Obstructive Sleep Apnea and Cardiovascular Disease

Timothy W. Jones, M.D.
Pulmonary, Critical Care, and Sleep Medicine
Program Director, Critical Care Medicine Fellowship
Faculty, Orlando Health Physician Group
Critical Care Medicine
Pulmonary and Sleep Medicine Physicians

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Disclosures – Timothy W. Jones, M.D.

I have no conflicts of interest related to this topic.

Obstructive Sleep Apnea

"**OSA** is characterized by repetitive episodes of complete (**apnea**) or partial (**hypopnea**) upper airway obstruction during sleep.

These events often result in **reductions in blood oxygen saturation** and are usually terminated by **brief arousals form sleep**."

ICSD 2nd Edition, 2005

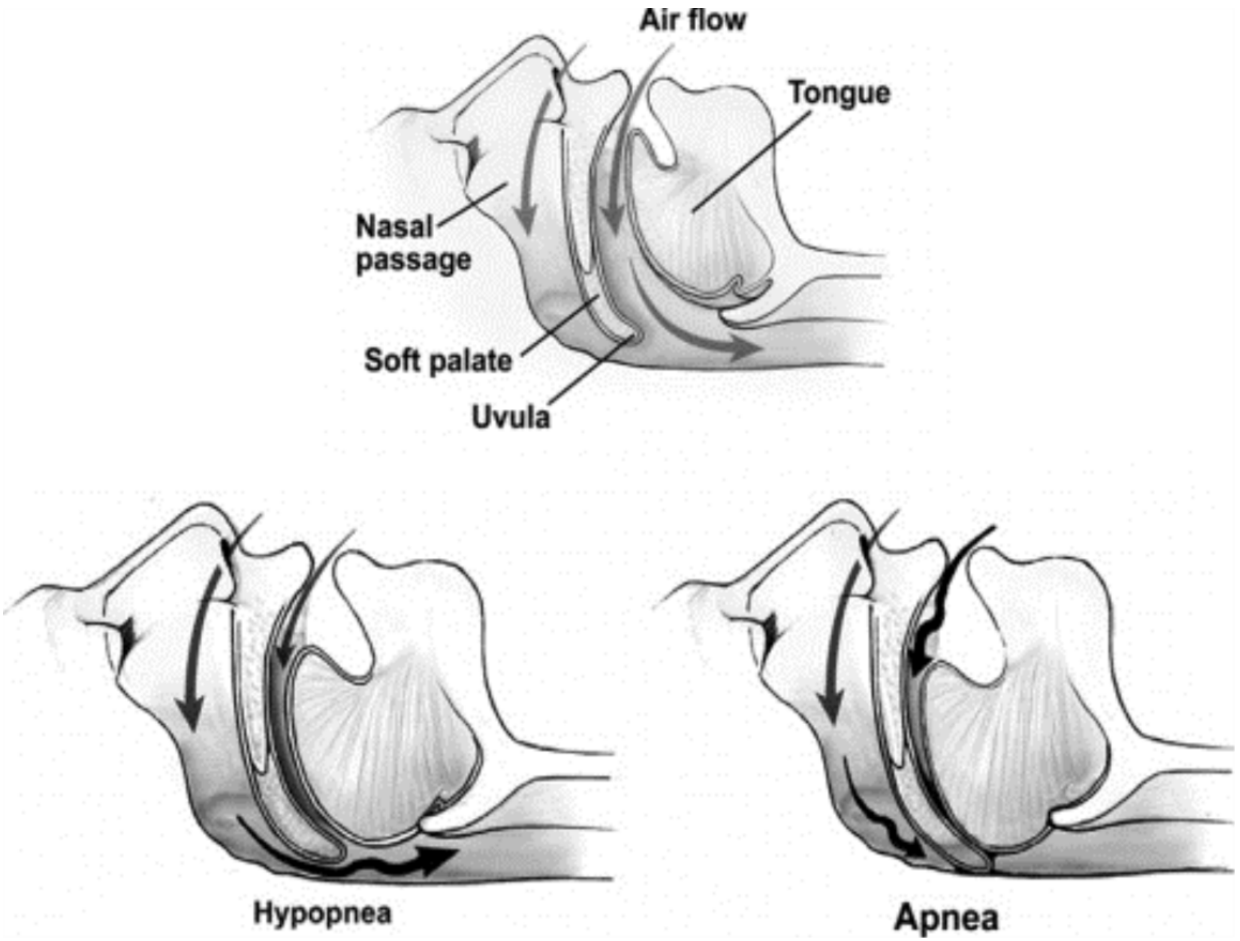
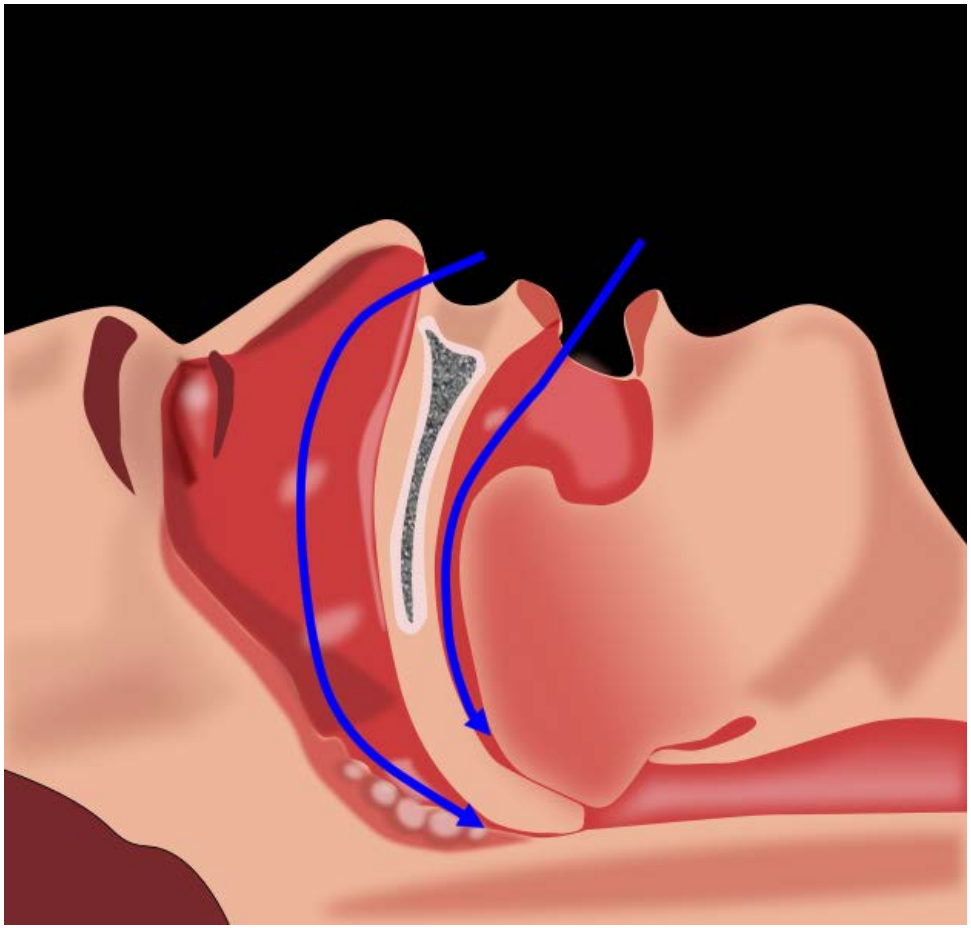


Figure Legend:

Partial and complete airway obstruction resulting in hypopnea and apnea, respectively. Reprinted from Hahn PY, Somers VK. Sleep apnea and hypertension. In: Lip GYH, Hall JE, eds. Comprehensive Hypertension. St. Louis, MO: Mosby; 2007:201–207. Copyright Elsevier 2007. Used with permission.

J Am Coll Cardiol. 2008;52(8):686-717. doi:10.1016/j.jacc.2008.05.002

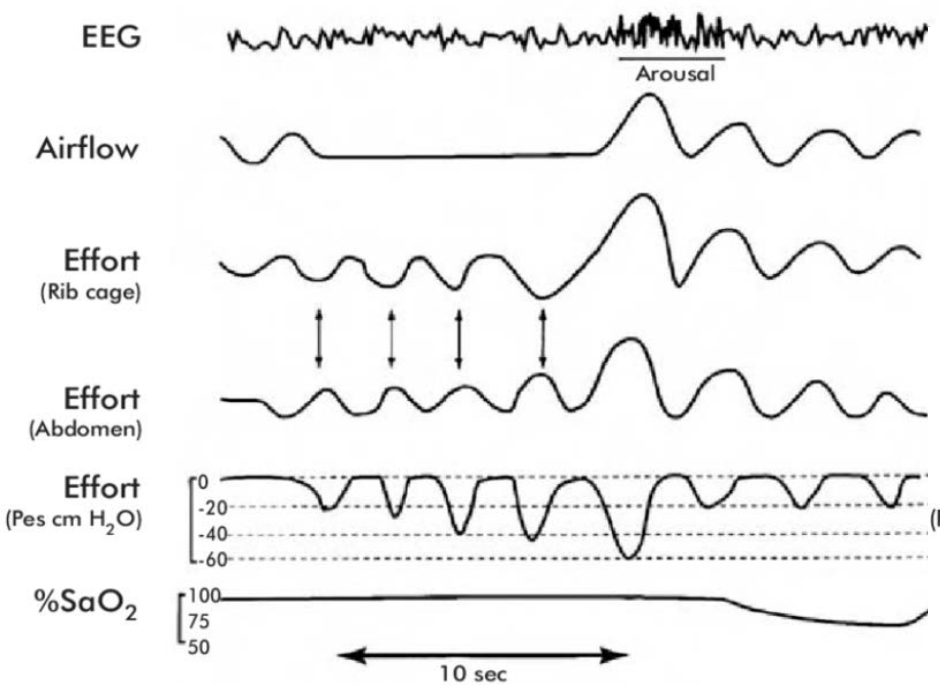
Obstructive Sleep Apnea: Anatomy



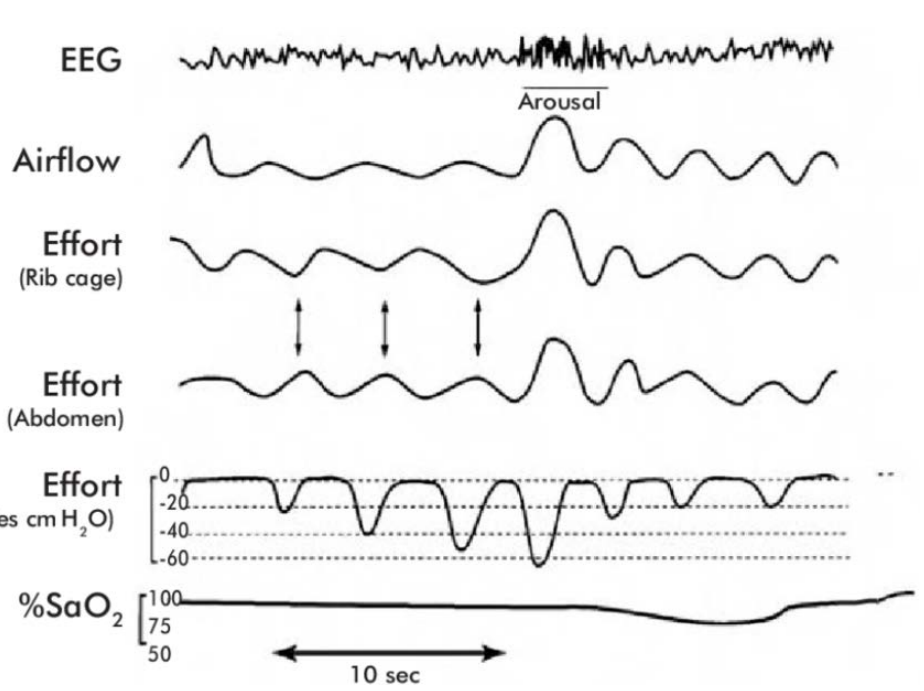
www.commons.wikimedia.org

Obstructive Sleep Apnea

Obstructive Apnea



Obstructive Hypopnea

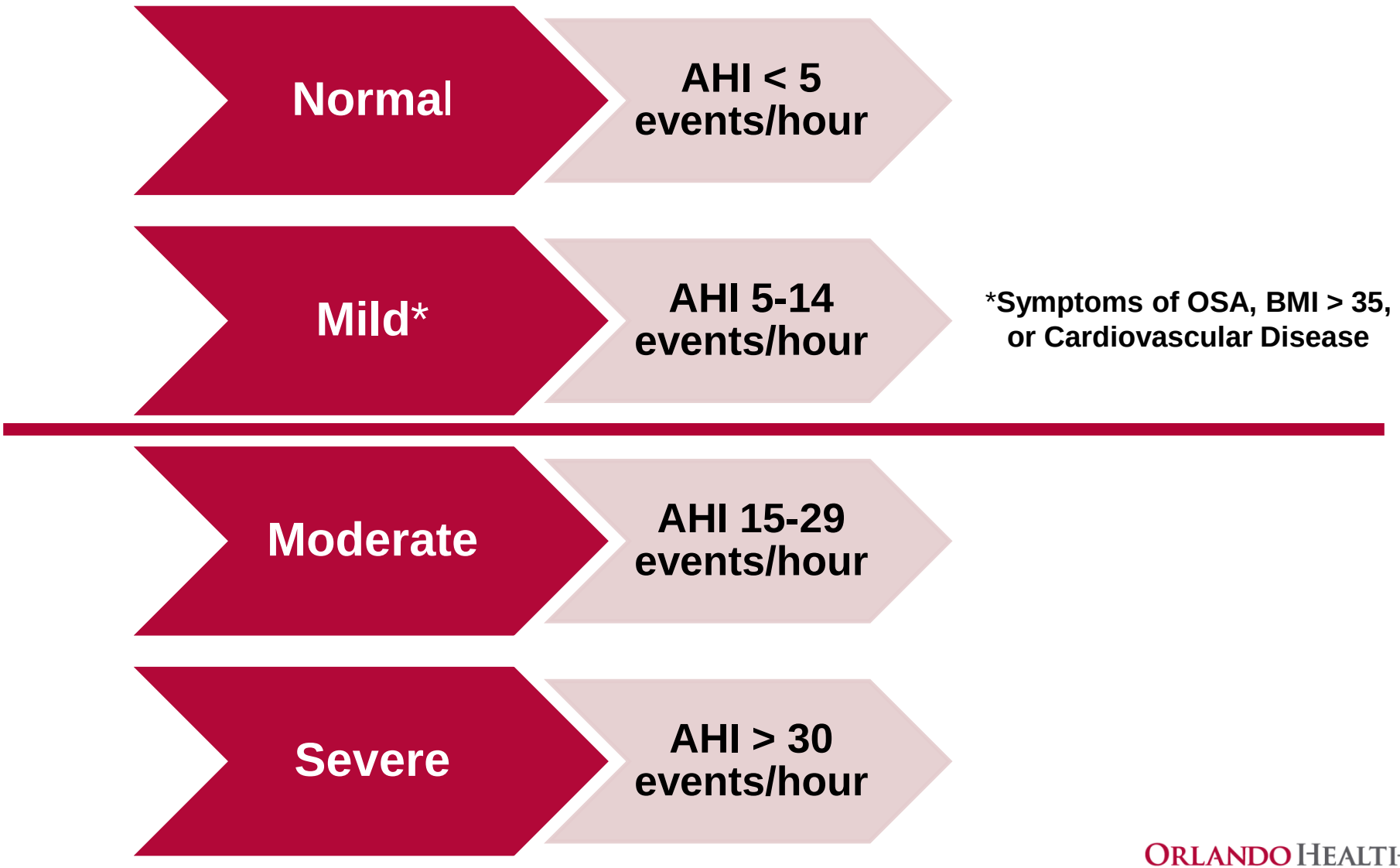


Obstructive Sleep Apnea: Apnea Hypopnea Index

Apnea Hypopnea Index (AHI)

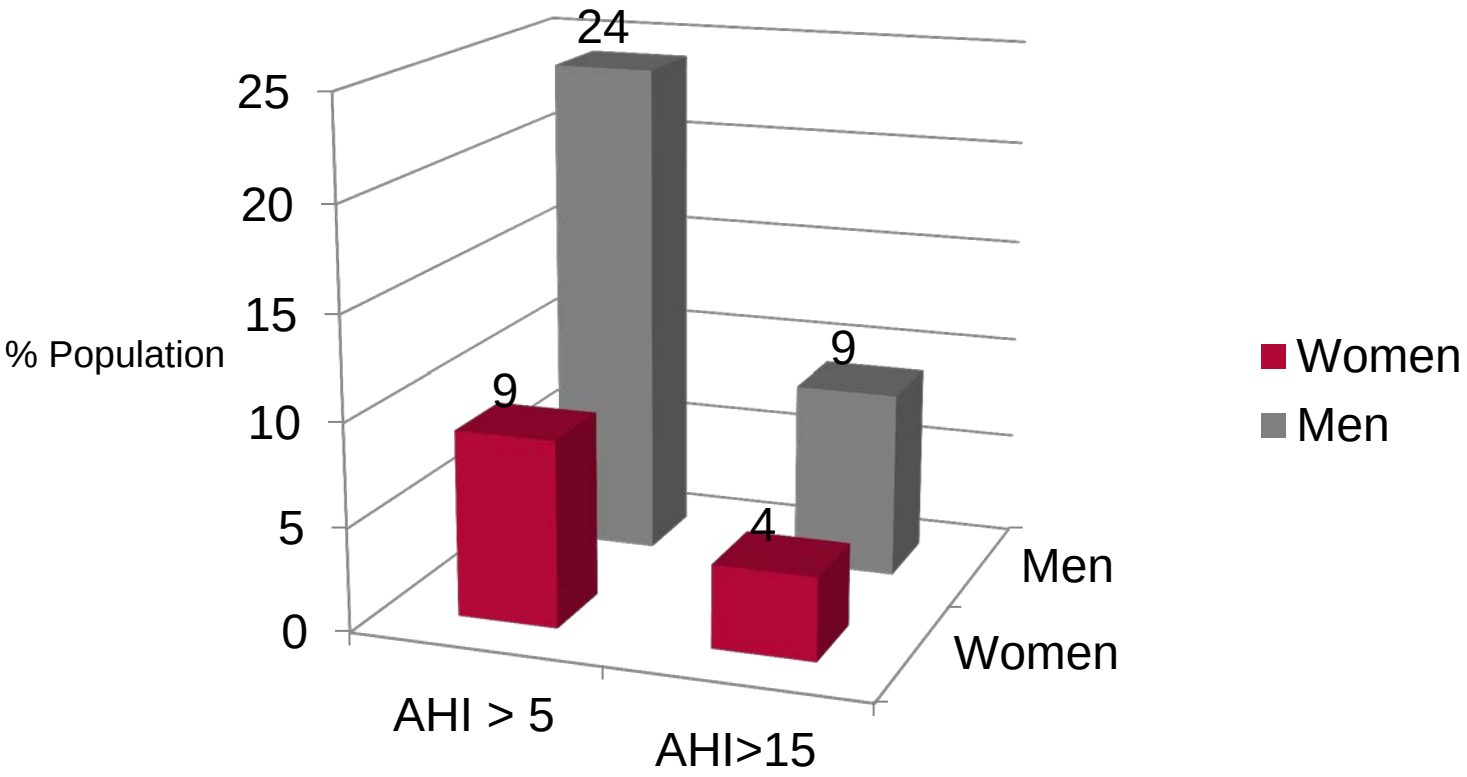
$$\frac{\#\text{Apneas} + \#\text{Hypopneas}}{\text{Total Sleep Time (hr)}}$$

Obstructive Sleep Apnea: Treatment



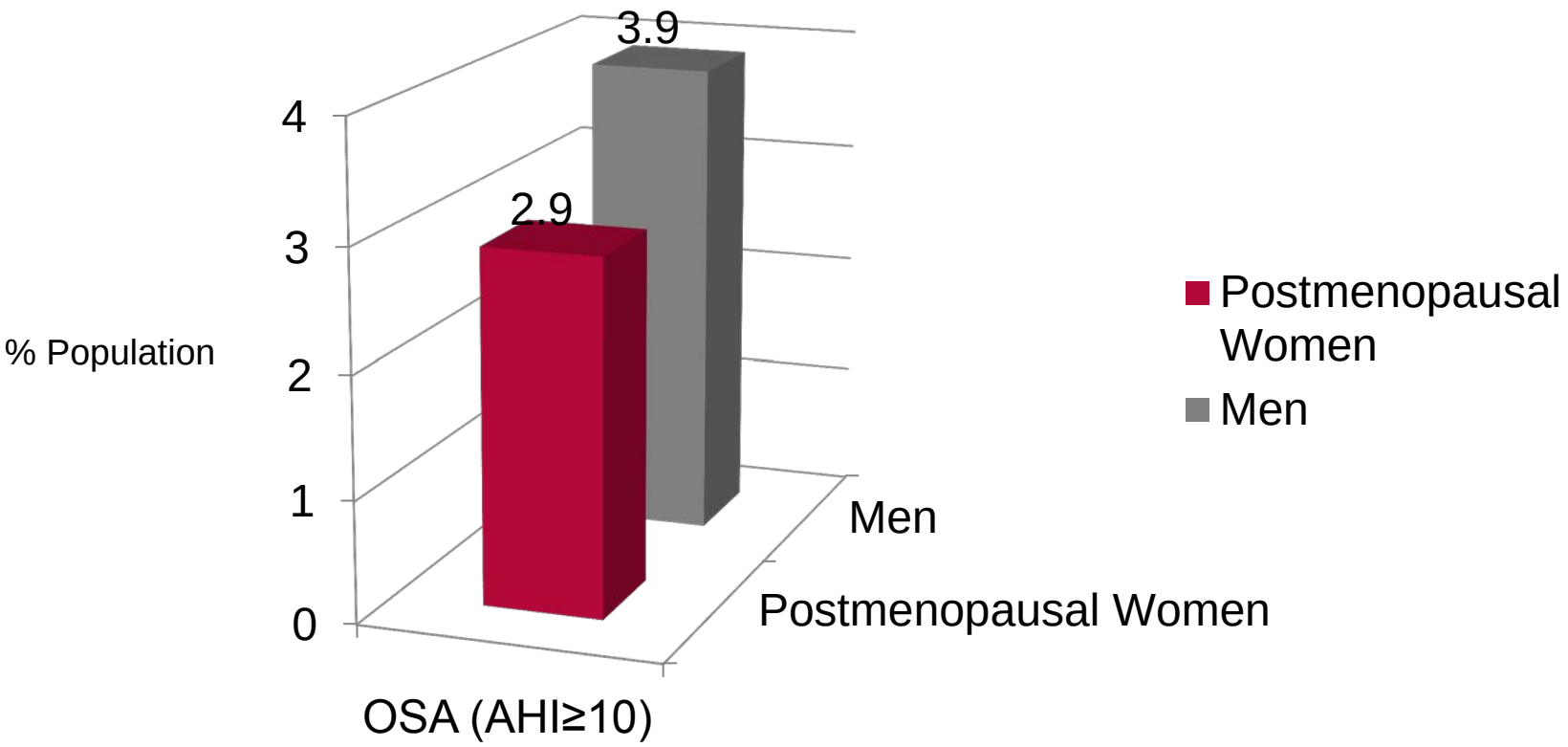
Obstructive Sleep Apnea: Prevalence

OSA Prevalence in Men and Women: Wisconsin Sleep Cohort Study



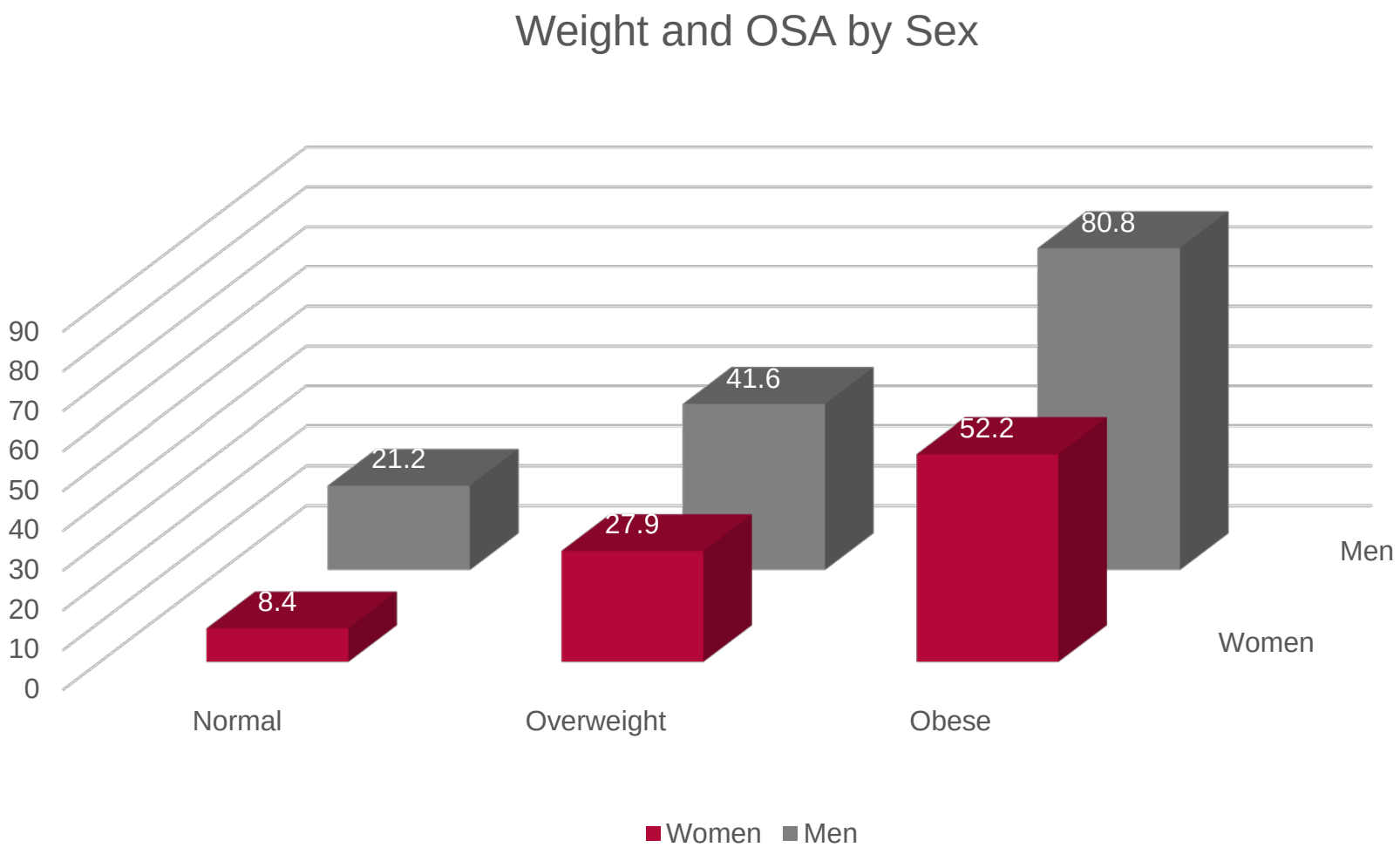
WMJ. 2009 Aug; 108(5): 246–249.

OSA in Postmenopausal Women vs Men



Am J Respir Crit Care Med. 2001;163(3 Pt 1):608.

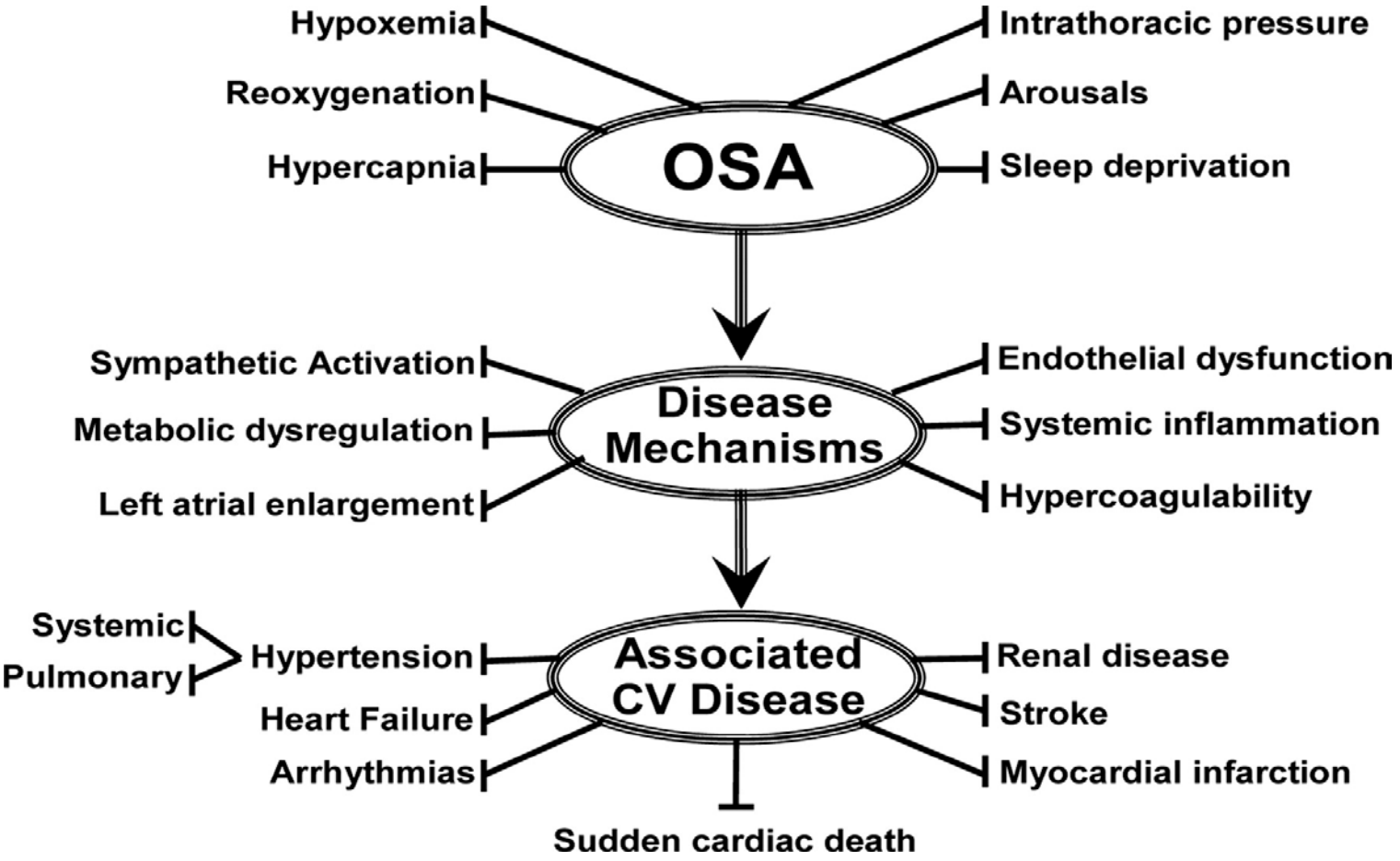
Prevalence of OSA in Men and Women by Weight



Sleep Medicine. 2010; 11(5):441-446.

Obstructive Sleep Apnea & Cardiovascular Disease

OSA and Cardiovascular Disease



Somers V K et al. *Circulation*. 2008;118:1080-1111

American Heart Association.

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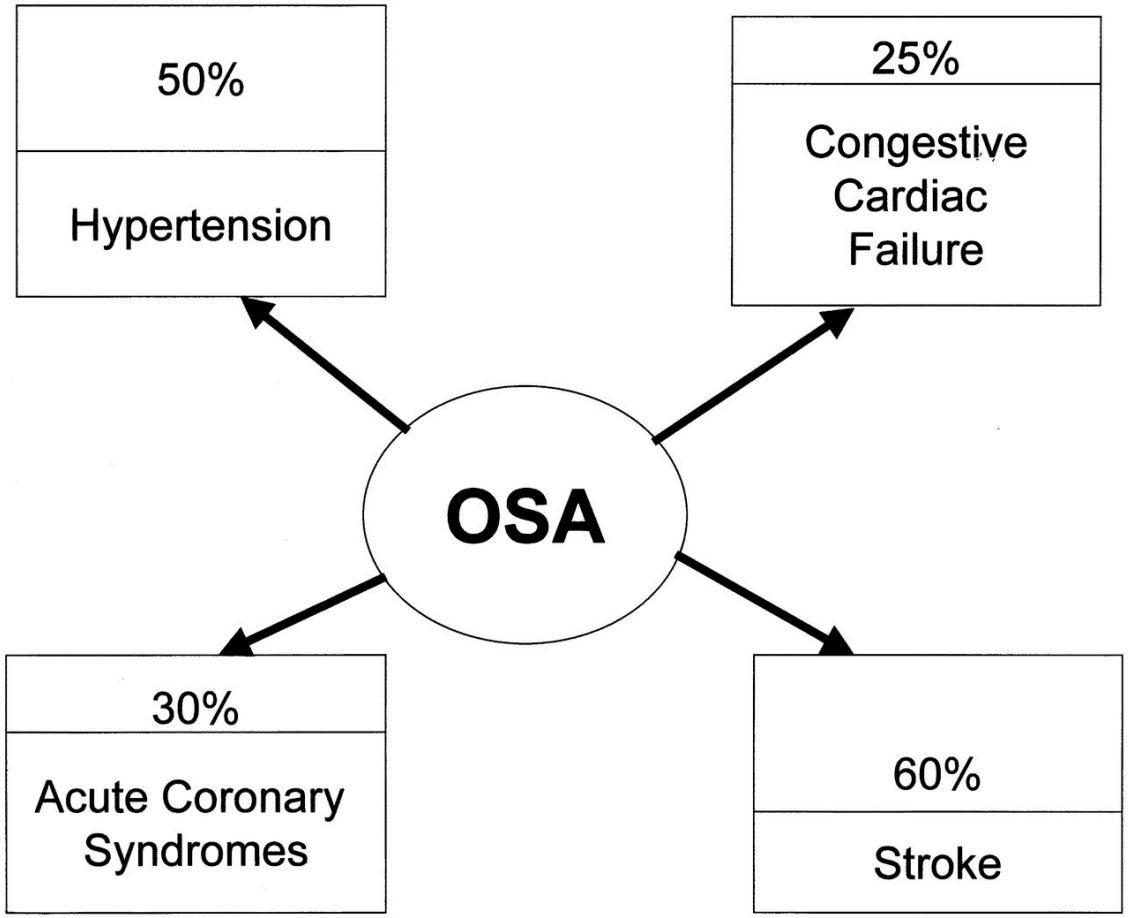
Prevalence of OSA in Patients with Cardiovascular and Cerebrovascular Disease



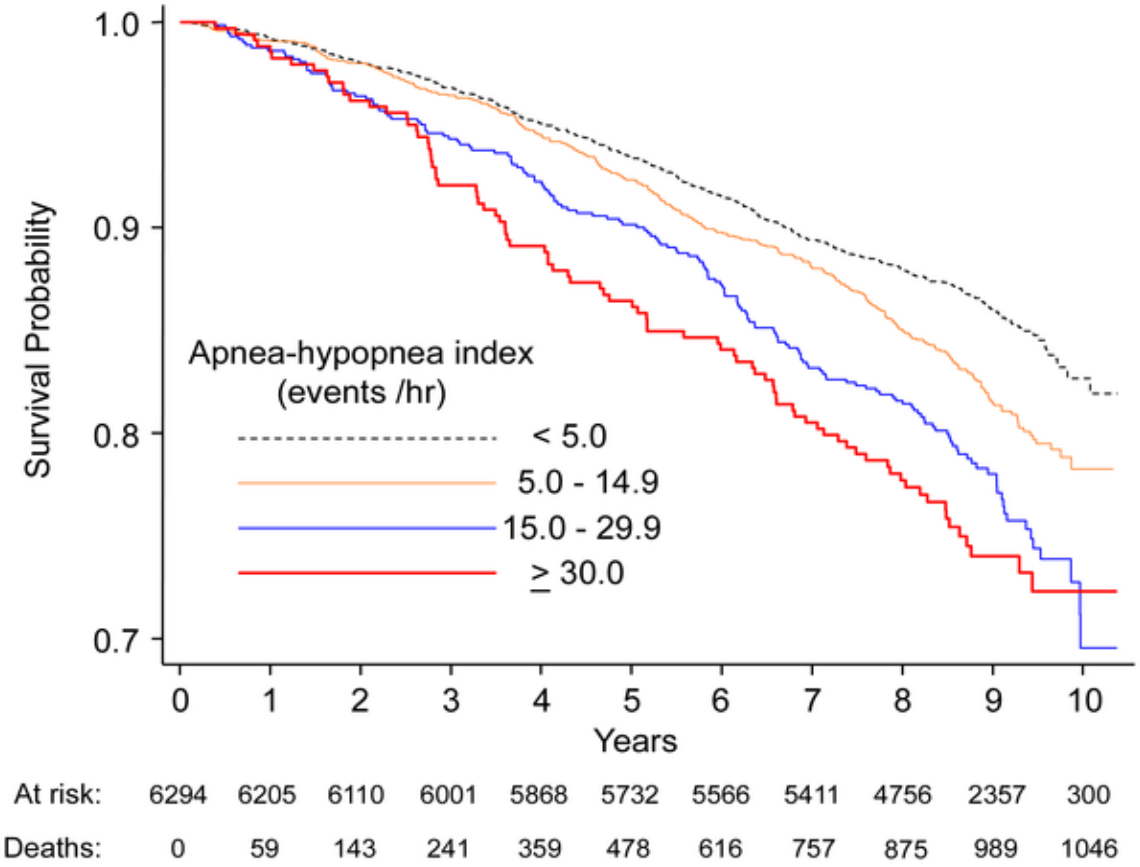
J.o-Dee L Lattimore et al. JACC 2003;41:1429-1437

OSA Increases Mortality

Sleep-Disordered Breathing and Mortality: A Prospective Cohort Study

Figure 1. Kaplan-Meier survival curves across categories of the apnea–hypopnea index (AHI).

N = 6,294



Punjabi NM, Caffo BS, Goodwin JL, Gottlieb DJ, et al. (2009) Sleep-Disordered Breathing and Mortality: A Prospective Cohort Study. PLoS Med 6(8): e1000132. doi:10.1371/journal.pmed.1000132
http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1000132

PLOS | MEDICINE

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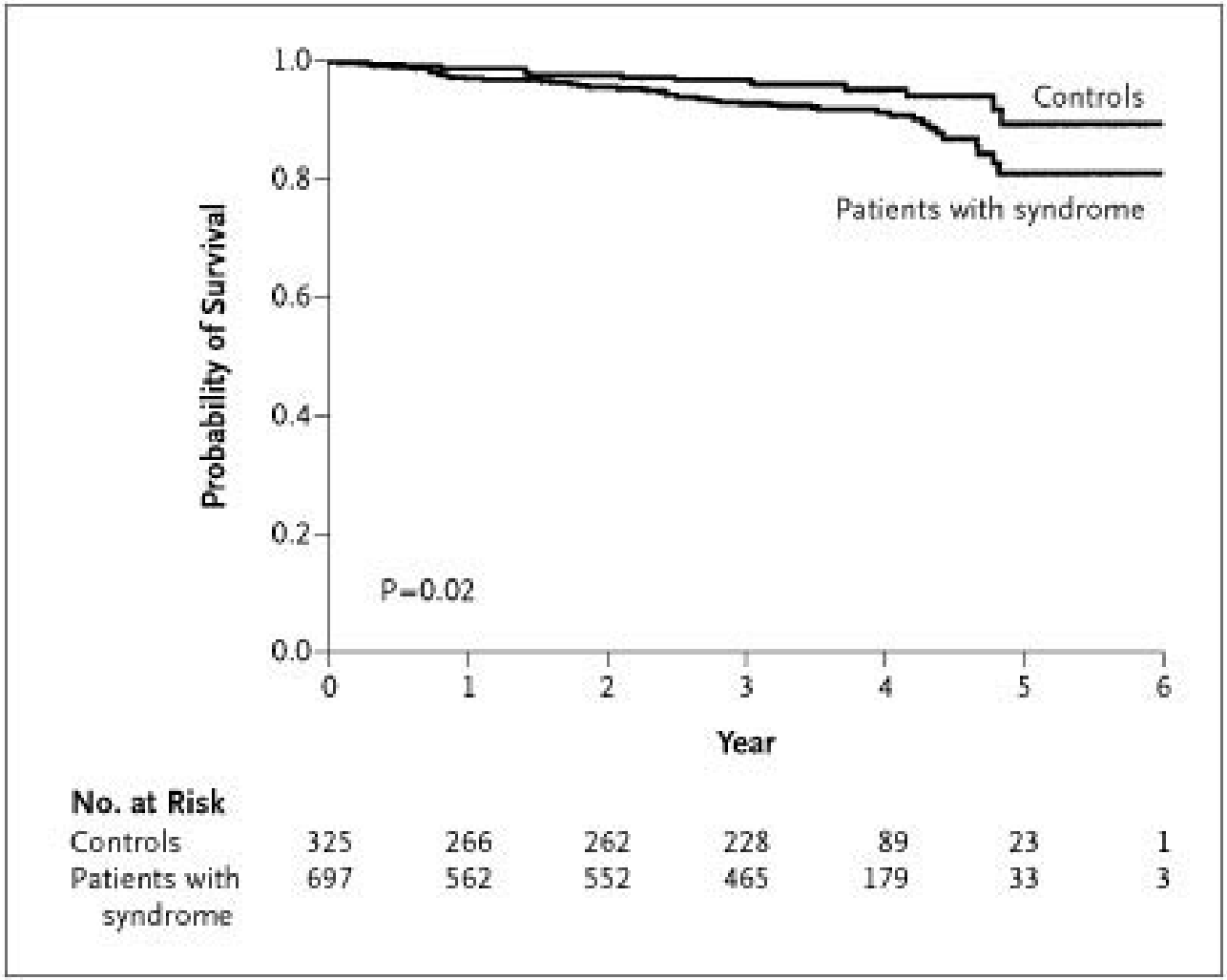
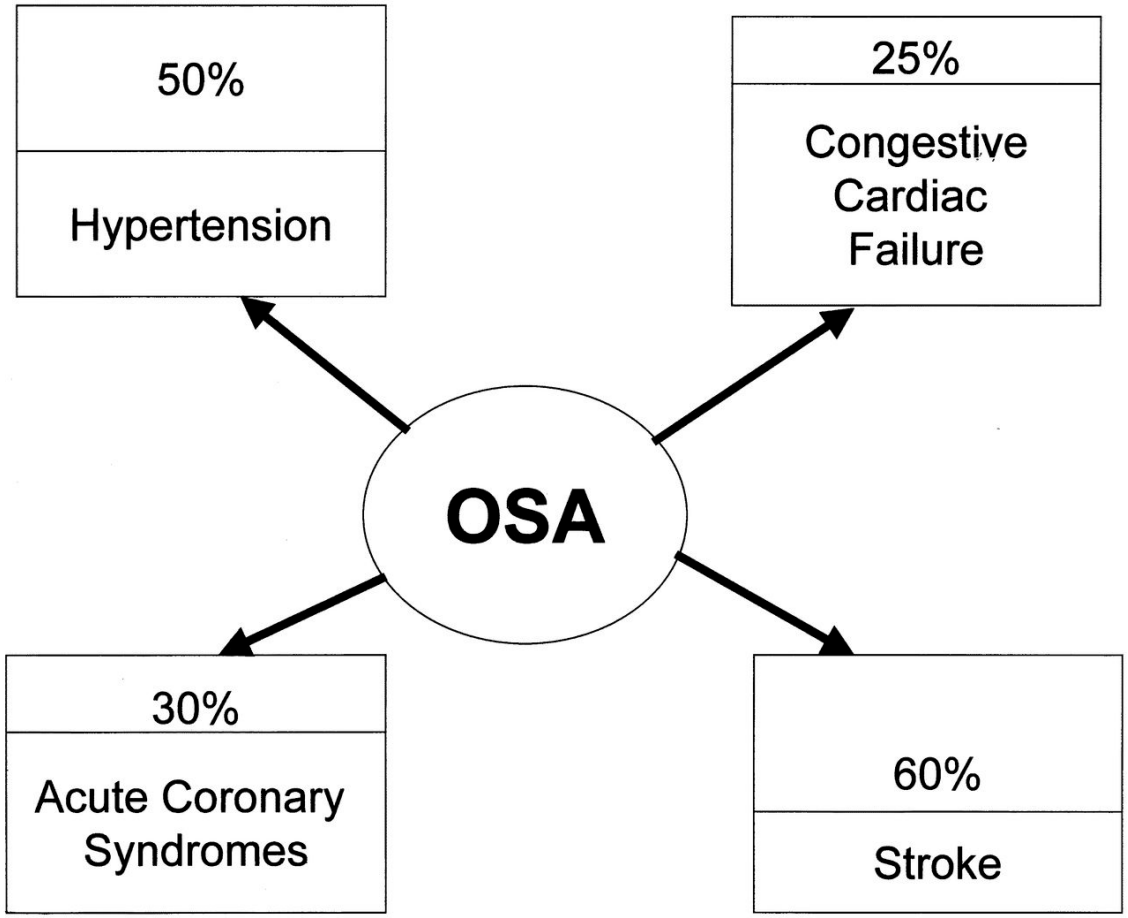
OSA Increases Mortality

OSA Probability of Survival



N Engl J Med 2005; 353:2034-2041

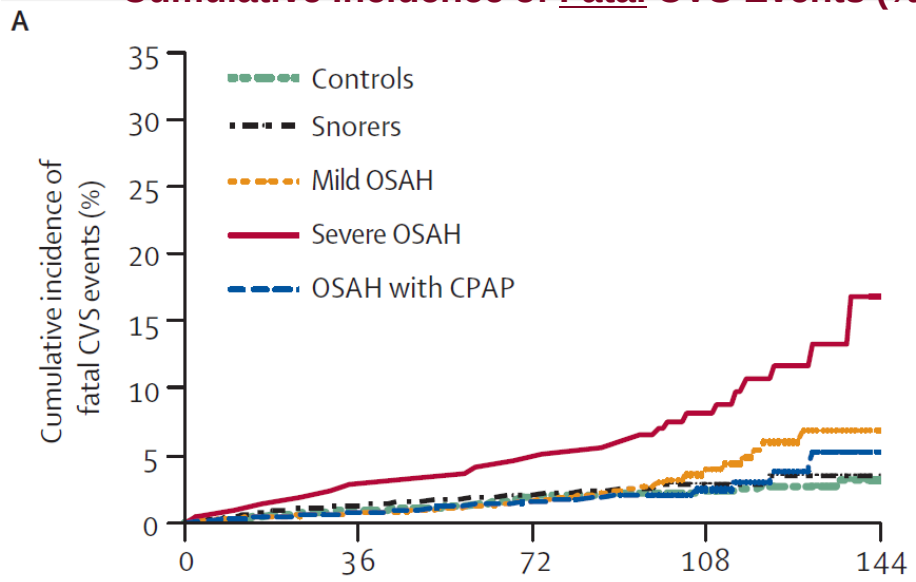
Prevalence of OSA in Patients with Cardiovascular and Cerebrovascular Disease



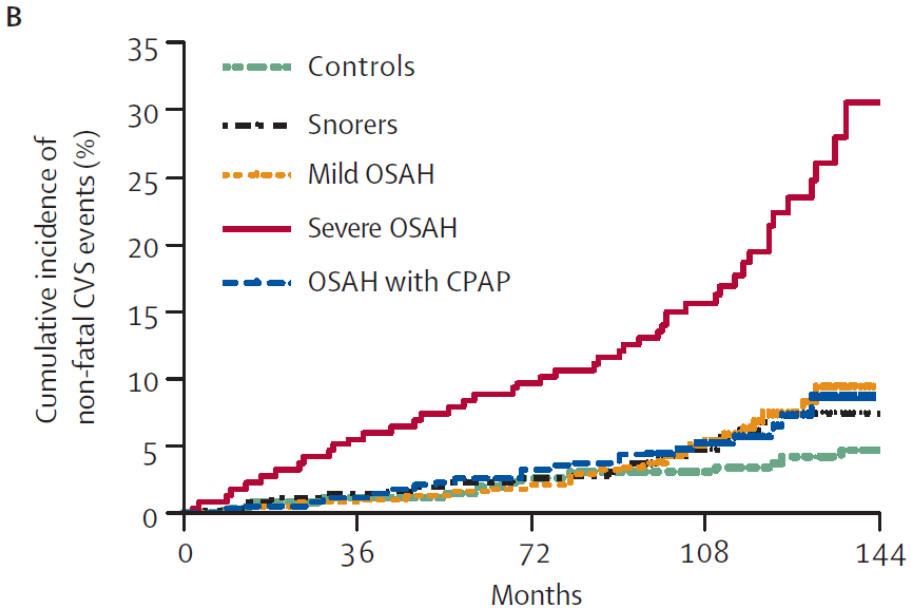
J.o-Dee L Lattimore et al. JACC 2003;41:1429-1437

OSA Increases Fatal & Non-Fatal Cardiovascular Events

Cumulative Incidence of Fatal CVS Events (%)



Cumulative Incidence of Non-Fatal CVS Events (%)



- Severe OSA has increased risk of fatal and non-fatal cardiovascular events.
- Treatment with CPAP reduced this risk.

THE LANCET

N = 1949

Lancet 2005:365:1046-53

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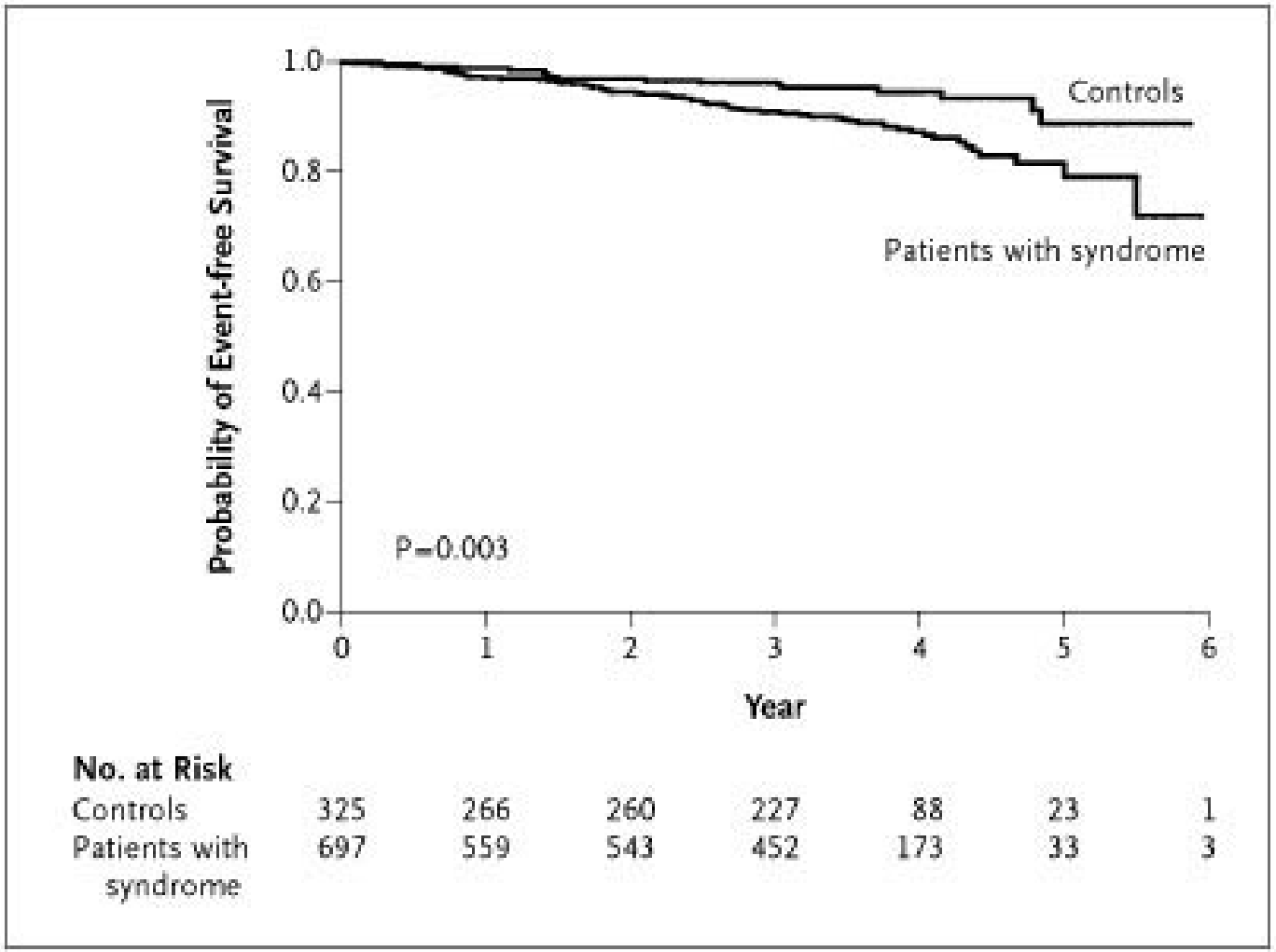
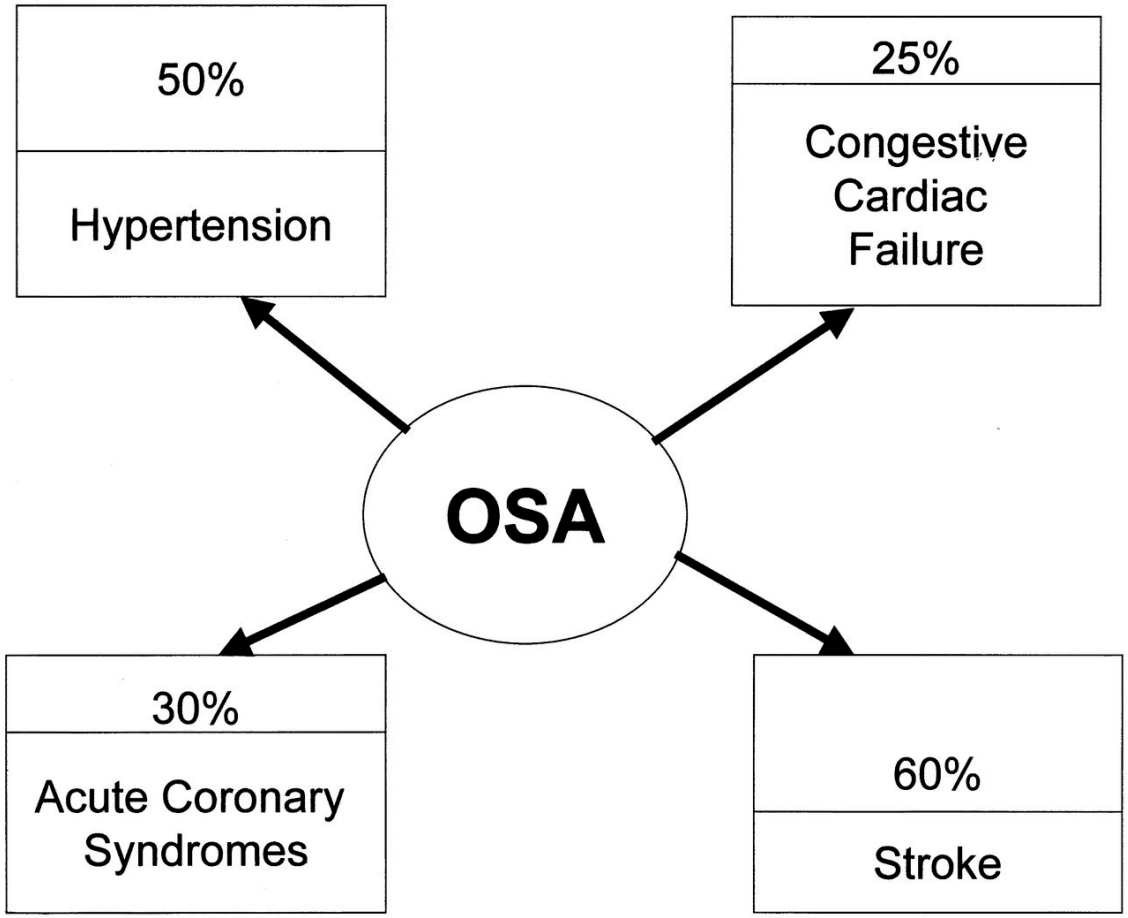
OSA Increases Strokes or All-Cause Mortality



N Engl J Med 2005; 353:2034-2041

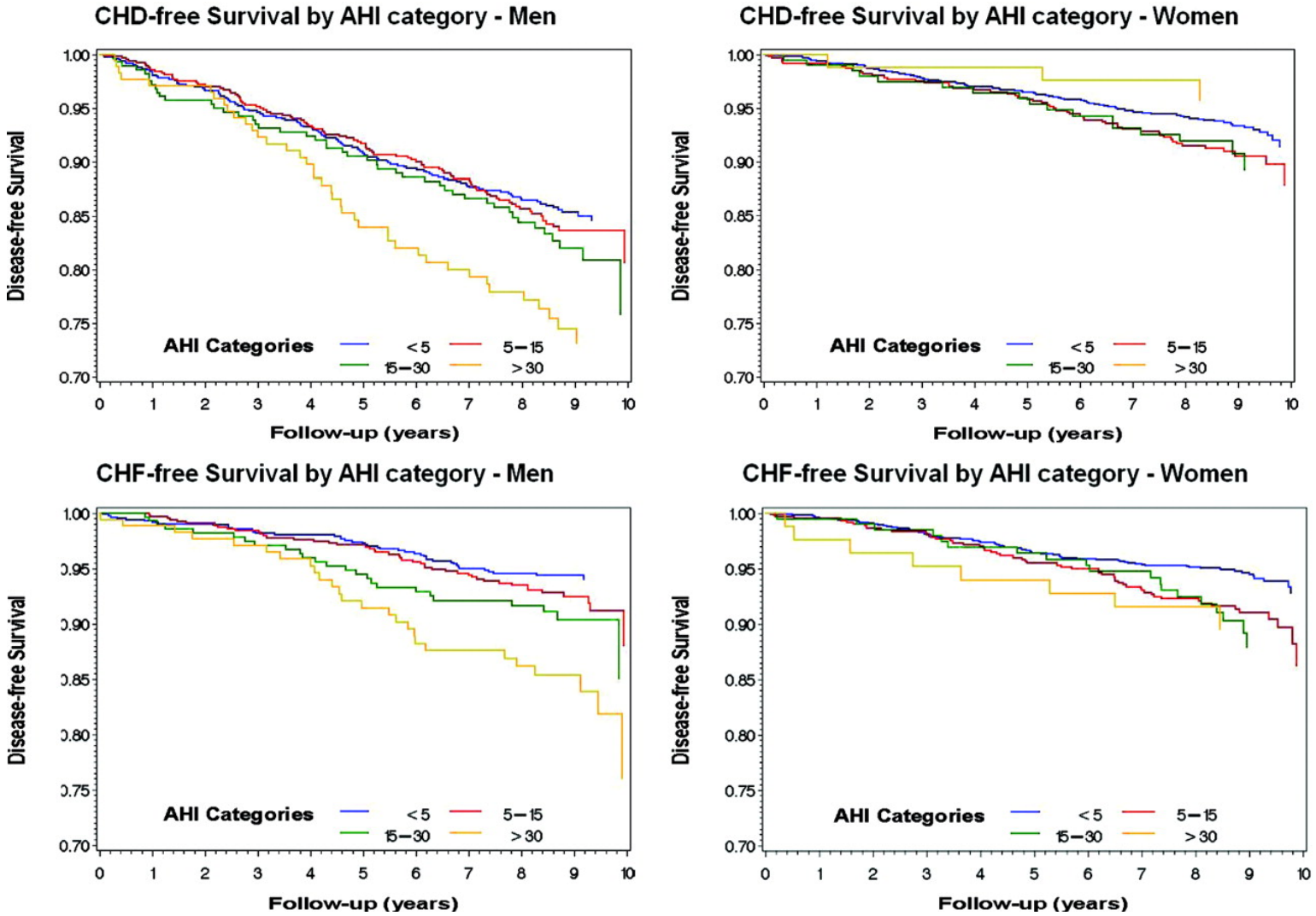
Prevalence of OSA in Patients with Cardiovascular and Cerebrovascular Disease



J.o-Dee L Lattimore et al. JACC 2003;41:1429-1437

CHD-free Survival and CHF-free Survival in Men and Women with OSA

Unadjusted Kaplan-Meier survival curves for AHI clinical categories, by sex and event type.



Gottlieb D J et al. *Circulation*. 2010;122:352-360

N = 4422

American Heart Association.

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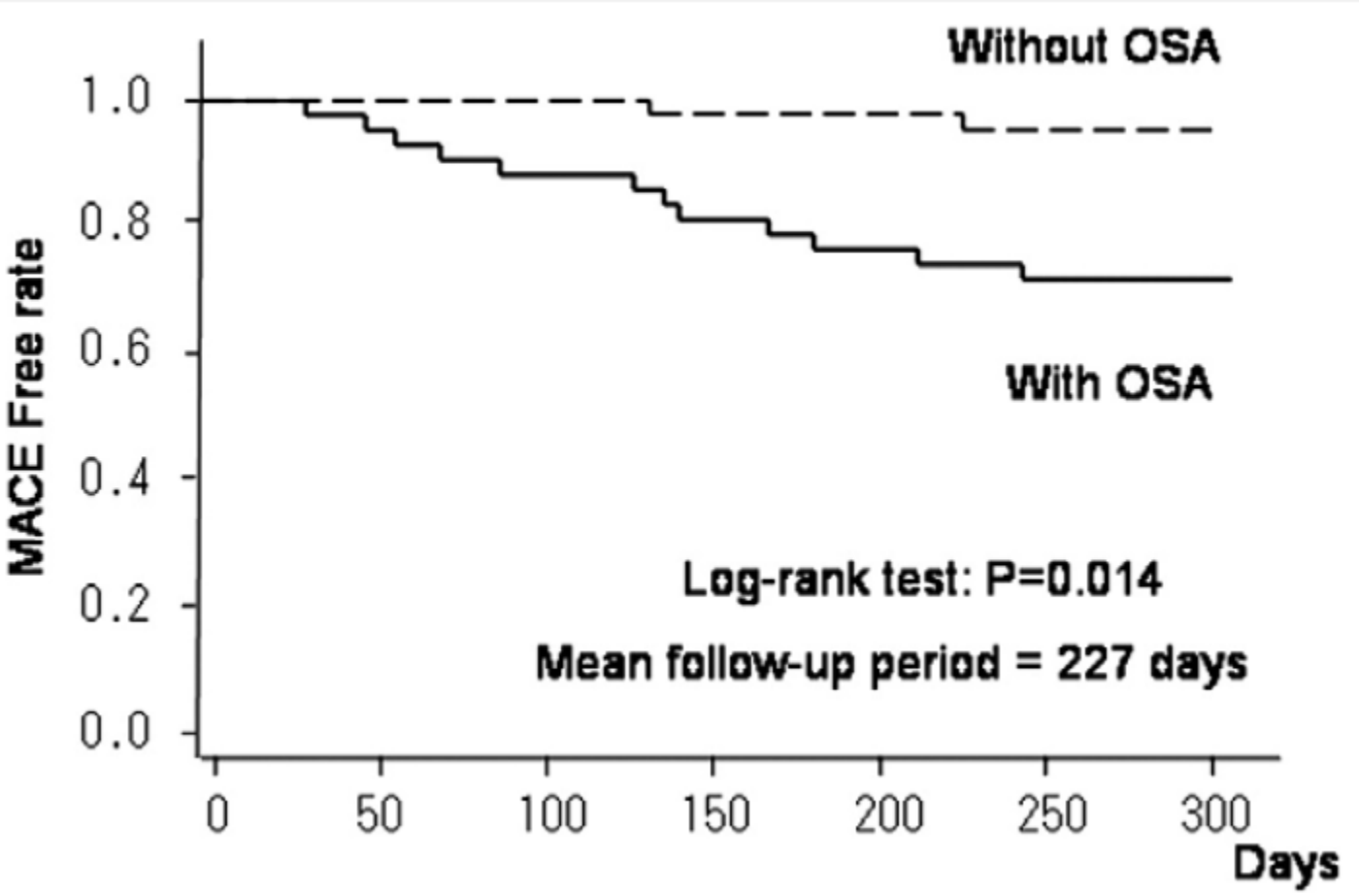
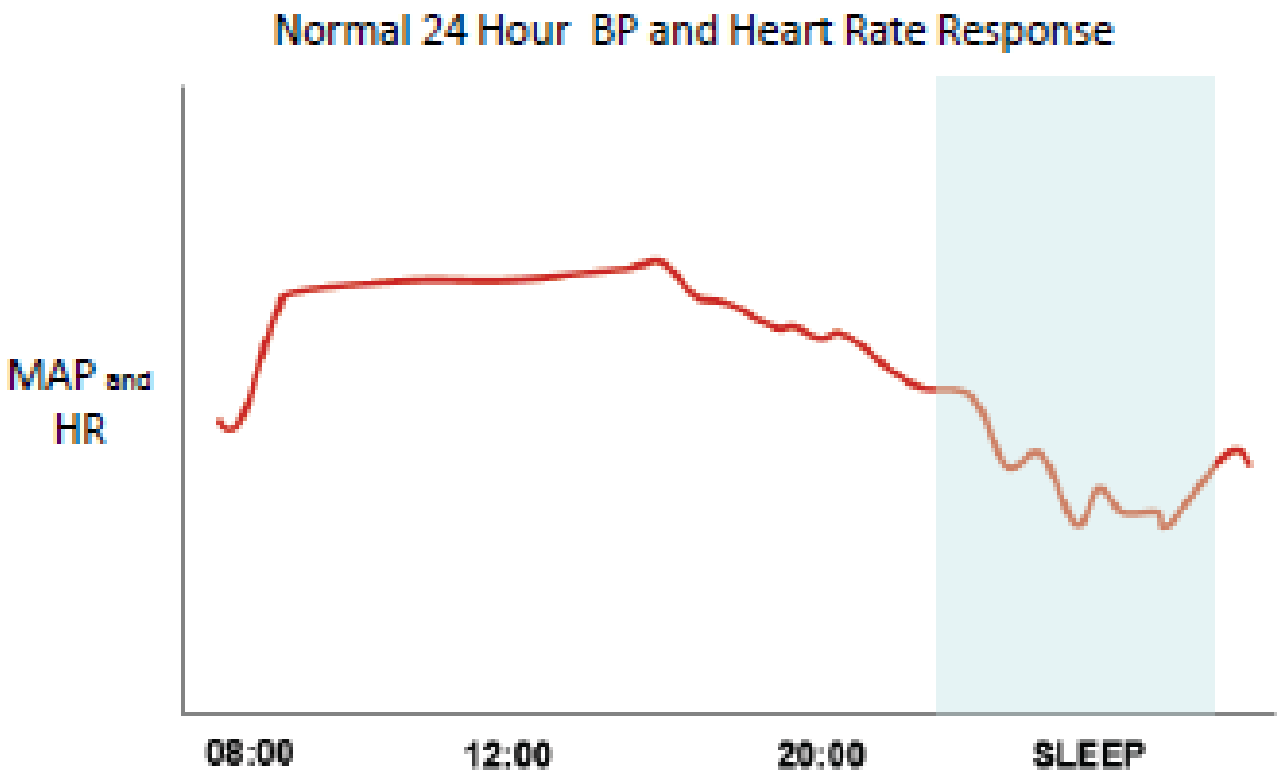
OSA Decreases Major Adverse Cardiac Event-Free Survival After Percutaneous Coronary Intervention



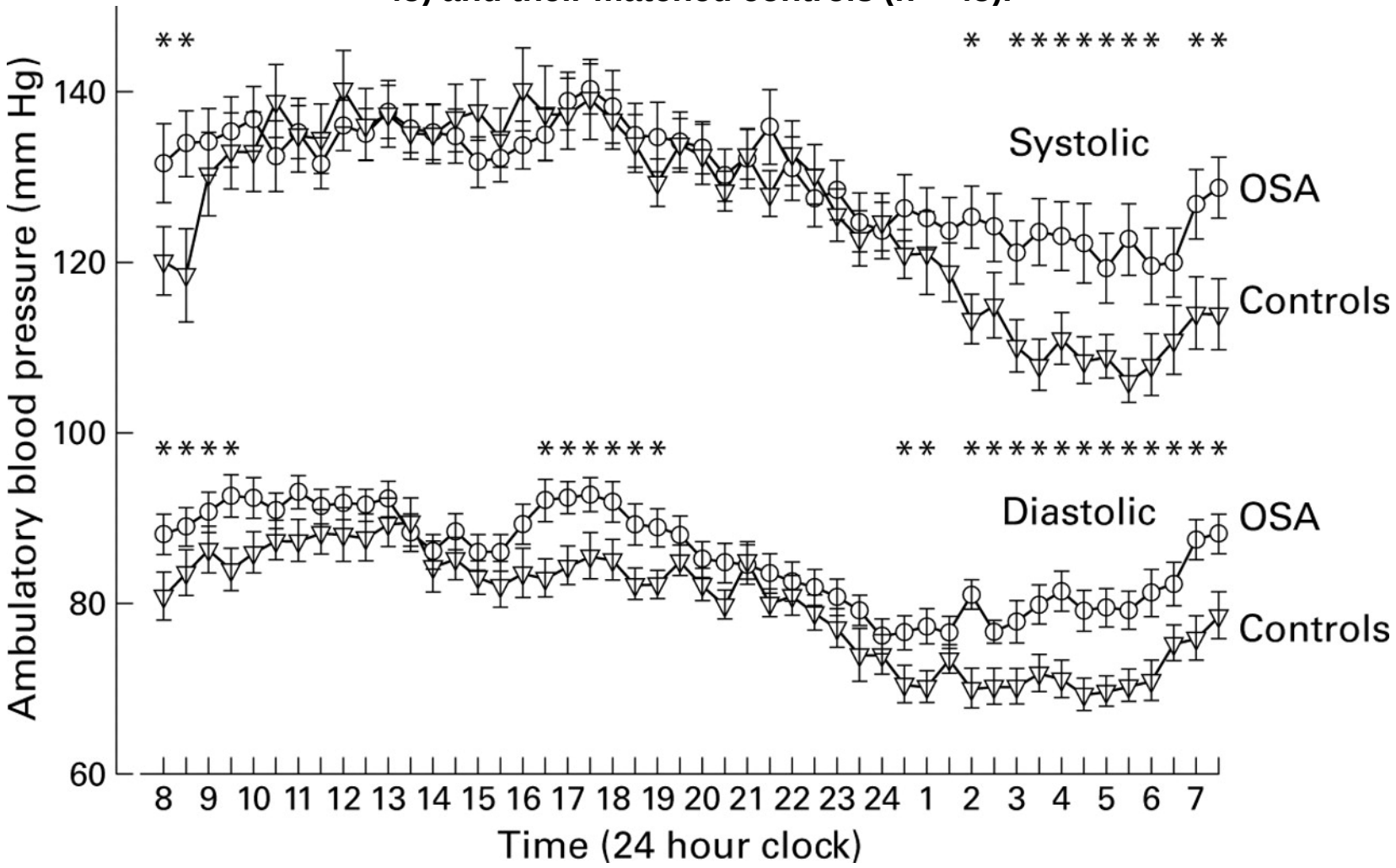
Am J. Cardiology. 2007;99:26-30

Normal BP and Heart Rate Response



OSA Increases Diastolic and Systolic Blood Pressure During Sleep

Mean (SE) 24 hour systolic and diastolic blood pressure profiles for patients with OSA (n = 45) and their matched controls (n = 45).



Christopher W H Davies et al. Thorax 2000;55:736-740

THORAX

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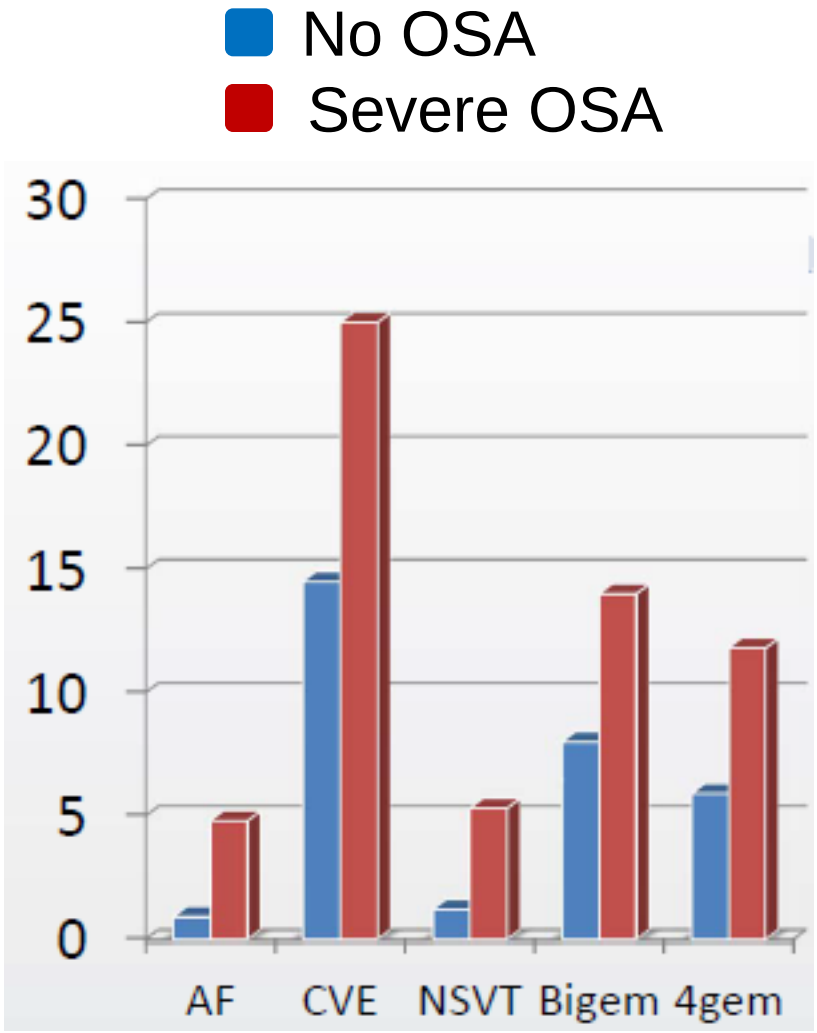
OSA Increases Risk of Arrhythmias

- Sleep Heart Health Study
- 2-4 times higher odds of arrhythmias in OSA



Am J Resp Crit Care Med 2006;173:910-916

OSA Increases Risk Atrial Fibrillation and Cardiovascular Ectopy

From: **Nocturnal Arrhythmias Across a Spectrum of Obstructive and Central Sleep-Disordered Breathing in Older Men: Outcomes of Sleep Disorders in Older Men (MrOS Sleep) Study**

Arch Intern Med. 2009;169(12):1147-1155. doi:10.1001/archinternmed.2009.138

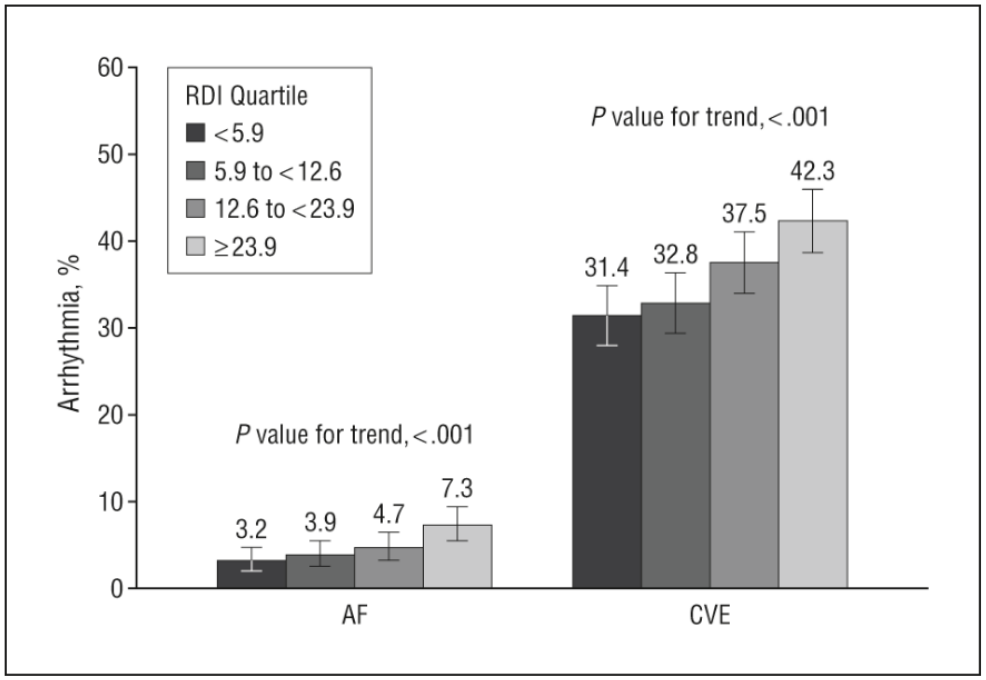
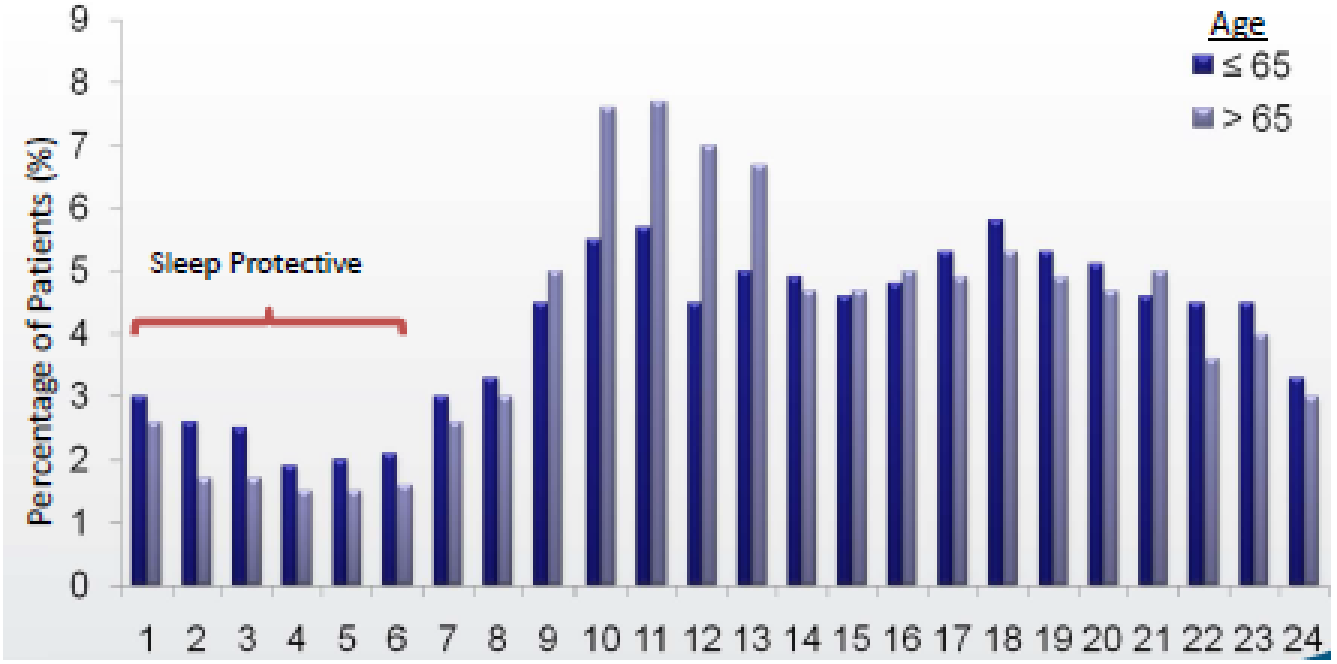


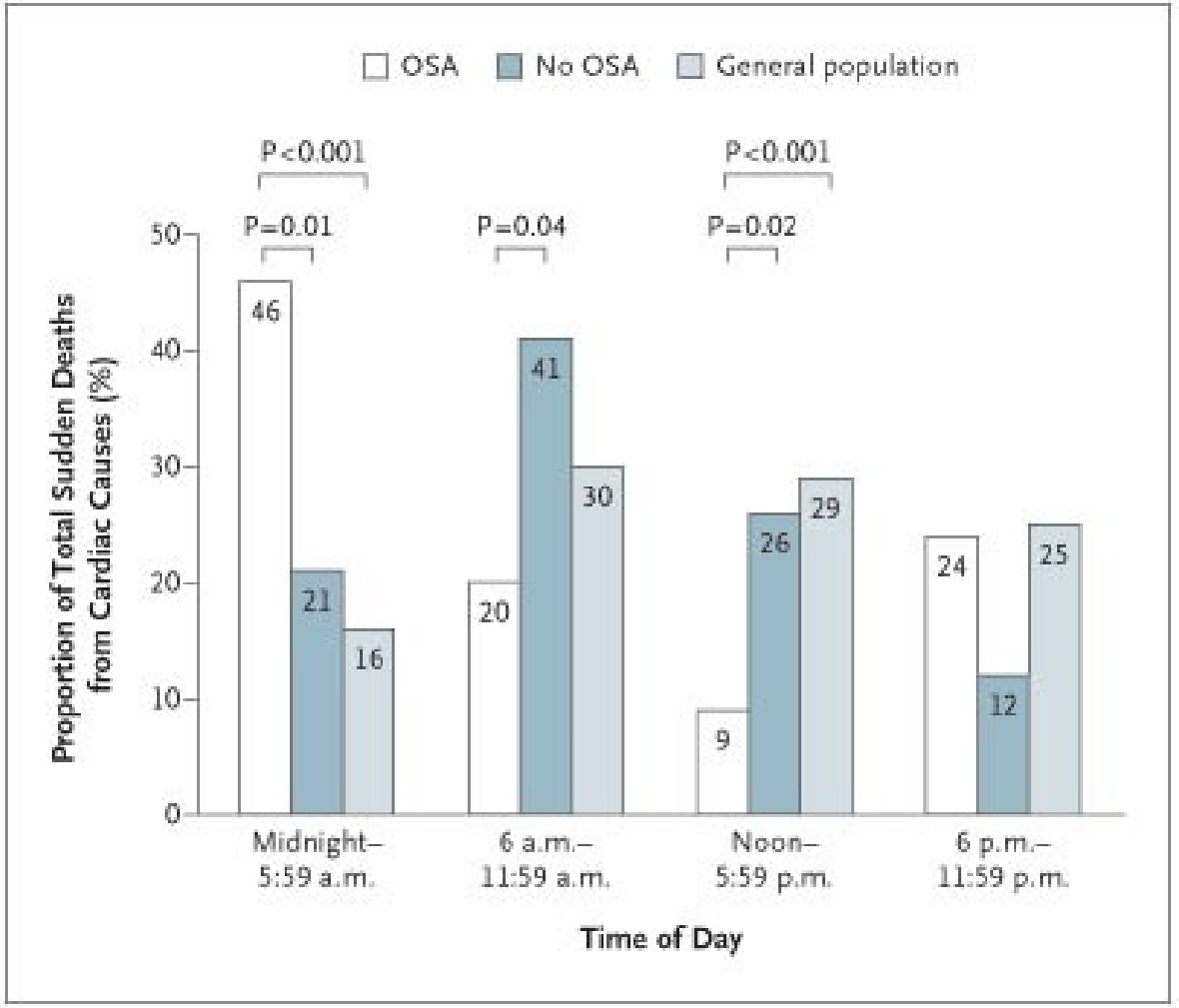
Figure Legend:

Arrhythmia by increasing Obstructive Apnea Index (OAI) quartile relative to atrial fibrillation or flutter (AF) and complex ventricular ectopy (CVE). The error bars indicate standard errors.

Sudden Cardiac Death: General Population



OSA Increases Risk of Sudden Cardiac Death At Night



N Engl J Med 2005; 352:1206-1214

OSA & Cardiovascular Disease: A Review

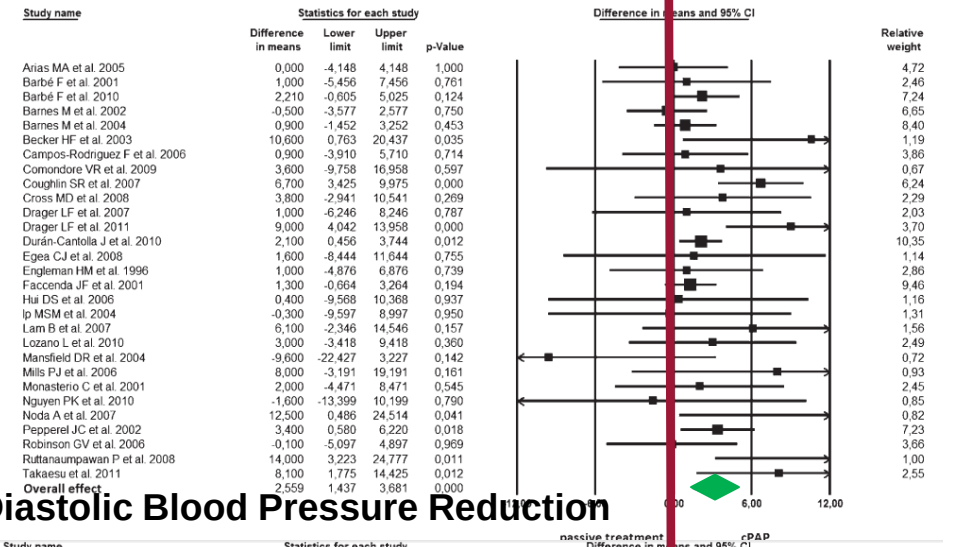
- OSA is Prevalent in Many Patients with Cardiovascular Disease
- Untreated OSA:
  - ↑ All-Cause Mortality
  - ↑ Cardiovascular Mortality
  - ↑ Non-fatal Cardiovascular Events
  - ↑ Risk of Coronary Heart Disease (esp. in Men)
  - ↑ Risk Congestive Heart Failure
  - ↑ Blood Pressure
  - ↑ Risk of Developing Arrhythmias
  - ↑ Risk of Sudden Cardiac Death (esp. at Night)

Obstructive Sleep Apnea: Treatment Effect on Cardiovascular Disease

Treatment of OSA Reduces Blood Pressure

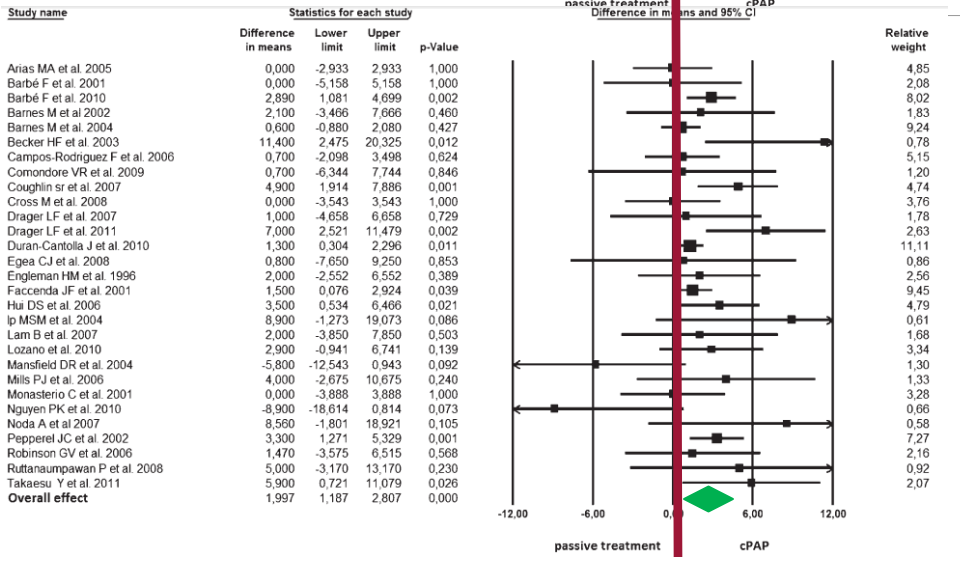
Passive Treatment **CPAP**

Systolic Blood Pressure Reduction



Study name	Difference in means	Lower limit	Upper limit	p-Value	Relative weight
Arias MA et al. 2005	0,000	-4,148	4,148	1,000	4,72
Barbé F et al. 2001	1,000	-5,456	7,456	0,761	2,46
Barbé F et al. 2010	2,210	-0,605	5,025	0,124	7,24
Barnes M et al. 2002	-0,500	-3,577	2,577	0,750	6,65
Barnes M et al. 2004	0,900	-1,452	3,252	0,453	8,40
Becker HF et al. 2003	10,600	0,763	20,437	0,035	1,19
Campos-Rodriguez F et al. 2006	0,900	-3,910	5,710	0,714	3,86
Comondore VR et al. 2009	3,600	-9,758	16,958	0,597	0,67
Coughlin SR et al. 2007	6,700	3,425	9,975	0,000	6,24
Cross MD et al. 2008	3,800	-2,941	10,541	0,269	2,29
Drager LF et al. 2007	1,000	-6,246	8,246	0,787	2,03
Drager LF et al. 2011	9,000	4,042	13,958	0,000	3,70
Durán-Cantolla J et al. 2010	2,100	0,456	3,744	0,012	10,35
Egea CJ et al. 2008	1,600	-8,444	11,644	0,755	1,14
Engleman HM et al. 1996	1,000	-4,876	6,876	0,739	2,86
Faccenda JF et al. 2001	1,300	-0,664	3,264	0,194	9,46
Hui DS et al. 2006	0,400	-9,568	10,368	0,937	1,16
Ip MSM et al. 2004	-0,300	-9,597	8,997	0,950	1,31
Lam B et al. 2007	6,100	-2,346	14,546	0,157	1,56
Lozano L et al. 2010	3,000	-3,418	9,418	0,360	2,49
Mansfield DR et al. 2004	-9,600	-22,427	3,227	0,142	0,72
Mills PJ et al. 2006	8,000	-3,191	19,191	0,161	0,93
Monasterio C et al. 2001	2,000	-4,471	8,471	0,545	2,45
Nguyen PK et al. 2010	-1,600	-13,399	10,199	0,790	0,85
Noda A et al. 2007	12,500	0,486	24,514	0,041	0,82
Pepperel JC et al. 2002	3,400	0,580	6,220	0,018	7,23
Robinson GV et al. 2006	-0,100	-5,097	4,897	0,969	3,66
Ruttanaumpawan P et al. 2008	14,000	3,223	24,777	0,011	1,00
Takaesu et al. 2011	8,100	1,775	14,425	0,012	2,55
Overall effect	2,559	1,437	3,681	0,000	

Diastolic Blood Pressure Reduction



Study name	Difference in means	Lower limit	Upper limit	p-Value	Relative weight
Arias MA et al. 2005	0,000	-2,933	2,933	1,000	4,85
Barbé F et al. 2001	0,000	-5,158	5,158	1,000	2,08
Barbé F et al. 2010	2,890	1,081	4,699	0,002	8,02
Barnes M et al 2002	2,100	-3,466	7,666	0,460	1,83
Barnes M et al. 2004	0,600	-0,880	2,080	0,427	9,24
Becker HF et al. 2003	11,400	2,475	20,325	0,012	0,78
Campos-Rodriguez F et al. 2006	0,700	-2,098	3,498	0,624	5,15
Comondore VR et al. 2009	0,700	-6,344	7,744	0,846	1,20
Coughlin sr et al. 2007	4,900	1,914	7,886	0,001	4,74
Cross M et al. 2008	0,000	-3,543	3,543	1,000	3,76
Drager LF et al. 2007	1,000	-4,658	6,658	0,729	1,78
Drager LF et al. 2011	7,000	2,521	11,479	0,002	2,63
Duran-Cantolla J et al. 2010	1,300	0,304	2,296	0,011	11,11
Egea CJ et al. 2008	0,800	-7,650	9,250	0,853	0,86
Engleman HM et al. 1996	2,000	-2,552	6,552	0,389	2,56
Faccenda JF et al. 2001	1,500	0,076	2,924	0,039	9,45
Hui DS et al. 2006	3,500	0,534	6,466	0,021	4,79
Ip MSM et al. 2004	8,900	-1,273	19,073	0,086	0,61
Lam B et al. 2007	2,000	-3,850	7,850	0,503	1,68
Lozano et al. 2010	2,900	-0,941	6,741	0,139	3,34
Mansfield DR et al. 2004	-5,800	-12,543	0,943	0,092	1,30
Mills PJ et al. 2006	4,000	-2,675	10,675	0,240	1,33
Monasterio C et al. 2001	0,000	-3,888	3,888	1,000	3,28
Nguyen PK et al. 2010	-8,900	-18,614	0,814	0,073	0,66
Noda A et al 2007	8,560	-1,801	18,921	0,105	0,58
Pepperel JC et al. 2002	3,300	1,271	5,329	0,001	7,27
Robinson GV et al. 2006	1,470	-3,575	6,515	0,568	2,16
Ruttanaumpawan P et al. 2008	5,000	-3,170	13,170	0,230	0,92
Takaesu Y et al. 2011	5,900	0,721	11,079	0,026	2,07
Overall effect	1,997	1,187	2,807	0,000	

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AMERICAN COLLEGE of CHEST PHYSICIANS

30 RCTs
N =1900 Patients

Chest. 2014;145(4):762.

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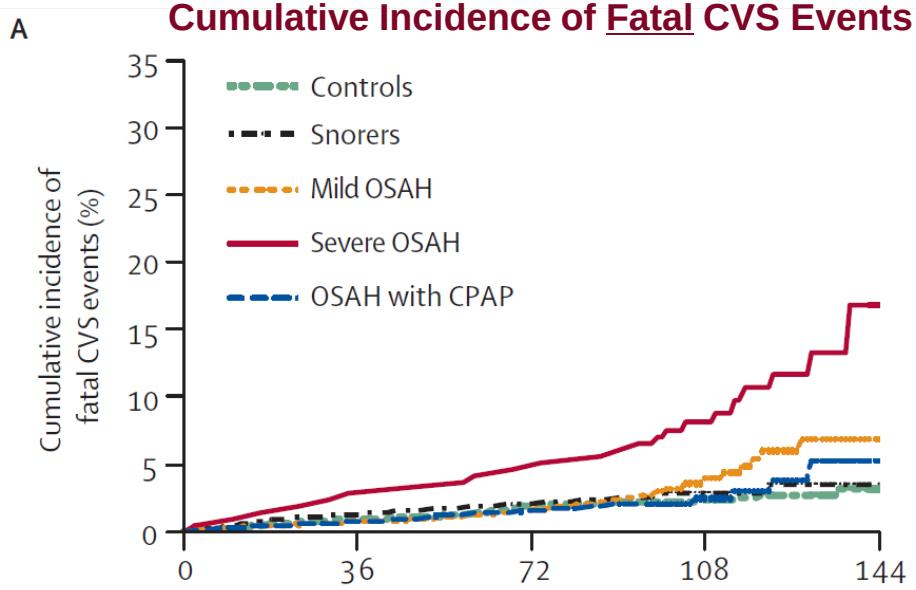
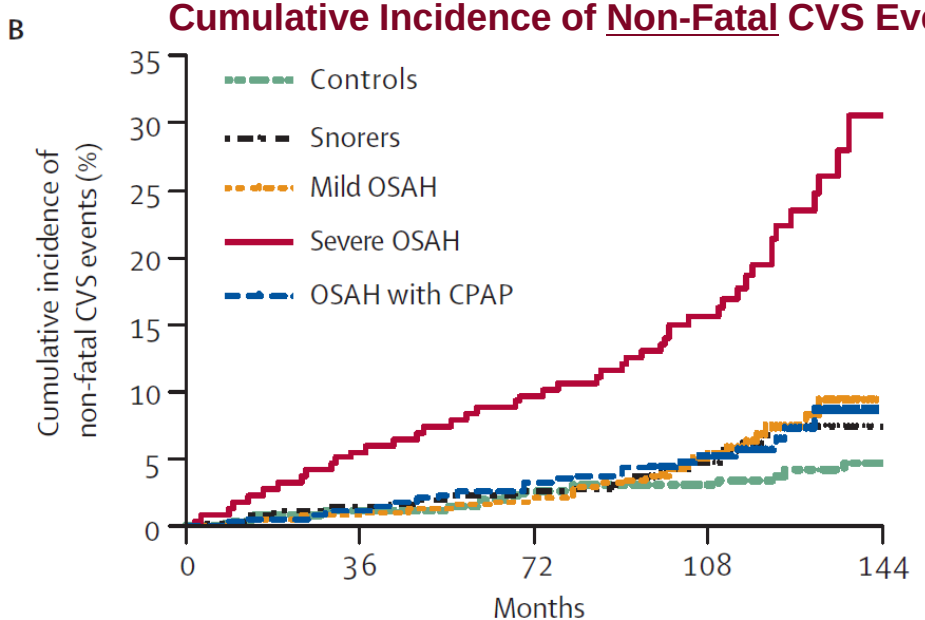
OSA and Fatal and Non-Fatal Cardiovascular Events





- Severe OSA has increased risk of fatal and non-fatal cardiovascular events.
- Treatment with CPAP reduced this risk.

THE LANCET

N = 1949

Lancet 2005:365:1046-53

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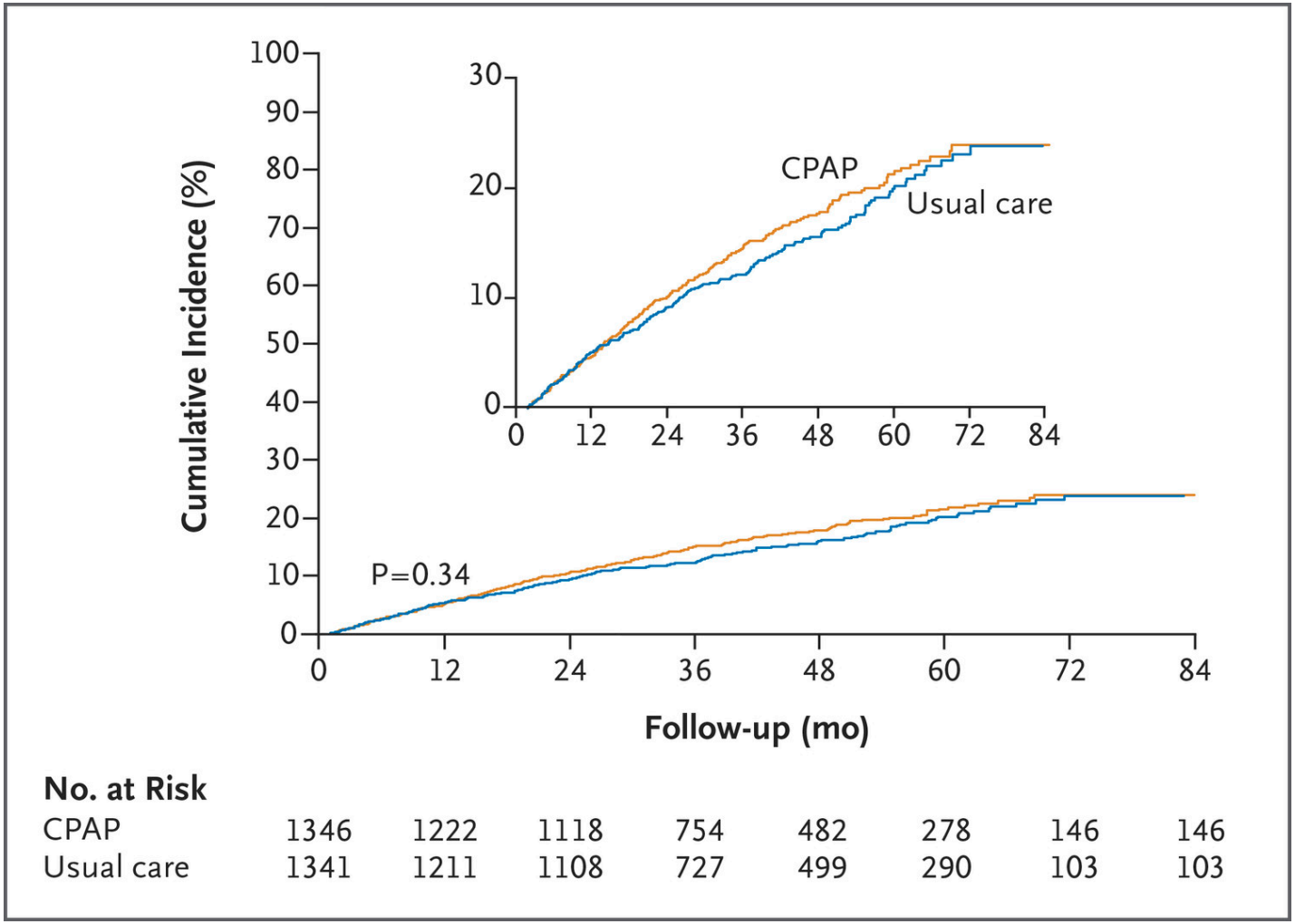
Incidence of Death From Cardiovascular Events in "Non-Sleepy" OSA Patients Treated with CPAP vs Usual Care

Cardiovascular Causes:

- Myocardial Infarction
- Stroke
- Hospitalization for Congestive Heart Failure
- Unstable Angina
- Transient Ischemic Attack

N = 2717



McEvoy RD et al. N Engl J Med 2016;375:919-931.

OSA & Cardiovascular Disease: A Review

- OSA is Prevalent in Many Patients with Cardiovascular Disease
- Untreated OSA:
  - ↑ All-Cause Mortality
  - ↑ Cardiovascular Mortality
  - ↑ Non-fatal Cardiovascular Events
  - ↑ Risk of Coronary Heart Disease (esp.. in Men)
  - ↑ Risk Congestive Heart Failure
  - ↑ Blood Pressure
  - ↑ Odds of Developing Arrhythmias
  - ↑ Risk of Sudden Cardiac Death (esp.. at Night)
- Treatment of OSA:
  - ↓ Blood Pressure
  - ↓ Cardiovascular Mortality (except maybe not in “non-sleepy” Adults.
  - ↓ Non-fatal Cardiovascular Events

Other Diseases Made Worse by OSA

- Diabetes
- GERD
- Depression
- COPD (Overlap Syndrome)
- Peripheral Vascular Disease (Carotid intimal thickness)
- Obesity
- Hypothyroidism
- Chronic Pain
- Divorce
- Sick Leave
- Facial Wrinkles
- Bed Partner Sleep
- Motor Vehicle Accidents

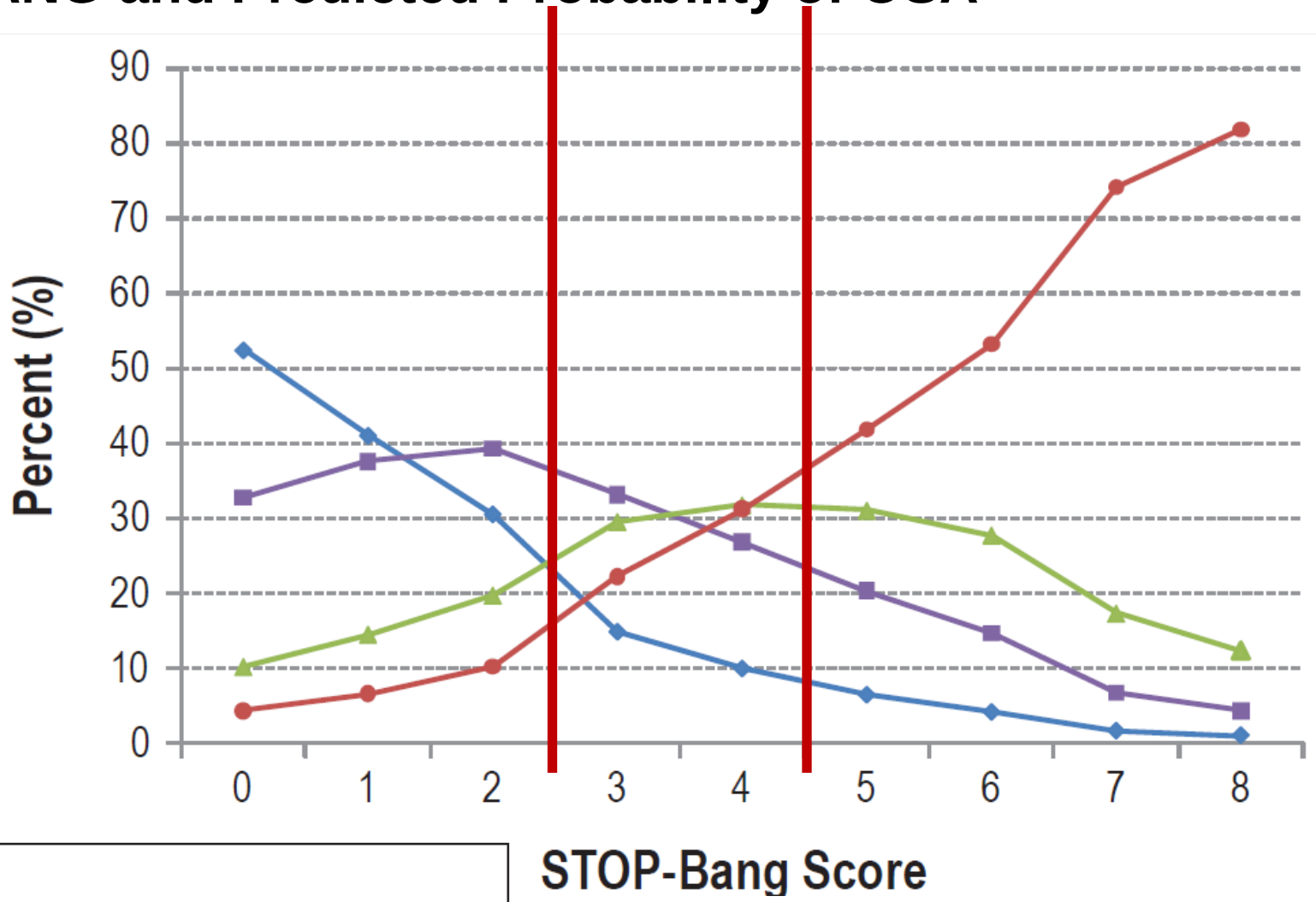
Obstructive Sleep Apnea: Screening

Screening: STOP BANG

- **S**noring
- **T**ired
- **O**bserved (Witnessed) Apneas
- **P**ressure

- **B**MI > 35 kg/m^2
- **A**ge > 50 years old
- **N**eck Circumference:
  - ♀ **> 16 inches (40 cm)**
  - ♂ **> 17 inches (43 cm)**
- **G**ender = Male

STOP BANG and Predicted Probability of OSA

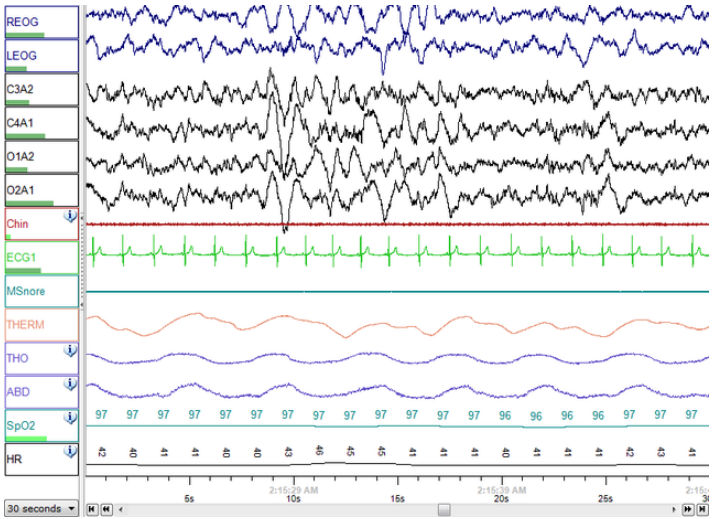


Sleep Med 2011; 7(5):459-465.

Obstructive Sleep Apnea: Testing

Obstructive Sleep Apnea: Testing

Polysomnogram



Home Sleep Testing

Apnea Hypopnea Index (AHI)

$$\frac{\#\text{Apneas} + \#\text{Hypopnea}}{\text{Total Sleep Time (hr)}}$$

Obstructive Sleep Apnea: Testing

Polysomnogram

- Gold Standard
- Evaluates Multiple Sleep Diagnoses
  - Sleep Disordered Breathing
    - OSA vs CSA
  - Movement/Behavior Disorders
  - Seizures
  - Arrhythmias
  - Sleep Time/Stages/Architecture
  - Medications Effects
  - Other Sleep Conditions
- Requires in-lab evaluation

Home Sleep Testing

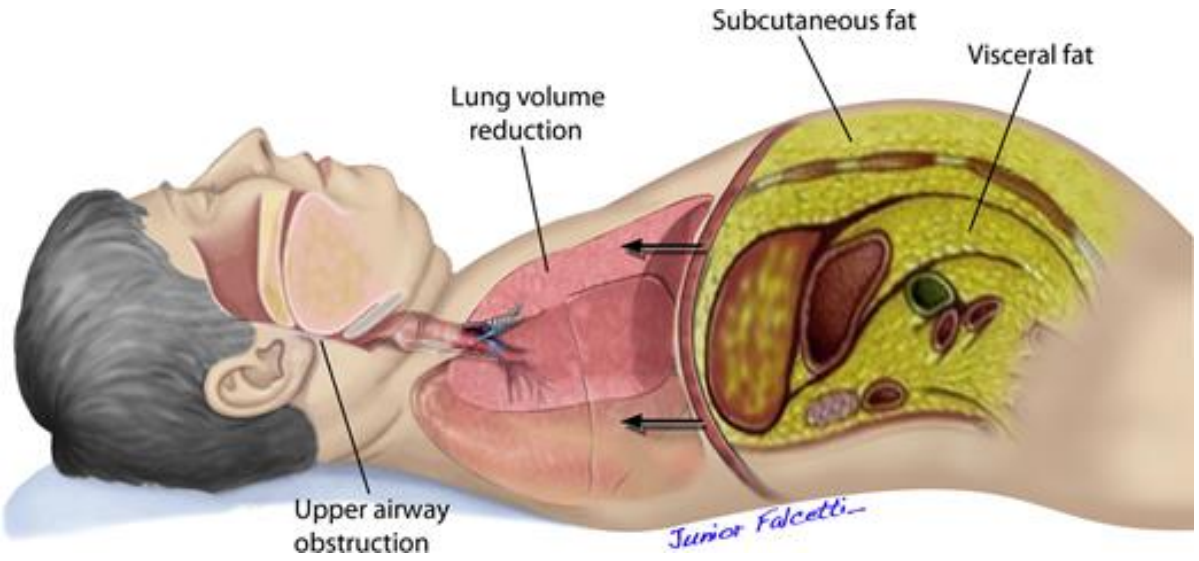
- **GOOD RULE-IN TEST** for OSA
- **BAD RULE-OUT TEST** for OSA
- Must Have HIGH PRE-TEST PROBABILITY
  - STOP BANG ≥ 3
- May Require In-lab PSG if Negative
- In-home Testing (Less expensive)
- Cannot Evaluate Other Sleep Conditions
- No serious comorbid conditions
  - Systolic CHF (EF < 45%)
  - Neuromuscular disease
  - Moderate-to Severe Pulmonary Disease
  - (Super) Morbid Obesity
- No comorbid sleep conditions
  - Central Sleep Apnea
  - Periodic Limb Movement Disorder
  - Insomnia
  - Parasomnias
  - Circadian Rhythm Disorders
  - Narcolepsy
- Must return equipment undamaged
- Must apply equipment correctly
  - Dexterity
  - Mental capacity

Obstructive Sleep Apnea: Treatment

Obstructive Sleep Apnea: Therapies
Behavioral Modification

Behavioral Modifications

- Weight Loss
- Sleep Position
- Alcohol Avoidance
- Concomitant Medications

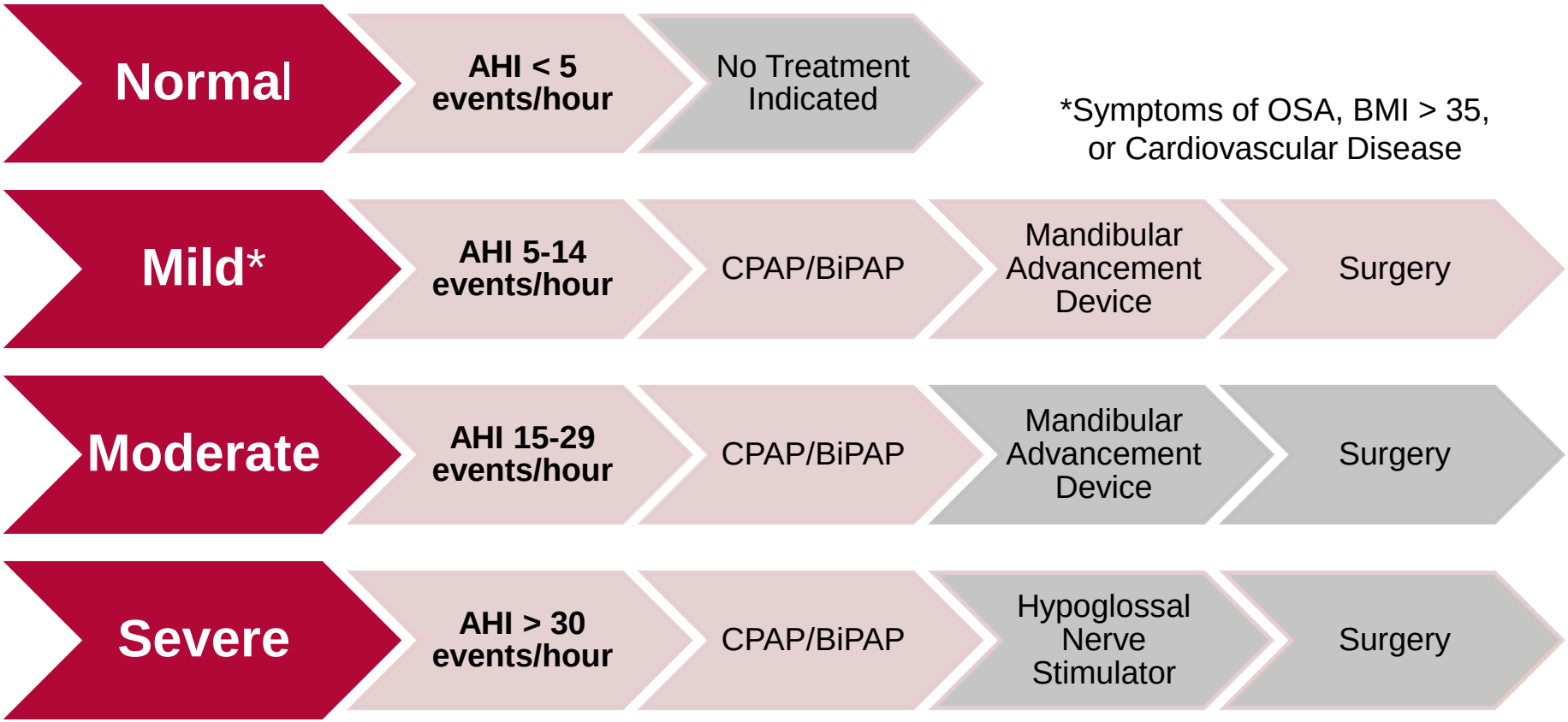


OSA Treatment: Positional Therapy

- Techniques
  - Tennis Ball
  - Alarm Training
  - Position Vests
  - Hospital Bed
  - (Bed partner's elbow)
- 38% compliance at 6 months
- Positional Sleep Apnea = 50% AHI Reduction

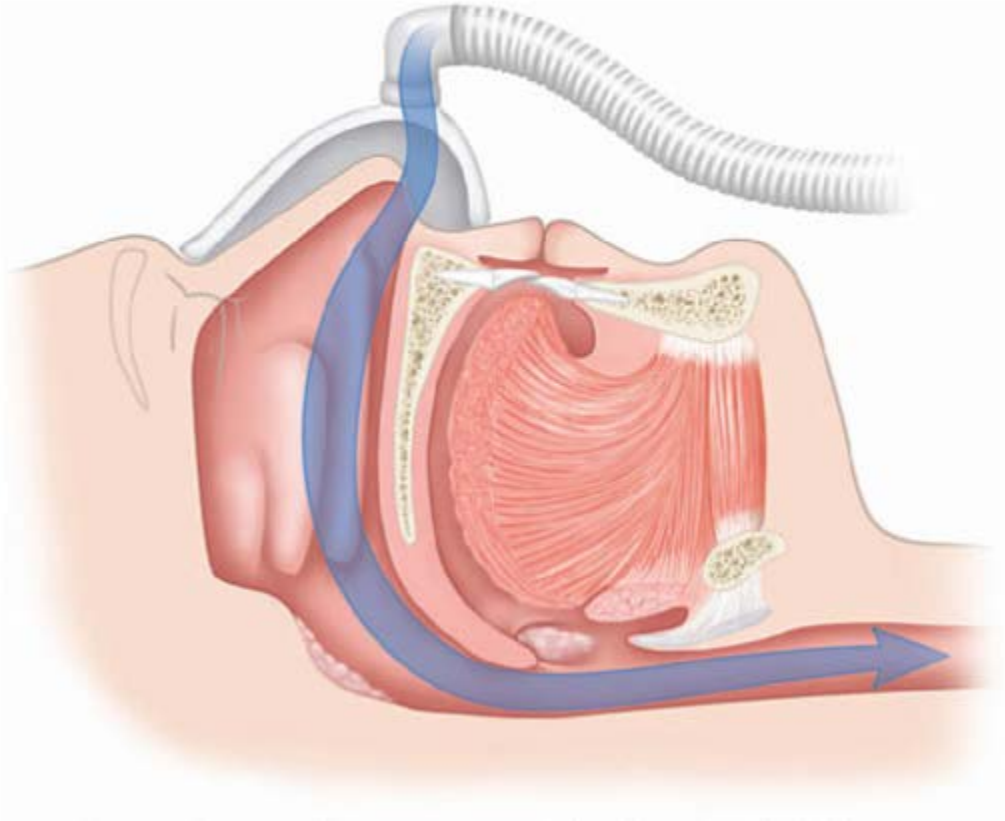
Obstructive Sleep Apnea: Positive Airway Pressure

Obstructive Sleep Apnea: Treatment



*Symptoms of OSA, BMI > 35, or Cardiovascular Disease

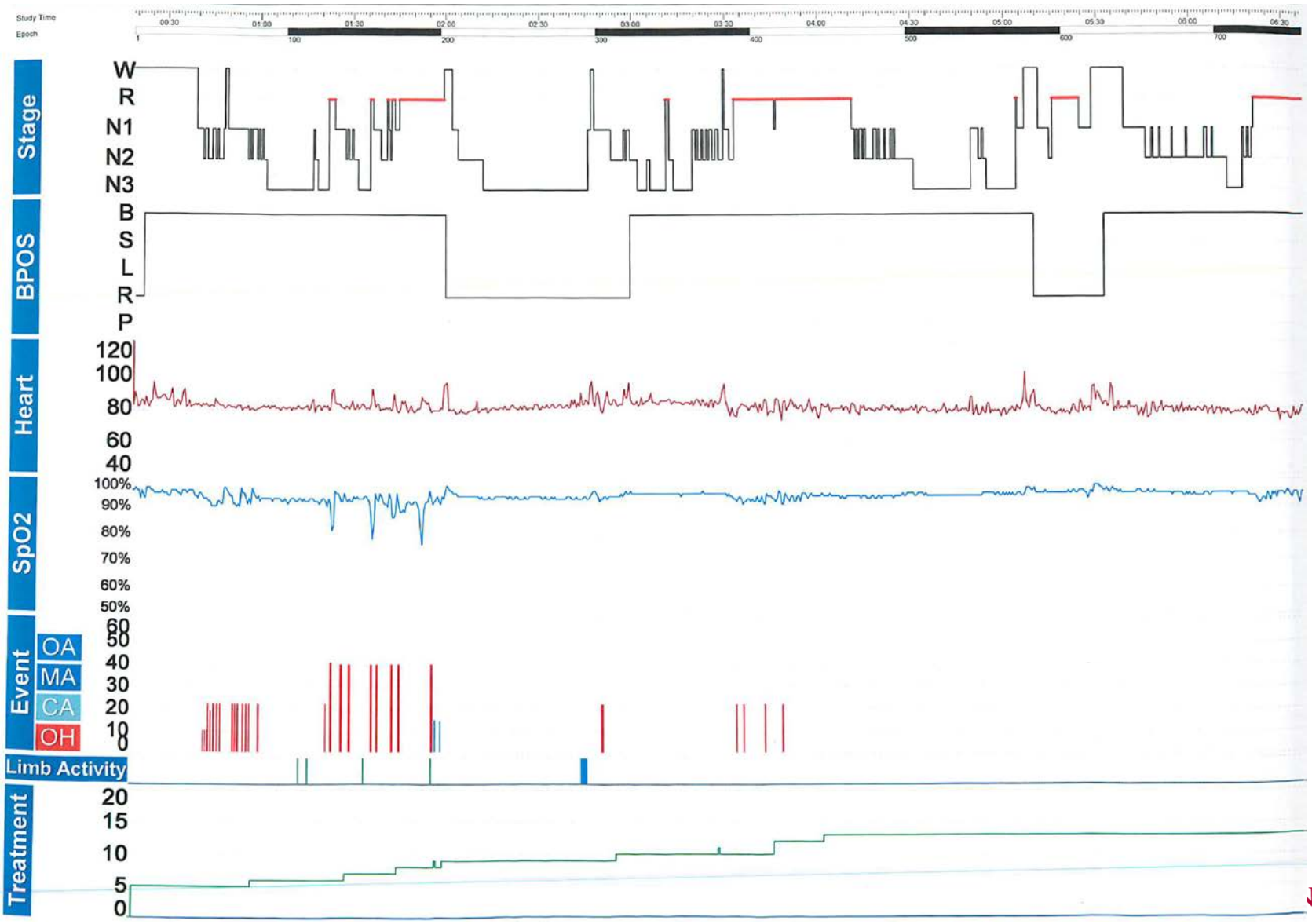
Continuous Positive Airway Pressure (CPAP)



Common CPAP Machines

CPAP Masks

OSA Treatment: CPAP Titration



OSA Treatment: CPAP Compliance Starts Early

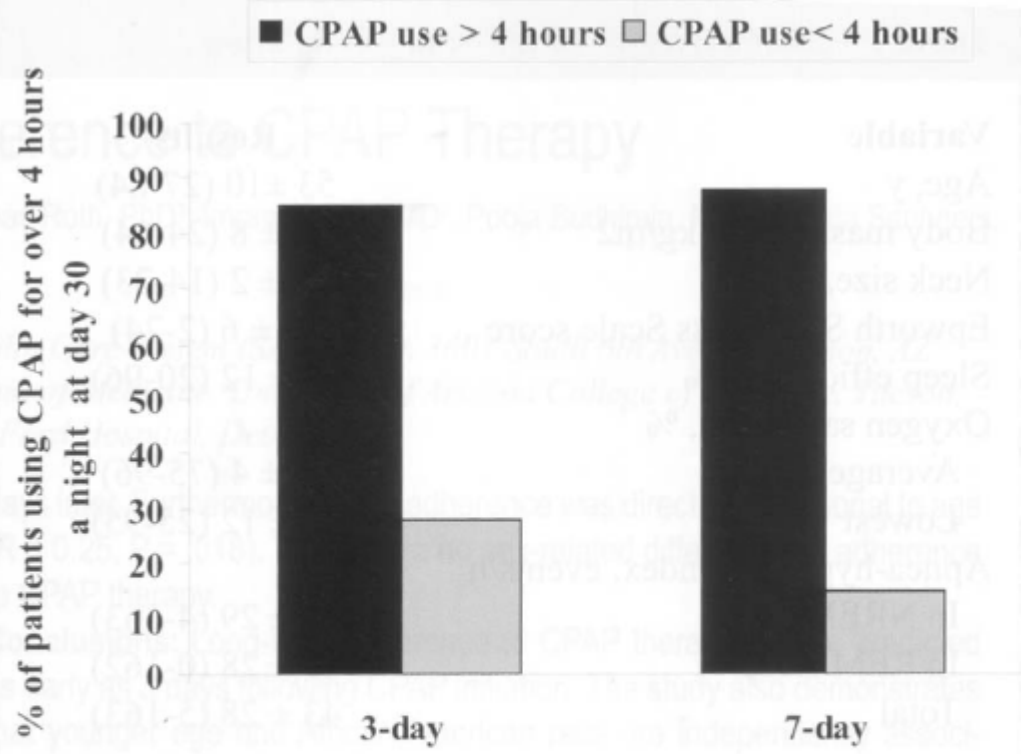


Figure 1—A significantly higher proportion of patients with good adherence to continuous positive airway pressure (CPAP use ≥ 4 night) at day 3 or day 7 were using CPAP for ≥ 4 h/night at day 30 than were patients with poor adherence to CPAP (CPAP use < 4 h/night) at these time points ($p < .001$ for all comparisons).

Sleep. 2007 Mar 1;30(3):320-4.

OSA Treatment: Sleep Medicine Consultation before CPAP

- CPAP Adherence is Significantly Increased with
  - Board-Certified Sleep Physician Consultation
  - Accredited Sleep Lab Use
  - All of the Above

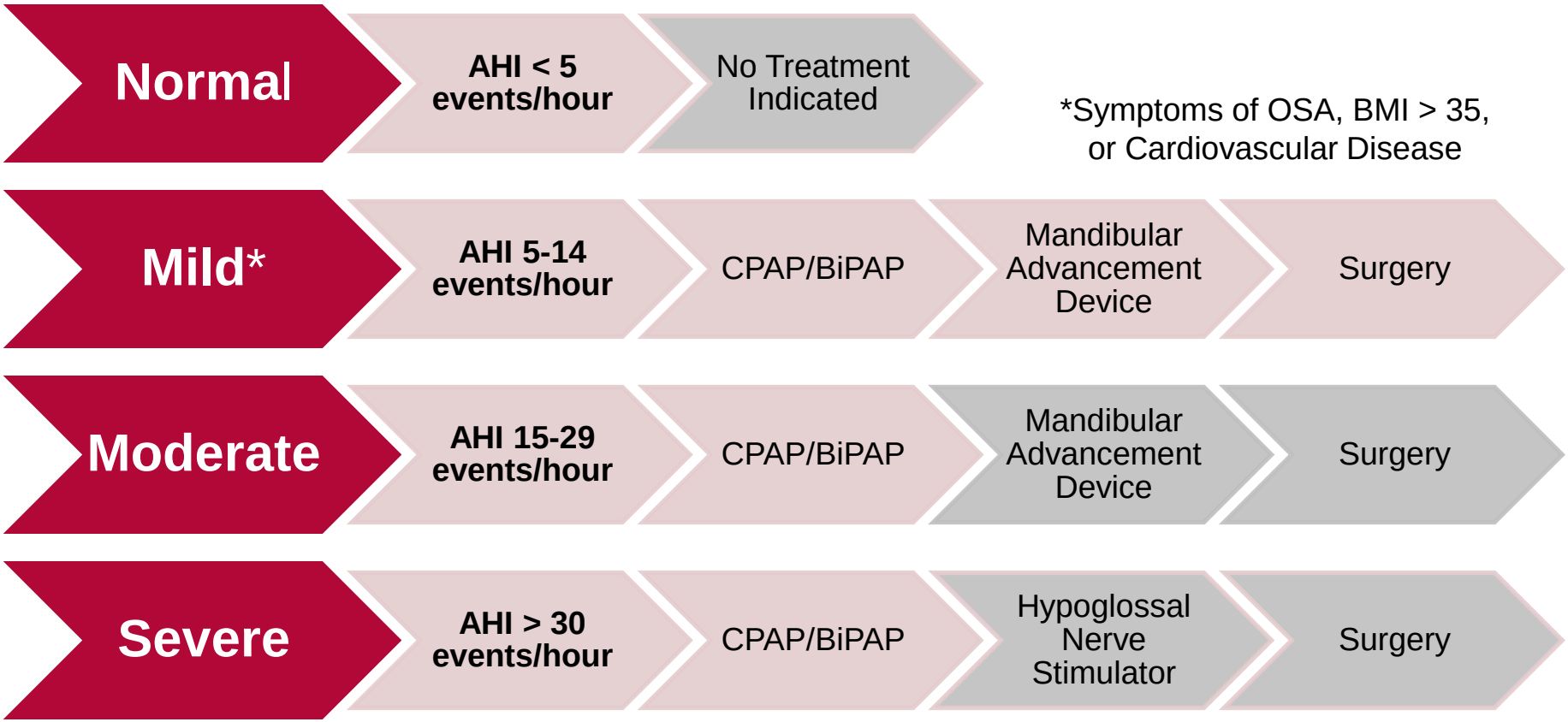
Odd Ratios of Determinants of CPAP Adherence

Variable	p value	Unadjusted odds ratio (95% CI)
Accreditation of center	0.004*	2.1 (1.3-3.5)
Sleep physician certification	0.047*	1.7 (1.0-2.7)
Accreditation-certification	0.001*	1.6 (1.2-2.1)

J Clin Sleep Med. 2014; 10(5):243–249.

Obstructive Sleep Apnea: Alternative Therapies

Obstructive Sleep Apnea: Treatment



*Symptoms of OSA, BMI > 35, or Cardiovascular Disease

OSA Treatment: Oral Appliances

http://orthodonticreviews.blogspot.com/2012/11/obstructive-sleep-apnea-osa-still.html#!/2012/11/obstructive-sleep-apnea-osa-still.html

OSA Treatment: Surgical Procedures

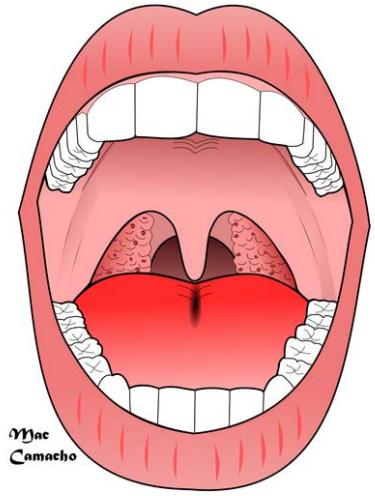
- Uvulopalatopharyngoplasty (UPPP)
- Maxillomandibular Advancement (MMA)
- Tonsillectomy (pediatrics)
- Hypoglossal Nerve Stimulator
- Tracheostomy

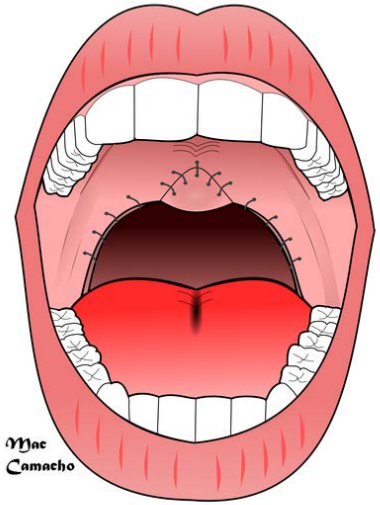
OSA Treatment: Uvulopalatopharyngoplasty (UPPP)

- In severe OSA, only 25% achieve AHI <5
- In severe OSA, only 33% achieve AHI <10
- Minimal study in mild OSA
- Eliminates Snoring
- Needs follow-up HST or PSG

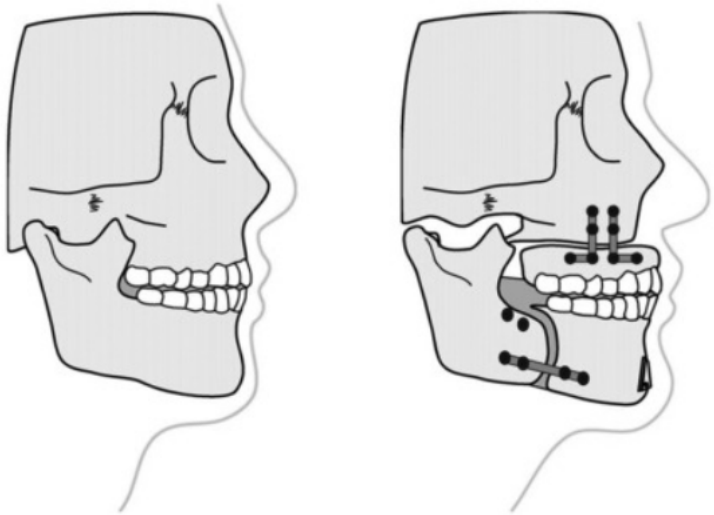
Mayo Clin Proc. 2009;84(9):795.

Sleep. 2010;33(10):1408





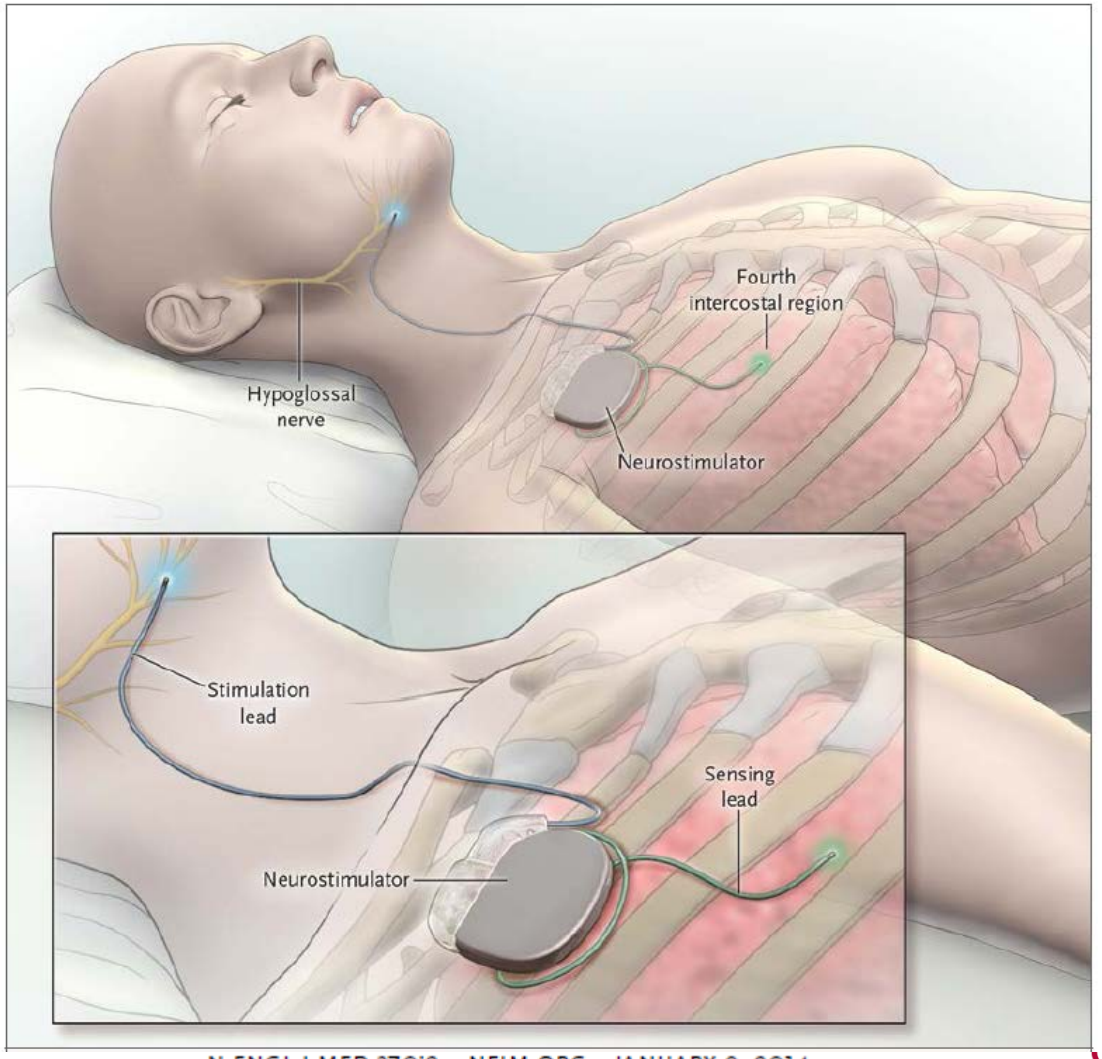
OSA Treatment: Maxillomandibular Advancement (MMA)



- Can be done with Uvulopalatopharyngoplasty (UPPP)
- Overnight hospital stay + temporary diet modification
- Patients like new “strong jaw line”

Berry R. Pearls in Sleep Medicine, 2014 (3rd edition)

OSA Treatment: Hypoglossal Nerve Stimulator



N ENGL J MED 370;2 NEJM.ORG JANUARY 9, 2014

OSA Treatment: Tracheostomy

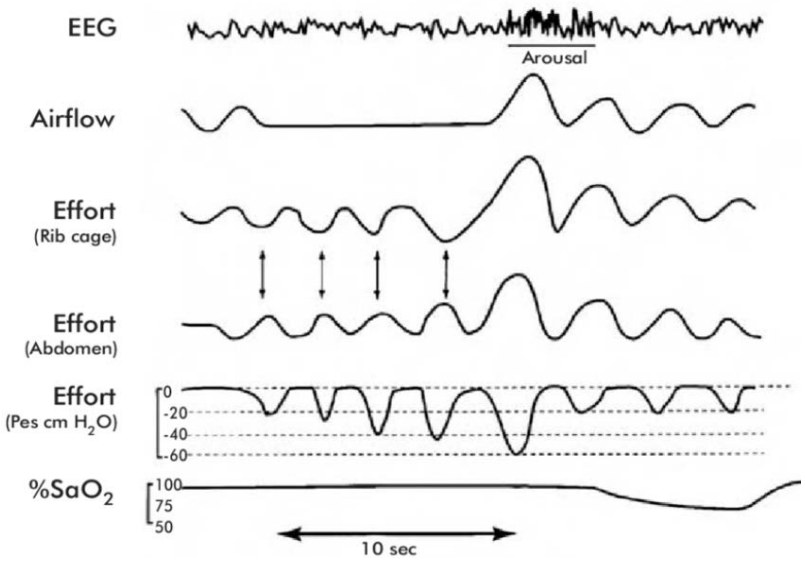
AASM Practice Parameters 2010:

"Tracheostomy has been shown to be an effective single intervention to treat obstructive sleep apnea. This operation should be considered only when other options do not exist, have failed, are refused, or when this operation is deemed necessary by clinical urgency."

Nocturnal Oxygen Is NOT a Treatment for OSA

- Oxygen Alone Does **NOT** control apneas.
- No change in Pulmonary Hypertension
- CAN be used with CPAP in patients with persistent hypoxia despite CPAP

Obstructive Apnea



Phillips, et al CHEST 1990; Gold et. Al. ARRD 1986

Take Home Messages

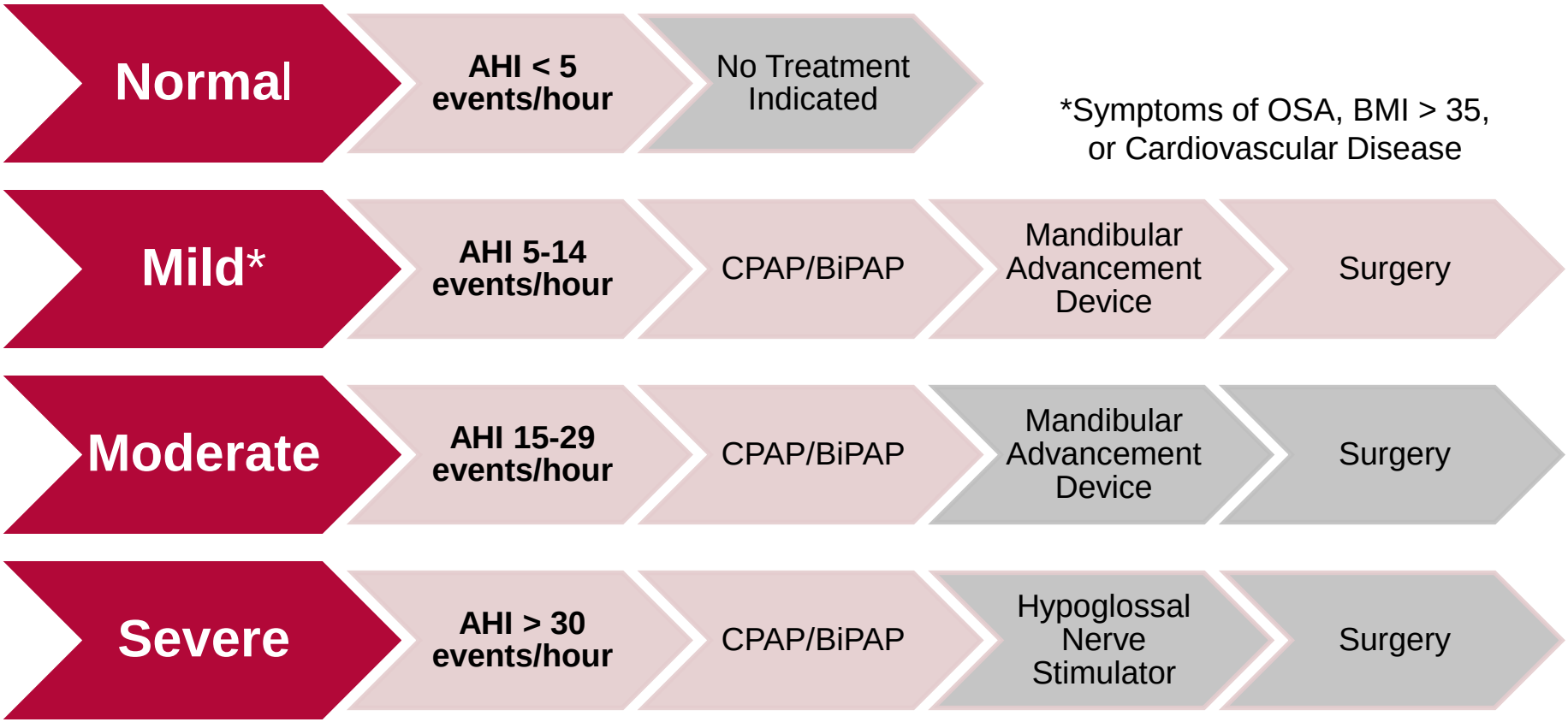
OSA & Cardiovascular Disease: A Review

- OSA is Prevalent in Many Patients with Cardiovascular Disease
- Untreated OSA:
  - ↑ All-Cause Mortality
  - ↑ Cardiovascular Mortality
  - ↑ Non-fatal Cardiovascular Events
  - ↑ Risk of Coronary Heart Disease (esp. in Men)
  - ↑ Risk Congestive Heart Failure
  - ↑ Blood Pressure
  - ↑ Odds of Developing Arrhythmias
  - ↑ Risk of Sudden Cardiac Death (esp. at Night)
- Treatment of OSA:
  - ↓ Blood Pressure
  - ↓ Cardiovascular Mortality (except maybe not in “non-sleepy” Adults.
  - ↓ Non-fatal Cardiovascular Events

Obstructive Sleep Apnea

- Diagnosis
  - STOP-BANG
  - Home Sleep Testing vs Polysomnogram
- Treatment
  - Behavioral Modifications
  - CPAP
  - Alternative Therapies
    - Mandibular Advancement Device
    - Surgery
    - Hypoglossal Nerve Stimulator

Obstructive Sleep Apnea: Treatment



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Review Questions

A 65 year-old male presents with snoring, witnessed apneas, and daytime hypersomnolence. He has hypertension treated with Lisinopril and a history of claustrophobia. He has a neck circumference of 18 inches and his BMI is 38 kg/m^2. He returns after home sleep study, which revealed an AHI of 4.4 events per hour. Which of the following should be done NEXT:

A. Recommend weight loss and follow up 6 months.
B. Referral to Dentist for mandibular advancement device (MAD) to control snoring as this can also treat OSA.
C. Repeat HST as patient is high risk for OSA.
D. Order in-lab polysomnogram as patient is high risk for OSA.
E. Order an adjustable (hospital) bed to avoid supine sleep.

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This afternoon you are seeing 10 patients in clinic. Each as a diagnosis of hypertension. You understand that untreated OSA increases their risk of cardiovascular events and that treatment of OSA can lower their blood pressure. How many patients do you expect to have hypertension and OSA in your clinic this afternoon?

A. 1 out of 10 hypertensive patients will likely have OSA.
B. 3 out of 10 hypertensive patients will likely have OSA.
C. 5 out of 10 hypertensive patients will likely have OSA.
D. 7 out of 10 hypertensive patients will likely have OSA.
E. 9 out of 10 hypertensive patients will likely have OSA.

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