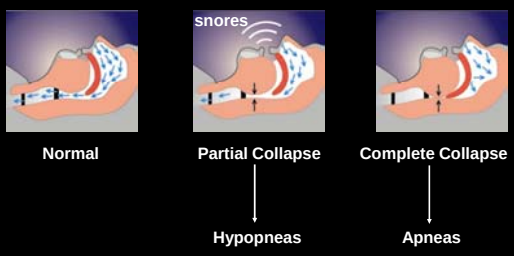
Sleep Apnea and Its Impact on Cardiovascular Disease Risk

Naresh M. Punjabi, MD, PhD
Johns Hopkins University, School of Medicine
Departments of Medicine and Epidemiology
Baltimore, Maryland (USA)

Definition of the Disorder

- Terminology:
  - Obstructive sleep apnea (OSA)
  - Sleep apnea (SA)
  - Sleep-disordered breathing (SDB)
  - Sleep apnea-hypopnea syndrome (SAS)

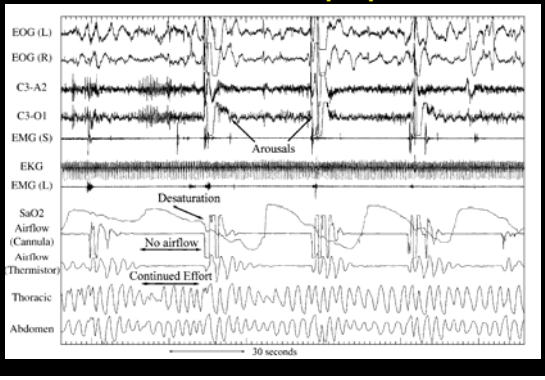
Pathophysiology of Sleep Apnea



Standard Diagnostic Test: Polysomnography

- Electro-oculogram (EOG)
- Electroencephalogram (EEG)
- Electromyogram (EMG)
- Electrocardiogram (ECG)
- Airflow (nasal and oral)
- Oxyhemoglobin Saturation (SaO_2)
- Chest and Abdominal Wall Effort
- Body Position
- (IN-LAB or IN-HOME)

Obstructive Sleep Apnea



Definition of the Disorder

Disease Defining Metric:

- Apnea-Hypopnea Index (AHI)
  - = Number of apneas and hypopneas per hour of sleep
- Respiratory Disturbance Index (RDI)
- "Normal": AHI or RDI < 5 events / hour

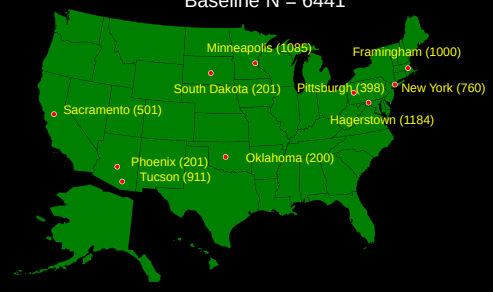
The Sleep Heart Health Study

- Design:
  - Prospective cohort study
  - Multi-center
  - Assessment of sleep on to ongoing cohort studies of cardiovascular and respiratory disease
  - Wide geographic and ethnic representation of middle-aged and older US adults

Quan et al: The Sleep Heart Health Study: Design, Methods, Rationale
Sleep 1997; 20(12) 1077-1085

The SHHS: Field Sites

Baseline N = 6441



National Heart Lung and Blood Institute (NHLBI). The Sleep Heart Health Study: Manuals of Operation. http://www.jhucct.com/shhs/manual/demographics/01jul02received/shhs1demo1jul02.pdf. Accessed July 18, 2007.

Cohort Eligibility

- Age ≥ 40 years
- Exclusion criteria:
  - Treatment with CPAP
  - Supplemental oxygen use
  - Tracheostomy
- Recruitment of men = women
- Minority/ethnic groups targeted

Quan et al: The Sleep Heart Health Study: Design, Methods, Rationale
Sleep 1997; 20(12) 1077-1085

System for Home Polysomnography

- P-series system Compumedics
- Recorded montage
  - EEG (C_3-A_2, C_4-A_1), EOG, chin EMG, EKG
  - Oximetry, thermocouple, respiratory inductive plethysmography
  - Body position and light sensors

Redline et al: Methods for Obtaining and Analyzing Unattended Polysomnography Data for a Multicenter Study
Sleep 1998; 21(7) 759-767 ;

Outcome and Covariate Data

- Prevalent disease
  - Cardiovascular disease, myocardial infarction, stroke, angina, PTCA, congestive heart failure, hypertension, diabetes, asthma and COPD
- Demographic
  - Age, race, education, marital status, occupation, etc.
- Health Habits
  - Smoking, alcohol use, caffeine, etc.

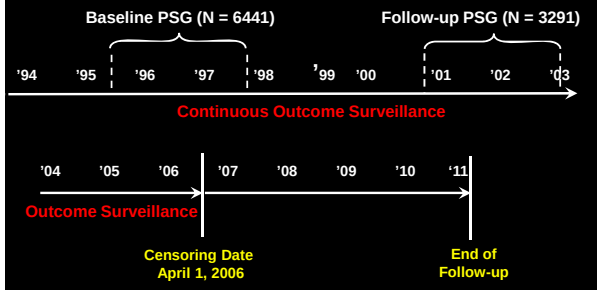
Quan et al: The Sleep Heart Health Study: Design, Methods, Rationale
Sleep 1997; 20(12) 1077-1085

Outcome and Covariate Data

- Anthropometrics (BMI, waist girth, hip circumferences)
- Medication use (prescription and non-prescription)
- Electrocardiogram
- Subset of the cohort
  - Echocardiogram
  - Holter data
  - Head MRI scans
  - Physical activity
  - Serum (fasting, non-fasting, post glucose challenge)
  - Spirometry

Quan et al: The Sleep Heart Health Study: Design, Methods, Rationale
Sleep 1997; 20(12) 1077-1085

SHHS: Longitudinal Design



Sleep apnea and Incident Hypertension

Prospective Study of Sleep-disordered Breathing and Hypertension

The Sleep Heart Health Study

George T. O'Connor[1], Brian Caffo[2], Anne B. Newman[3], Stuart F. Quan[4,5], David M. Rapoport[6], Susan Redline[7], Helaine E. Resnick[8], Jonathan Samet[2], and Eyal Shahar[9]

[1]Pulmonary Center, Boston University School of Medicine, Boston, Massachusetts; [2]Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland; [3]University of Pittsburgh, Pittsburgh, Pennsylvania; [4]Arizona Respiratory Center, University of Arizona, Tucson, Arizona; [5]Division of Sleep Medicine, Harvard Medical School, Boston, Massachusetts; [6]Department of Medicine, New York University School of Medicine, New York, New York; [7]Department of Medicine, Case Western Reserve University, Cleveland, Ohio; [8]American Association of Homes and Services for the Aging, Washington, D.C.; and [9]Division of Epidemiology and Biostatistics, Mel and Enid Zuckerman College of Public Health, University of Arizona, Tucson, Arizona

O'Connor et al. Am J Respir Crit Care Med Vol 179. pp 1159–1164, 2009

Sleep apnea and Incident Hypertension

TABLE 4. ADJUSTED ODDS RATIOS FOR INCIDENT HYPERTENSION AMONG SLEEP HEART HEALTH STUDY SUBJECTS WHO WERE NORMOTENSIVE AT BASELINE, ACCORDING TO BASELINE APNEA-HYPOPNEA INDEX, STRATIFIED BY BODY MASS INDEX

	BMI ≤27.3		BMI >27.3	
Baseline AHI	n	OR (95% CI)	n	OR (95% CI)
0–4.9	887	—	541	—
5–14.9	213	0.89 (0.59–1.34)	378	0.92 (0.67–1.27)
15–29.9	58	0.93 (0.46–1.90)	164	1.13 (0.76–1.68)
≥30	21	2.71 (1.24–5.93)	65	1.18 (0.64–2.19)

O'Connor et al. Am J Respir Crit Care Med Vol 179. pp 1159–1164, 2009

Epidemiology and Prevention

Prospective Study of Obstructive Sleep Apnea and Incident Coronary Heart Disease and Heart Failure

The Sleep Heart Health Study

Daniel J. Gottlieb, MD, MPH; Gayane Yenokyan, MD, PhD; Anne B. Newman, MD, MPH; George T. O'Connor, MD, MSc; Naresh M. Punjabi, MD, PhD; Stuart F. Quan, MD; Susan Redline, MD, MPH; Helaine E. Resnick, PhD, MPH; Elisa K. Tong, MD, MA; Marie Diener-West, PhD; Eyal Shahar, MD, MPH

Gottlieb et al. Circulation 2010; 122: 325-360

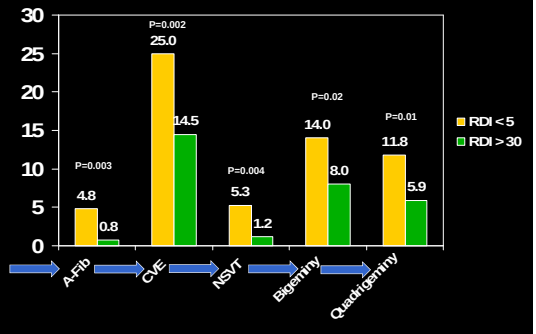
Sleep Apnea: Incident CVD

Men: Age < 70 years

Outcome	Predictor Variable	Hazard Ratio	95 % CI
Incident CVD	AHI < 5 vs. AHI ≥ 30	1.68	1.02 – 2.76
	AHI continuous (per 10 unit increase)	1.10	1.00 – 1.21

Gottlieb et al. Circulation 2010; 122: 325-360

Sleep Apnea and Arrhythmias: SHHS



Mehra et al. *AJRCCM*. 2006; 170: 910-916

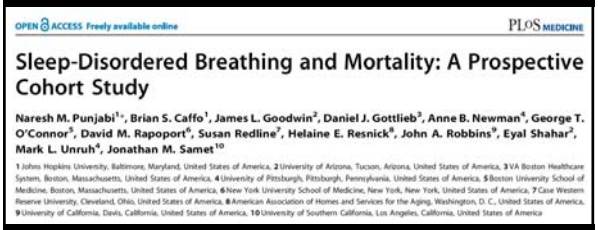
Sleep Apnea and Stroke in Men

Covariate	Unadjusted	Age-Adjusted	Fully-Adjusted*
Quartile of OAHI			
IV: 19.13 – 164.5	3.91 (1.55 – 9.86)	3.05 (1.21 – 7.72)	2.86 (1.10 – 7.39)
III: 9.50 – 19.12	2.35 (0.89 – 6.20)	1.97 (0.74 – 5.21)	1.86 (0.70 – 4.95)
II: 4.05 – 9.49	1.96 (0.71 – 5.40)	1.86 (0.68 – 5.13)	1.86 (0.67 – 5.12)
I: 0.00 – 4.04)	1.00	1.00	1.00

*Adjusted for age, BMI, smoking status, SBP, blood pressure medications, diabetes, and race

Redline et al. Am J Respir Crit Care Med Vol 182. pp 269–277, 2010

Sleep Apnea and All-Cause Mortality



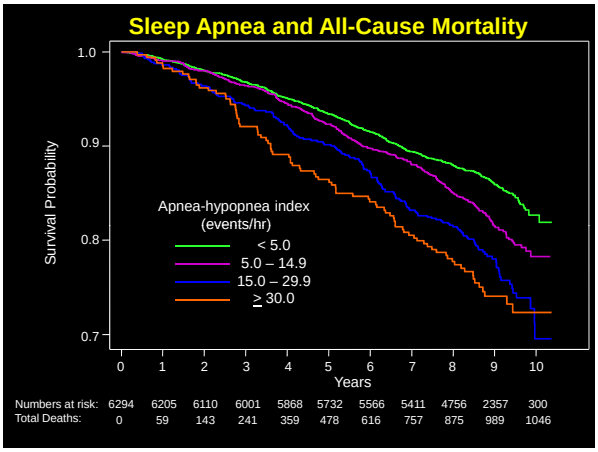
OPEN ACCESS Freely available online PLoS MEDICINE

Sleep-Disordered Breathing and Mortality: A Prospective Cohort Study

Naresh M. Punjabi[1*], Brian S. Caffo[1], James L. Goodwin[2], Daniel J. Gottlieb[3], Anne B. Newman[4], George T. O'Connor[5], David M. Rapoport[6], Susan Redline[7], Helaine E. Resnick[8], John A. Robbins[9], Eyal Shahar[3], Mark L. Unruh[4], Jonathan M. Samet[10]

1 Johns Hopkins University, Baltimore, Maryland, United States of America, 2 University of Arizona, Tucson, Arizona, United States of America, 3 VA Boston Healthcare System, Boston, Massachusetts, United States of America, 4 University of Pittsburgh, Pittsburgh, Pennsylvania, United States of America, 5 Boston University School of Medicine, Boston, Massachusetts, United States of America, 6 New York University School of Medicine, New York, New York, United States of America, 7 Case Western Reserve University, Cleveland, Ohio, United States of America, 8 American Association of Homes and Services for the Aging, Washington, D. C., United States of America, 9 University of California, Davis, California, United States of America, 10 University of Southern California, Los Angeles, California, United States of America

Sleep Apnea and All-Cause Mortality



Sleep Apnea and All-Cause Mortality

AHI (events/hr)	N	Person years	Deaths	Mortality Rate	Adjusted Odds Ratios (95% CI)
Men ≤ 70 years					
< 5.0	985	8,220	91	11.1	1.00
5.0 – 14.9	694	5,697	82	14.4	1.24 (0.90 – 1.71)
15.0 – 29.9	322	2,623	47	17.9	1.45 (0.98 – 2.14)
> 30.0	168	1,355	28	20.7	2.09 (1.31 – 3.33)
Men > 70 years					
< 5.0	277	2,055	125	60.8	1.00
5.0 – 14.9	282	2,176	111	51.0	0.92 (0.70 – 1.20)
15.0 – 29.9	140	1,029	67	65.1	1.23 (0.90 – 1.68)
> 30.0	74	517	36	69.6	1.27 (0.86 – 1.86)

Normal Sleep = Cardiovascular Health