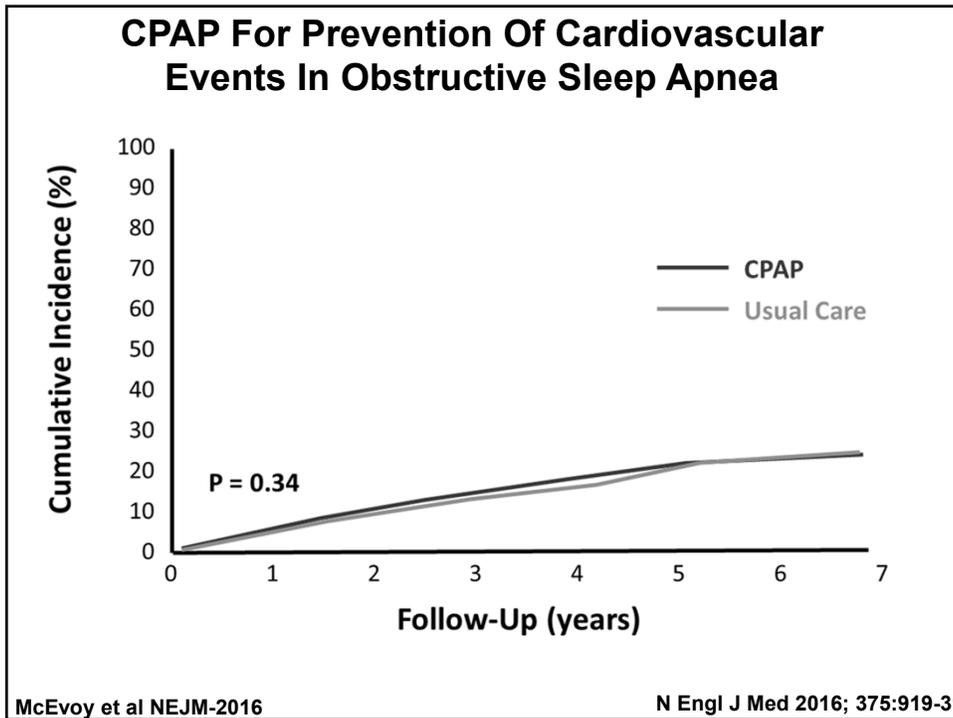
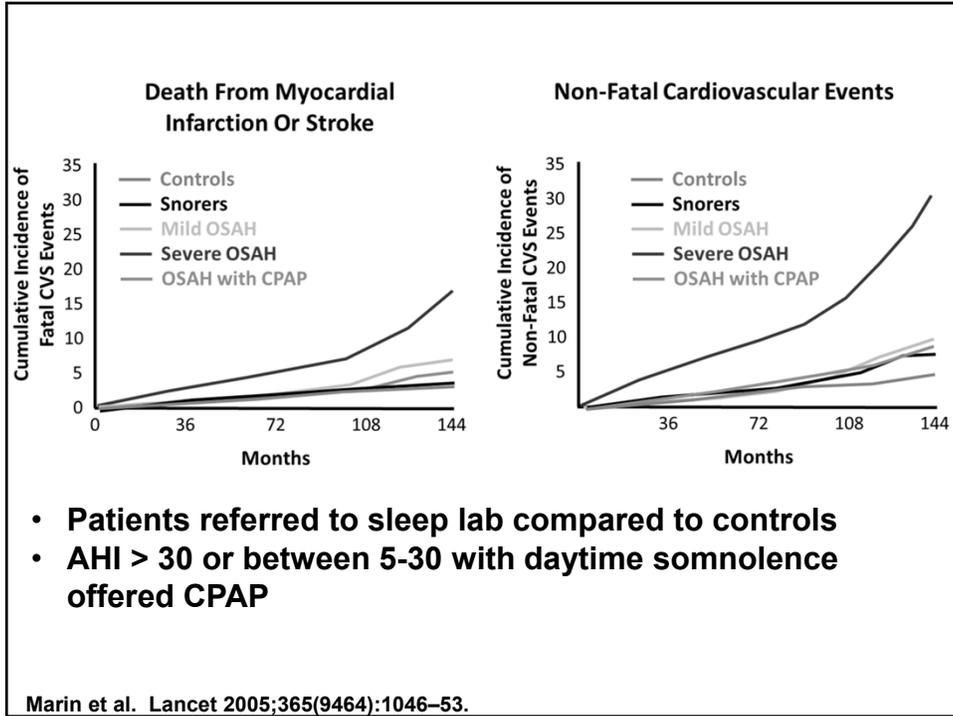
## Cerebrovascular Accidents (CVA)

- High prevalence of SDB in stroke/TIA patients
  - Meta analysis demonstrated frequency of AHI > 5 was 72%, and AHI > 20 was 38%
  - Wisconsin Sleep Cohort Study showed AHI > 20 associated with 4 fold increase risk of having CVA
- Several potential mechanisms
  - ✓ Hypertension, diabetes, inflammation effects
  - ✓ Atrial fibrillation association with stroke and SDB
  - ✓ Intracranial hemodynamic changes as a result of blood pressure surges, transient hypoxia and resulting drop in cerebral perfusion

Johnson KG et al. J Clin Sleep Med 2010;6(2):131-7.  
Arzt M et al. Am J Respir Crit Care Med 2005;172(11):1447-51.  
Franklin KA. Sleep Med Rev 2002;6(6):429-41.

## Pathways of Cardiovascular Disease in Sleep Apnea





## **If OSA is a Cardiovascular Risk Factors, Why are the RCTs negative?**

- **Is CPAP an effective treatment for OSA?**
- **Dose of CPAP in the RCTs was not adequate**
- **Power and duration of follow up are not adequate**
- **Outcomes measured are not representative**
- **Populations studied are not appropriate**

## **Treatment options**

- **Mandibular advancement devices**
- **Surgery**
  - **UPPP**
  - **Jaw advancement surgeries**
  - **Bariatric procedures**
  - **Tracheostomy**
- **Neurostimulation: Inspire®**
- **Positional therapy**
- **Weight loss**

## **Treatment of OSA in Patients with Cardiovascular Disease**

- **CPAP remains the mainstay of treatment**
- **CPAP has the most available data on safety and efficacy**
- **Improvement in blood pressure, atrial fibrillation control and endothelial dysfunction are reported only with CPAP**
- **Tolerance of CPAP is likely increased with improved technology of device and interface**

## **Evaluation for OSA**

- **Patients at high risk for OSA should be evaluated for OSA symptoms**
  - **Obesity (BMI > 35)**
  - **Congestive heart failure**
  - **Atrial fibrillation**
  - **Refractory hypertension**
  - **Type II diabetes**
  - **Nocturnal dysrhythmias**
  - **Stroke**
  - **Pulmonary hypertension**
  - **High risk driving populations**
  - **Preoperative evaluation**

Epstein et al. JCSM Vol 5, No 3; 2009

## **OSA symptoms that should be evaluated during a comprehensive sleep evaluation**

- **Witnessed apneas**
- **Snoring**
- **Gaspings/choking at night**
- **Excessive sleepiness**
- **Nonrefreshing sleep**
- **Total sleep amount**
- **Sleep fragmentation**
- **Nocturia**
- **Morning headaches**
- **Decreased concentration**
- **Memory loss**
- **Decreased libido**
- **Irritability**

- **CPAP is effective in improving symptoms of SDB**
  - **Sleepiness; insomnia; cognitive; mood; and functional parameters**
- **CPAP must be viewed as a highly personalized intervention:**
  - **Exposure time**
  - **Sleep time**
  - **Residual AHI**
- **Traditional CVD biomarkers may not reflect actual CPAP effects**
- **Subpopulations of OSA patients who benefit most from CPAP need to be identified.**