# **Obstructive Sleep Apnea and Cardiovascular Disease**

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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 2<sup>nd</sup> Edition, 2005

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#### 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

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### **Obstructive Sleep Apnea: Anatomy**



### **Obstructive Sleep Apnea**

**Obstructive Apnea** 

**Obstructive Hypopnea** 



**Obstructive Sleep Apnea: Apnea Hypopnea Index** 

## Apnea Hypopnea Index (AHI)

<u>#Apneas + #Hypopneas</u> Total Sleep Time (hr)

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## **Obstructive Sleep Apnea: Treatment**



## **Obstructive Sleep Apnea: Prevalence**

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### 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

Weight and OSA by Sex



■Women ■Men

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

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# Obstructive Sleep Apnea & Cardiovascular Disease

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# OSA and Cardiovascular Disease



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



## 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).



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



## **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





Months

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



N = 1949

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Lancet 2005:365:1046-53

18

1812

1828



N Engl J Med 2005; 353:2034-2041

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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



CHD-free Survival by AHI category - Men CHD-free Survival by AHI category - Women 1.00 100 0.95 0.95 Disease-free Survival Disease-free Survival 0.90 0.90 0.85 0.85 0.80 0.80 0.75 0.75 **AHI Categories** AHI Categories 5-15 > 30 > 30 0.70 0.70 0 n Follow-up (years) Follow-up (years) CHF-free Survival by AHI category - Men CHF-free Survival by AHI category - Women 1.00 0.95 0.95 Disease-free Survival **Disease-free Survival** 0.90 0.90 0.85 0.85 0.80 0.80 0.75 0.75 **AHI Categories AHI Categories** 5—15 - 15 > 30 > 30 0.70 0.70 ٥ 0 2 Follow-up (years) Follow-up (years) American Gottlieb D J et al. Circulation. 2010;122:352-360 = 4422Heart ssociation

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

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



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

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### **Normal BP and Heart Rate Response**



Normal 24 Hour BP and Heart Rate Response

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### **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).



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THORAX

# **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

#### 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



Time of Day (Hrs)



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
  - A 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**

D

Study name	s	tatistics fo	r each stud	у			Difference in	eans and 9	5% CI		
	Difference in means	Lower limit	Upper limit	p-Value							Relative weight
Arias MA et al. 2005	0.000	-4 1/18	4 148	1 000	1		ı —		1	1	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					- 1		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			I		<u> </u>		3,86
Comondore VR et al. 2009	3,600	-9,758	16,958	0,597					_	<b>→</b>	0,6
Coughlin SR et al. 2007	6,700	3,425	9,975	0,000						-	6,2
Cross MD et al. 2008	3,800	-2,941	10,541	0,269			I —		_	- 1	2,2
Drager LF et al. 2007	1,000	-6,246	8,246	0,787			H				2,0
Drager LF et al. 2011	9,000	4,042	13,958	0,000						<b>→</b>	3,7
Durán-Cantolla J et al. 2010	2,100	0,456	3,744	0,012							10,3
Egea CJ et al. 2008	1,600	-8,444	11,644	0,755					_		1,1
Engleman HM et al. 1996	1,000	-4,876	6,876	0,739					-		2,8
Faccenda JF et al. 2001	1,300	-0,664	3,264	0,194							9,4
Hui DS et al. 2006	0,400	-9,568	10,368	0,937					_	- 1	1,1
lp MSM et al. 2004	-0,300	-9,597	8,997	0,950			-		<u> </u>		1,3
Lam B et al. 2007	6,100	-2,346	14,546	0,157			· -		-		1,5
Lozano L et al. 2010	3,000	-3,418	9,418	0,360					_	•	2,4
Mansfield DR et al. 2004	-9,600	-22,427	3,227	0,142	←	-					0,7
Mills PJ et al. 2006	8,000	-3,191	19,191	0,161			I —				0,9
Monasterio C et al. 2001	2,000	-4,471	8,471	0,545					<u> </u>		2,4
Nguyen PK et al. 2010	-1,600	-13,399	10,199	0,790	+					- 1	0,8
Noda A et al. 2007	12,500	0,486	24,514	0,041					<u> </u>		0,8
Pepperel JC et al. 2002	3,400	0,580	6,220	0,018							7,2
Robinson GV et al. 2006	-0,100	-5,097	4,897	0,969					-		3,6
Ruttanaumpawan P et al. 2008	14,000	3,223	24,777	0,011							1,0
Takaesu et al. 2011	8,100	1,775	14,425	0,012							2,5
		1,437	3,681	0,000		4:-			00.8	12.00	
Iastolic Bio	oa Pre	255	ure	Re	auc	τio	ก		0,00	12,00	
Study name	Stat	istics for e	ach study			nass	Ve treatment Difference in m	ans and 95	% CI		
Study name	S <u>tati</u> Difference in means	istics for e Lower limit	ach study Upper limit	p-Value		nassi	ve treatment Difference in m	ans and 95	<u>cPΔP</u> % Cl		Relativ
Study name	S <u>tati</u> Difference in means	Lower limit	upper limit	p-Value	I	nassi	ve treatment Difference in m	ans and 95	<u>« C</u> I	1	Relativ weigh
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passive treatment

cPAP



### 30 RCTs N =1900 Patients

Chest. 2014;145(4):762.

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### **OSA and Fatal and Non-Fatal Cardiovascular Events**



Months

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

THE	LANCET

N = 1949

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Lancet 2005:365:1046-53

32

### Incidence of Death From Cardiovascular Events in "<u>Non-Sleepy</u>" 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**

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# **Screening: STOP BANG**

- **S**noring
- Tired
- Observed (Witnessed) Apneas
- Pressure
- **B**MI > 35 kg/m<sup>2</sup>
- Age > 50 years old
- Neck Circumference:
  - ♀ > 16 inches (40 cm)
  - ♂ > 17 inches (43 cm)
- Gender = Male

## STOP BANG and Predicted Probability of OSA



# **Obstructive Sleep Apnea: Testing**

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## **Obstructive Sleep Apnea: Testing**

## Polysomnogram





## Home Sleep Testing



## Apnea Hypopnea Index (AHI)

<u>#Apneas + #Hypopnea</u> Total Sleep Time (hr)

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# **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

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# **Obstructive Sleep Apnea: Treatment**

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# **Obstructive Sleep Apnea: Therapies Behavioral Modification**

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# **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







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# **Obstructive Sleep Apnea: Positive Airway Pressure**

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# **Obstructive Sleep Apnea: Treatment**



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# **Continuous Positive Airway Pressure (CPAP)**



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# **Common CPAP Machines**





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# **CPAP Masks**













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# **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  $\geq$  4 night) at day 3 or day 7 were using CPAP for  $\geq$  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.

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# **Obstructive Sleep Apnea: Alternative Therapies**

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# **Obstructive Sleep Apnea: Treatment**



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# **OSA Treatment: Oral Appliances**





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

# **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.

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# **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. <u>Pearls in Sleep Medicine</u>, 2014 (3<sup>rd</sup> edition)

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# **OSA Treatment: Hypoglossal Nerve Stimulator**





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

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## **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."





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- Oxygen Alone Does <u>NOT</u> 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

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# **Take Home Messages**

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# **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

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# **Obstructive Sleep Apnea: Treatment**



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# **Review Questions**

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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<sup>2</sup>. 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.

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<sup>2</sup>. He returns after home sleep study, which revealed an AHI of 4.4 events per hour. Which of the following should be done NEXT:

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- 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.

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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