Sleep Apnea in Older Adults

Barbara Phillips, MD, MSPH, FCCP

October 5, 2015

Disclosures

Current Funding: none

Leadership position

- American College of Chest Physicians, President-elect
- National Board of Respiratory Care

Expert Witness

- Kinnard, Clayton, Beveridge LLC (perioperative death from OSA)
- Kinkead Stiltz, PLLC (noisy bar below condominium)

Honorarium

- CHEST Review, CCM International

Conflicts of Interest: I personally am not getting any younger.

Overview

Significance

State-of-the-art knowledge

Knowledge gaps

Research opportunities

SDB with Aging (Young T, 2002)

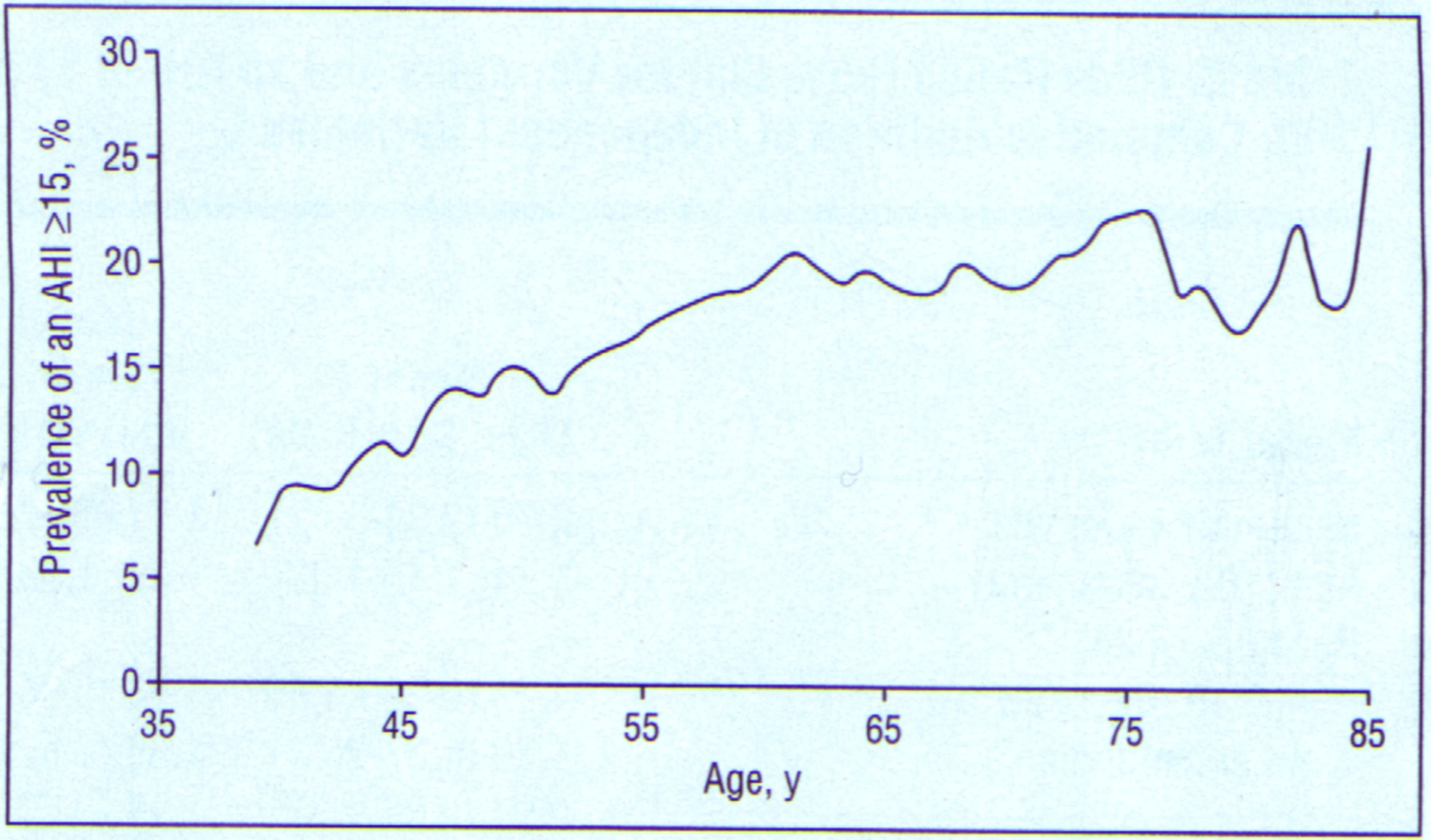
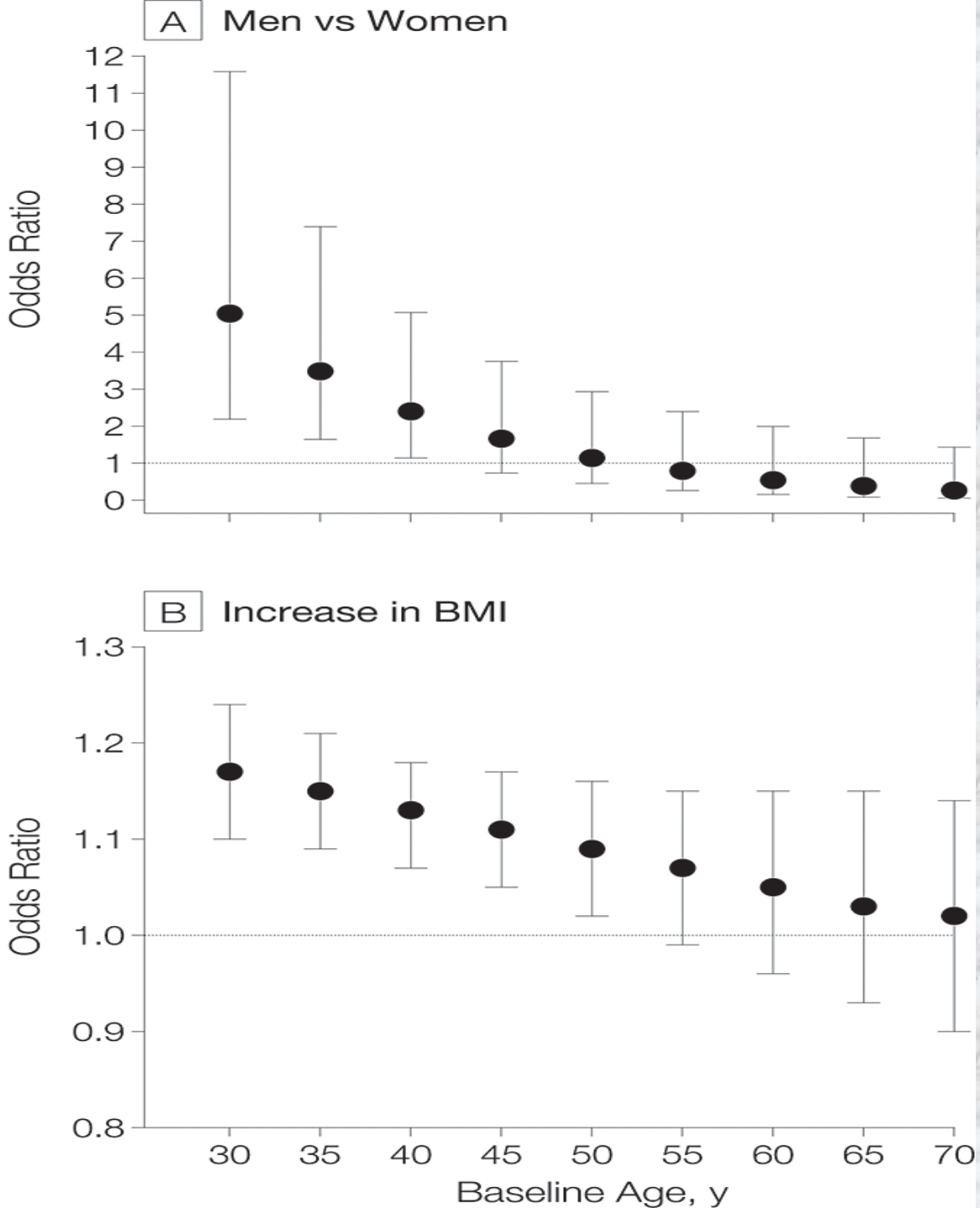


Figure 1. Smoothed plot (5-year moving average) of the prevalence of an apnea-hypopnea index (AHI) of 15 or greater by age.



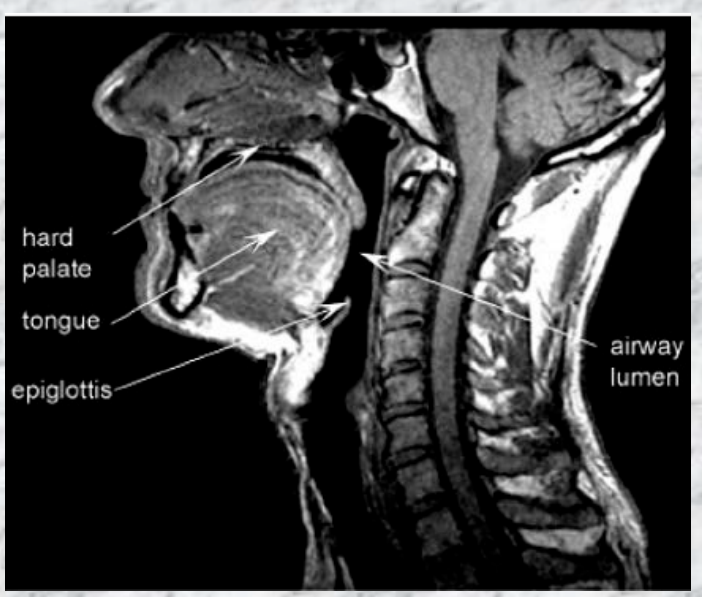
- The effects of gender and BMI change with aging.
- AFTER THE AGE OF 50, *GENDER* BECOMES LESS IMPORTANT
- AFTER THE AGE OF 60, *BMI* BECOMES LESS IMPORTANT
- Weight is a more important risk factor for men than for women
- Age is a more important risk factor for women than for men.
- (Tishler P, 2003)

Potential Factors for Increased OSA Risk in Older People

- Increased body weight
- Reduced pulmonary function
- Impaired ventilatory control
- Increased upper airway collapsibility
- Reduced muscular endurance
- Impaired thyroid function
- Increased sleep fragmentation
- Reduced slow wave sleep

Changes in airway anatomy with age - MRI findings

- Soft palate gets longer
- Pharyngeal fat pads increase in size
- Shape of bony structures around pharyngeal airway change
- Response of genioglosus muscle to negative pressure stimulation diminishes



Midsagittal magnetic resonance image illustrating anatomic structures of interest

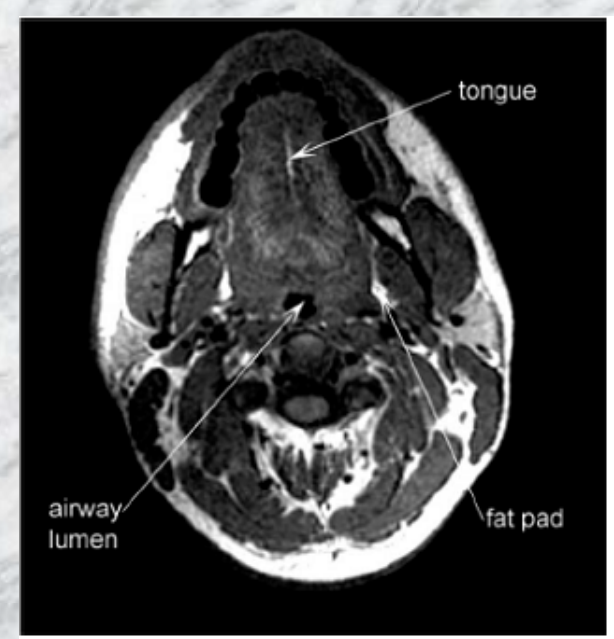
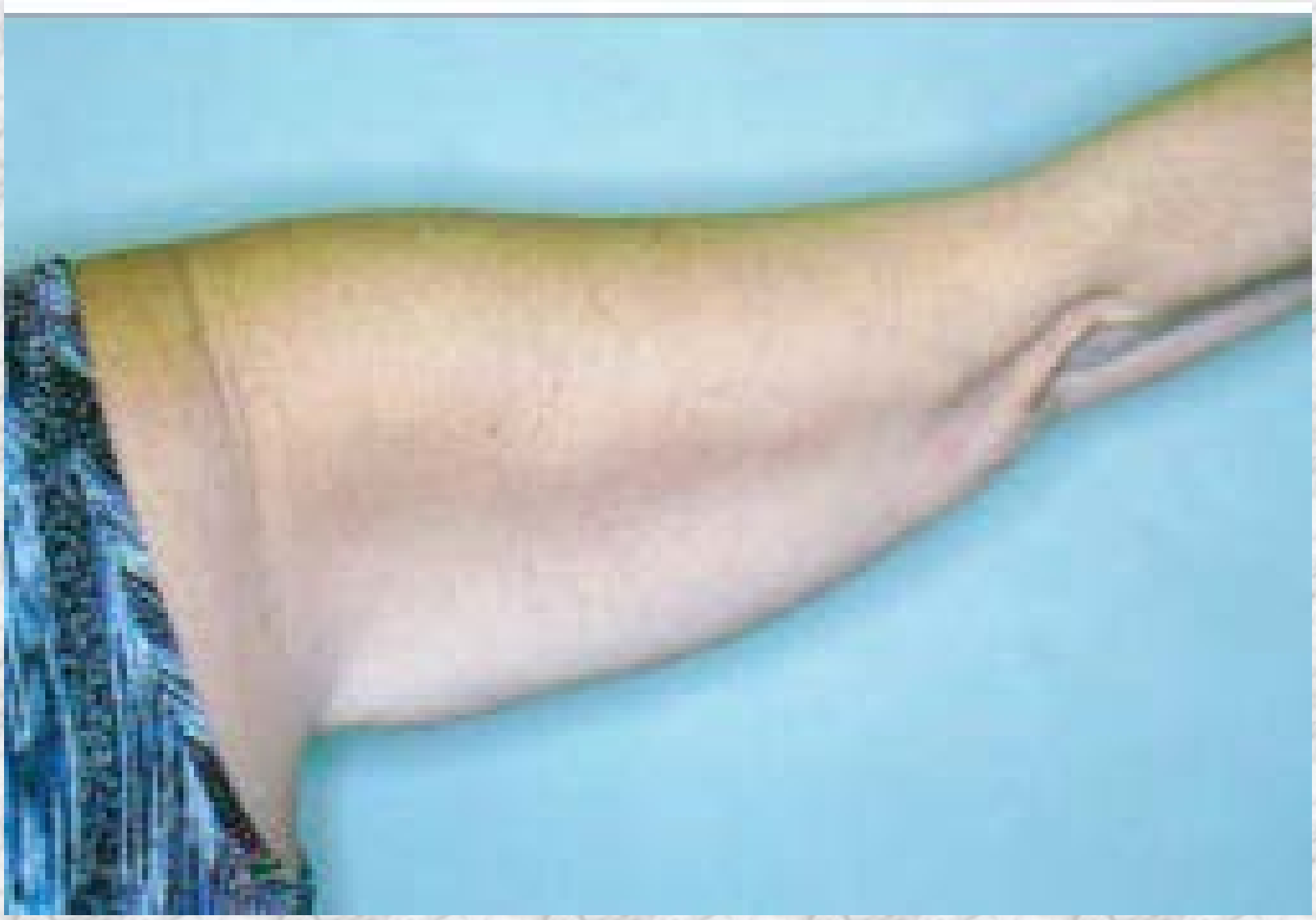


Figure 2 Axial magnetic resonance image illustrating structures relevant to pharyngeal collapse.

Malhotra A. *Am J. Med*, 2006.



Consequences of Sleep Apnea: Most Data is from Middle-Aged People

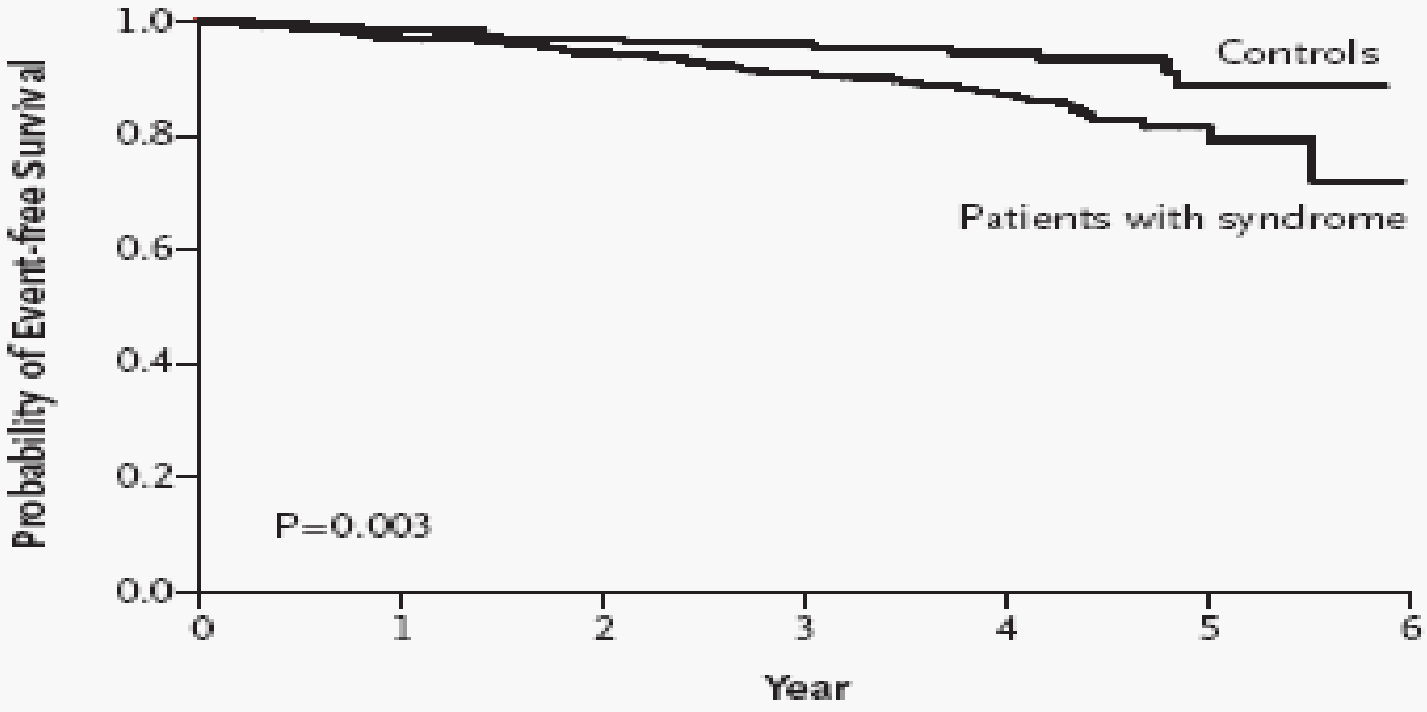
- Sleepiness
- Impaired quality of life
- Decreased cognitive function
- Increased hospitalizations and health care costs
- Increased car accidents
- Impaired glucose control
- Hypertension
- Increased cardiac risk
- Increased mortality rate
- Impotence

What About Studies or Conditions of Older People?

- Stroke
- Atrial fibrillation
- Nocturia
- Hypertension
- Cardiovascular disease
- Death

Stroke or Death with OSA

Yaggi HK, N Engl J Med 2005, n=1022, mean age ~ 60

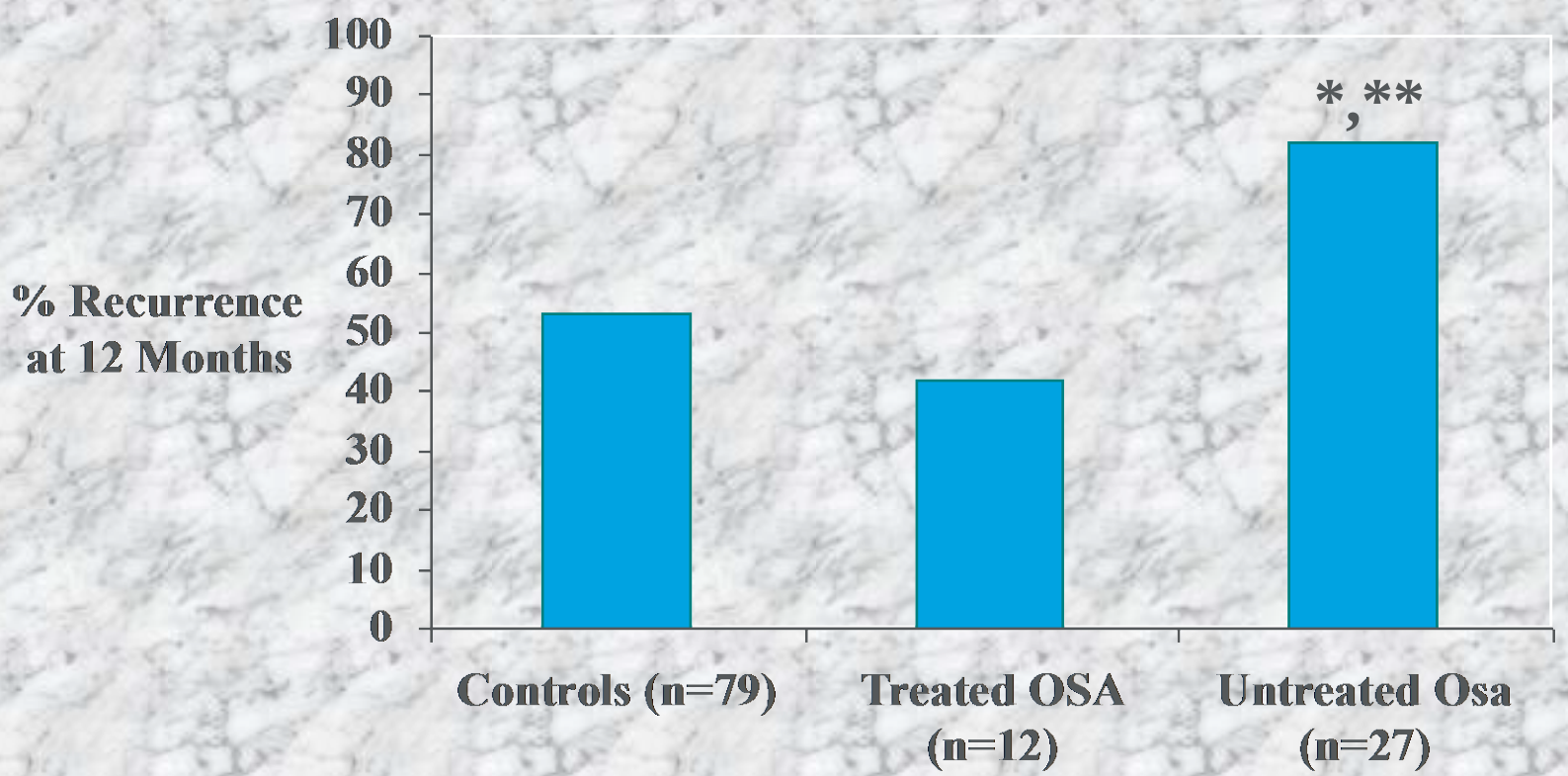


No. at Risk							
Controls	325	266	260	227	88	23	1
Patients with syndrome	697	559	543	452	173	33	3

Figure 1. Kaplan–Meier Estimates of the Probability of Event-free Survival among Patients with the Obstructive Sleep Apnea Syndrome and Controls.

Recurrence of Atrial Fibrillation Following Cardioversion in Patients with OSA

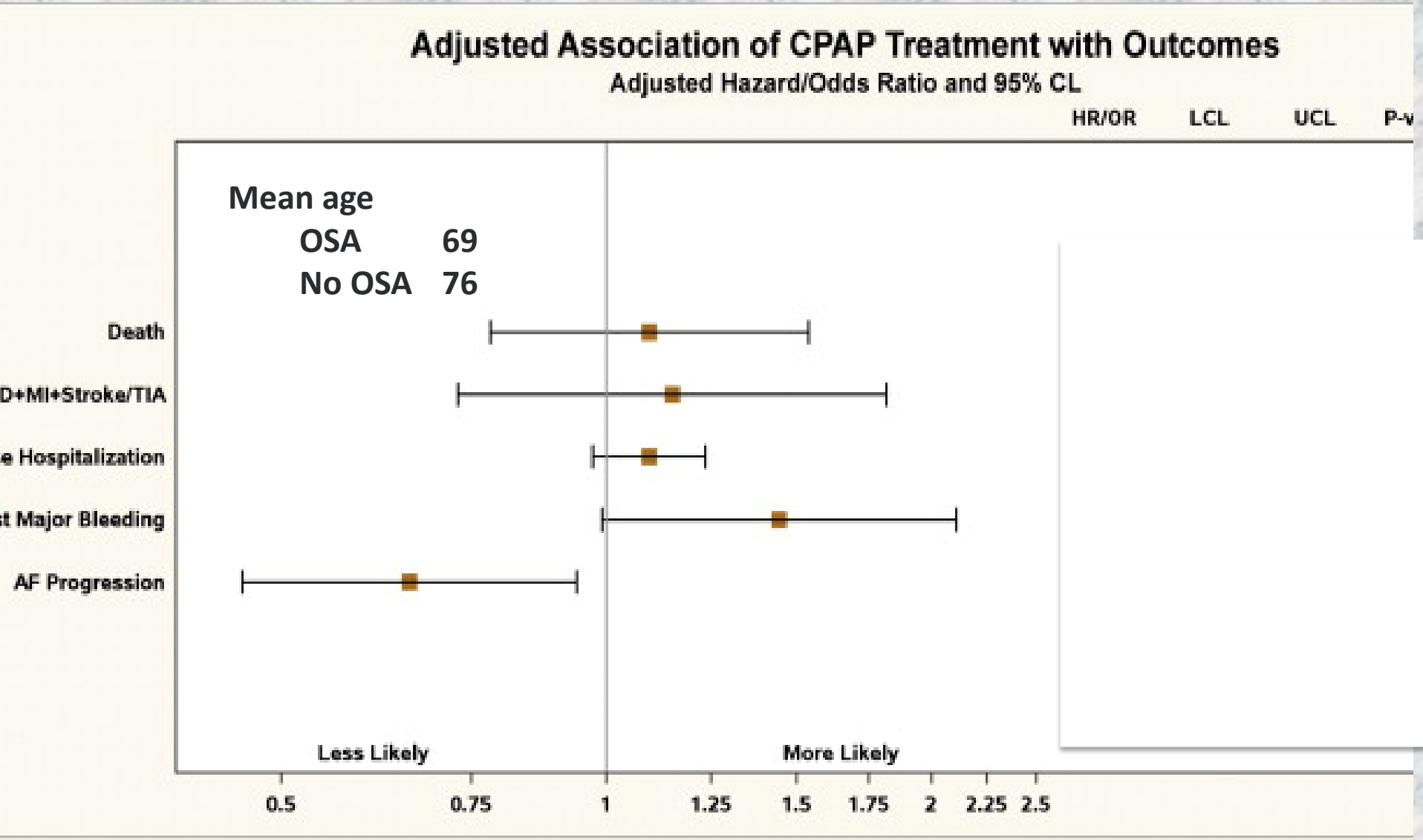
(Kanagala Circ 2003, Mean age 66 years)



*p<0.009 compared to controls

**p<0.013 compared to treated OSA

CPAP Associated with Less Likelihood of Chronic AF
(Holmqvist F, Am Heart J 2015, n=10,132)



Nocturia Correlates (Weakly) with RDI

(Margel D, Urology 2006)

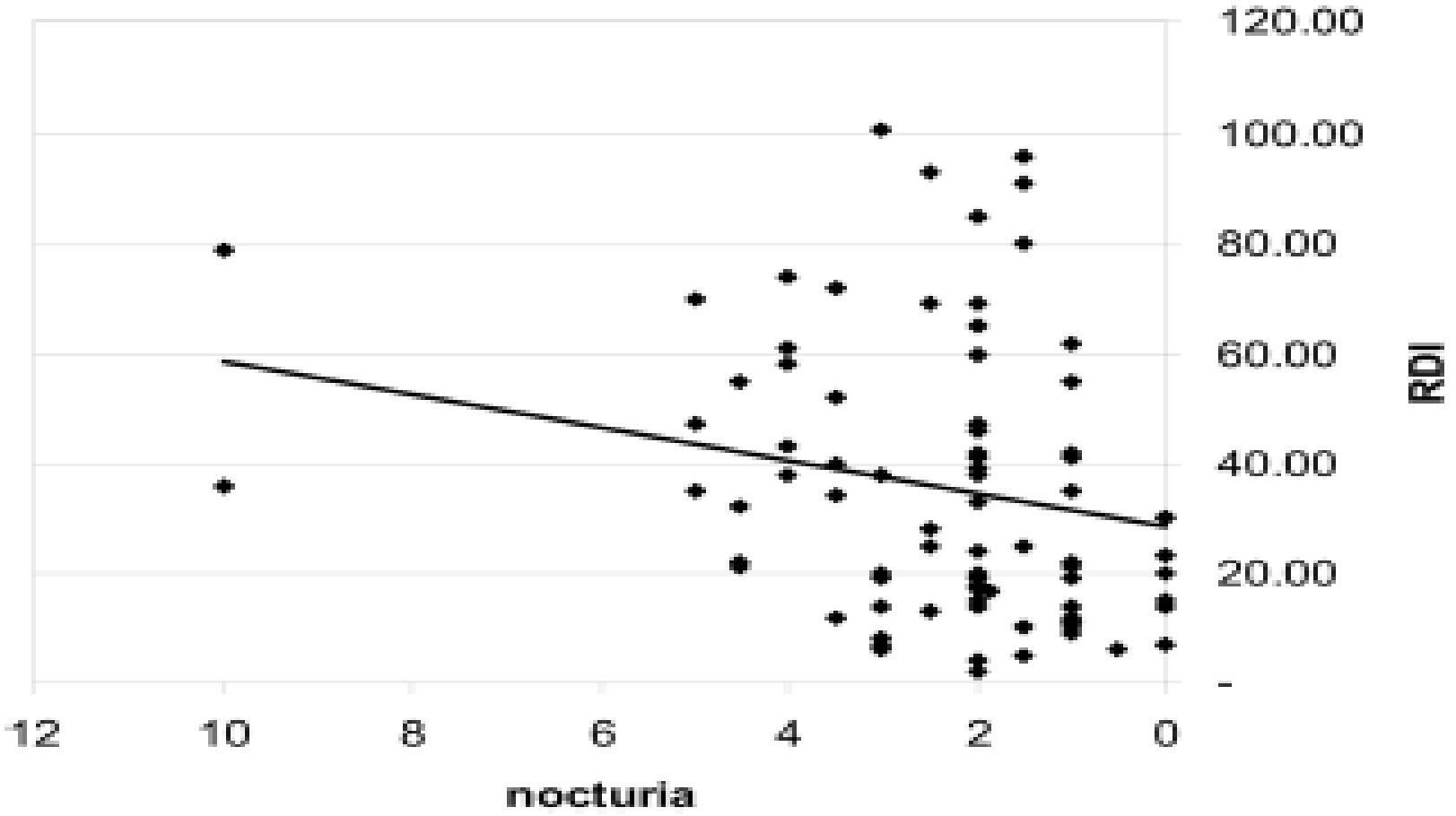


FIGURE 1. *Correlation between number of awakenings to void before treatment with respiratory disturbance index (r = 0.25, P = 0.01).*

CPAP Improves Nocturia

(Margel D, Urology, 2006; n=50, mean age 55)

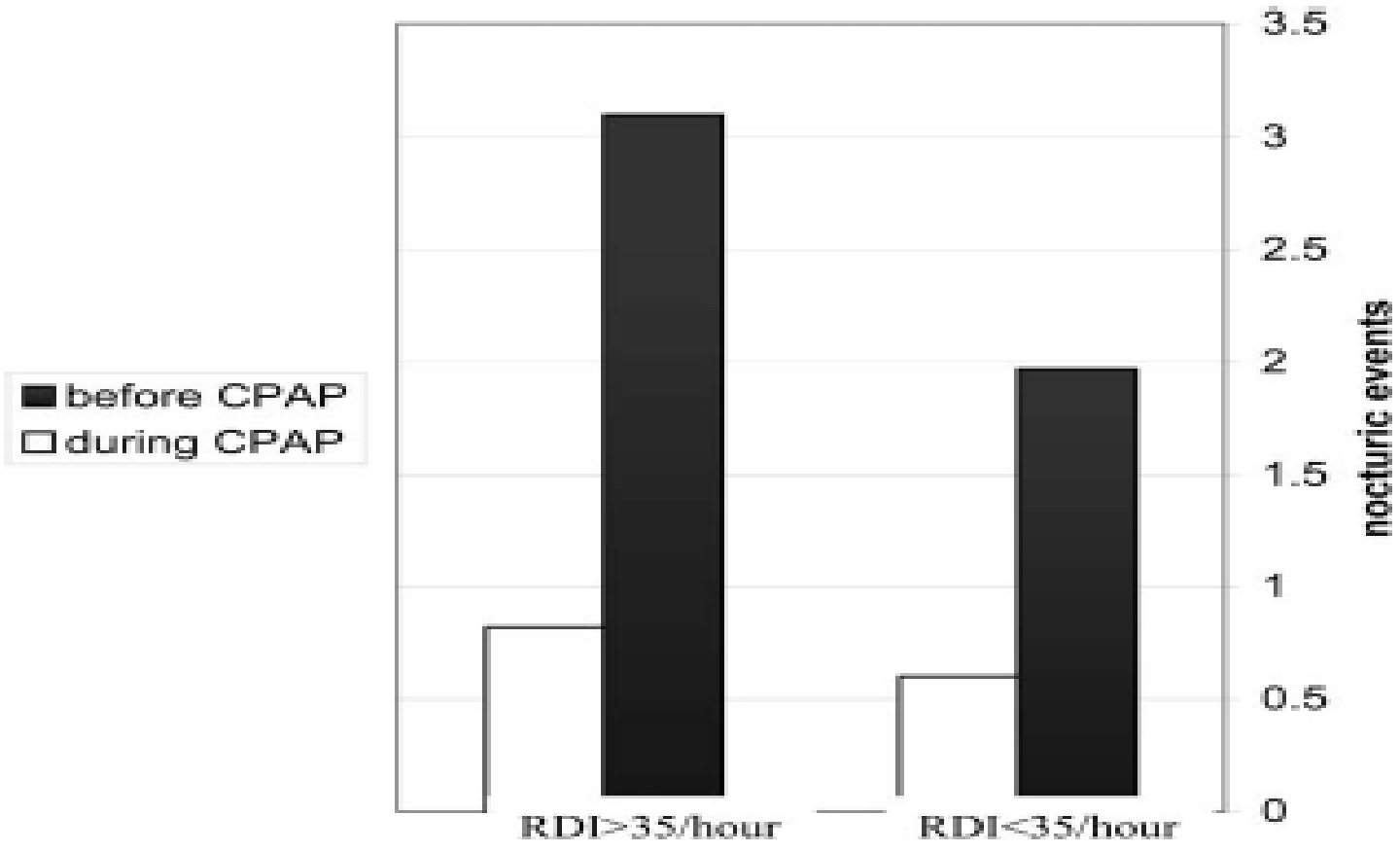


FIGURE 2. *Comparison of outcomes of 50 patients with mild to moderate OSA (RDI less than 35/hr) and 47 with severe OSA (RDI greater than 35/hr).*

From The Joint National Committee on Hypertension 7

Prehypertension	120–139	or	80–89
Hypertension, Stage 1	140–159	or	90–99
Hypertension, Stage 2	≥160	or	≥100

* See *Blood Pressure Measurement Techniques* (reverse side)

Key: SBP = systolic blood pressure DBP = diastolic blood pressure

Diagnostic Workup of Hypertension

- Assess risk factors and comorbidities.
- Reveal identifiable causes of hypertension.
- Assess presence of target organ damage.
- Conduct history and physical examination.
- Obtain laboratory tests: urinalysis, blood glucose, hematocrit and lipid panel, serum potassium, creatinine, and calcium. Optional: urinary albumin/creatinine ratio.
- Obtain electrocardiogram.

Assess for Major Cardiovascular Disease (CVD) Risk Factors

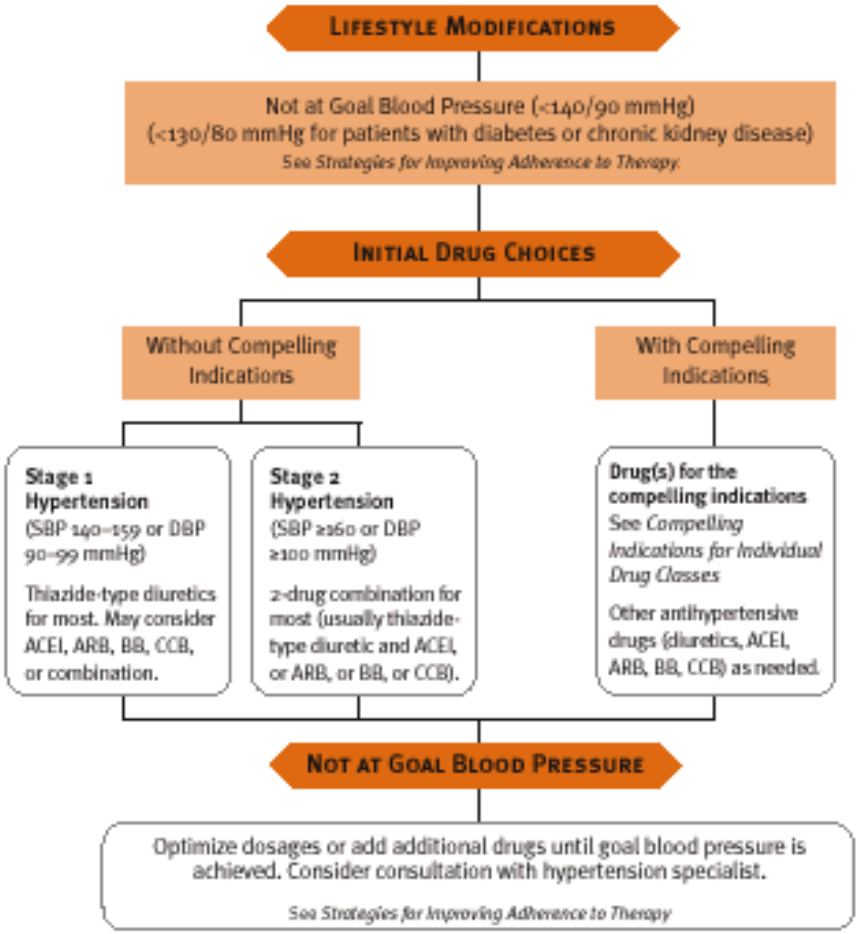
- Hypertension
- Obesity (body mass index ≥30 kg/m²)
- Dyslipidemia
- Diabetes mellitus
- Cigarette smoking
- Physical inactivity
- Microalbuminuria, estimated glomerular filtration rate <60 mL/min
- Age (>55 for men, >65 for women)
- Family history of premature CVD (men age <55, women age <65)

Assess for Identifiable Causes of Hypertension

- Sleep apnea
- Drug induced/related
- Chronic kidney disease
- Primary aldosteronism
- Renovascular disease
- Cushing's syndrome or steroid therapy
- Pheochromocytoma
- Coarctation of aorta
- Thyroid/parathyroid disease

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health
National Heart, Lung, and Blood Institute

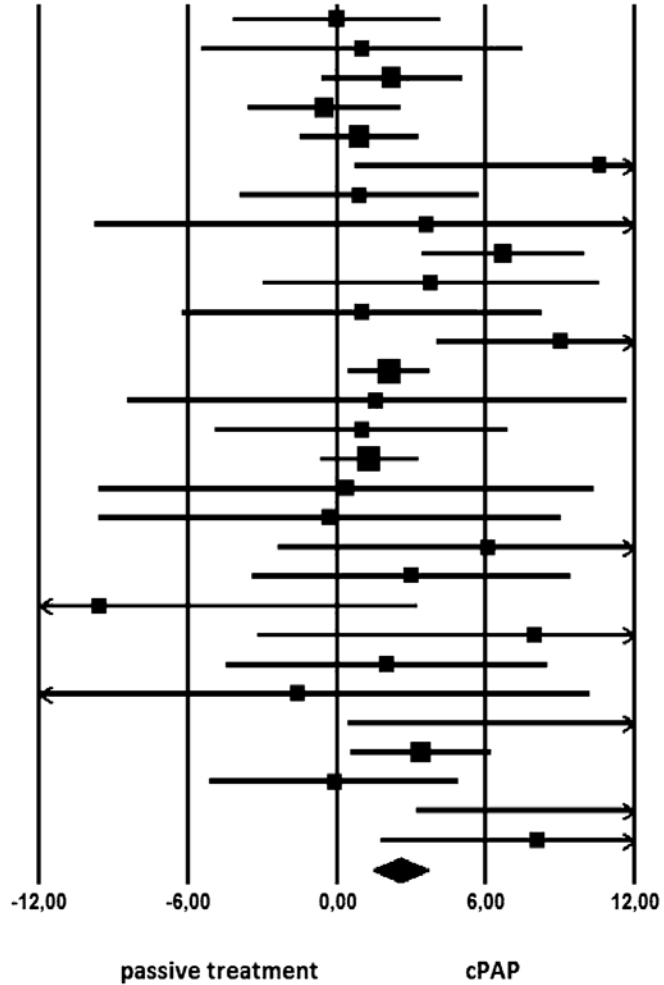
Algorithm for Treatment of Hypertension



Meta-analysis of CPAP and Systolic Blood Pressure (Fava C Chest 2014)

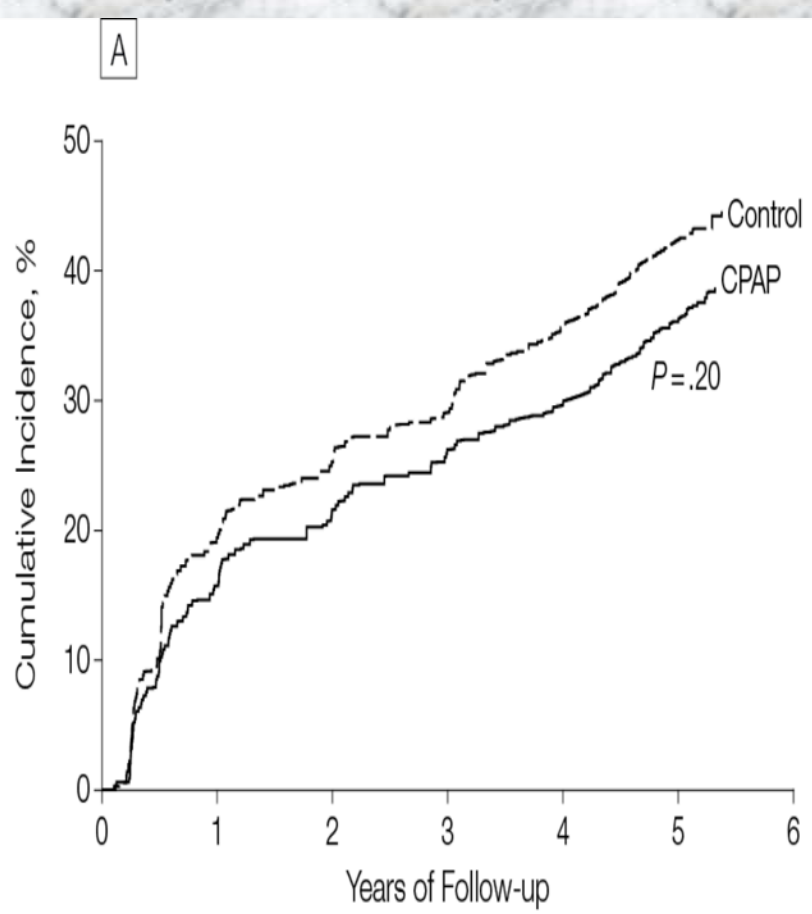
t

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	



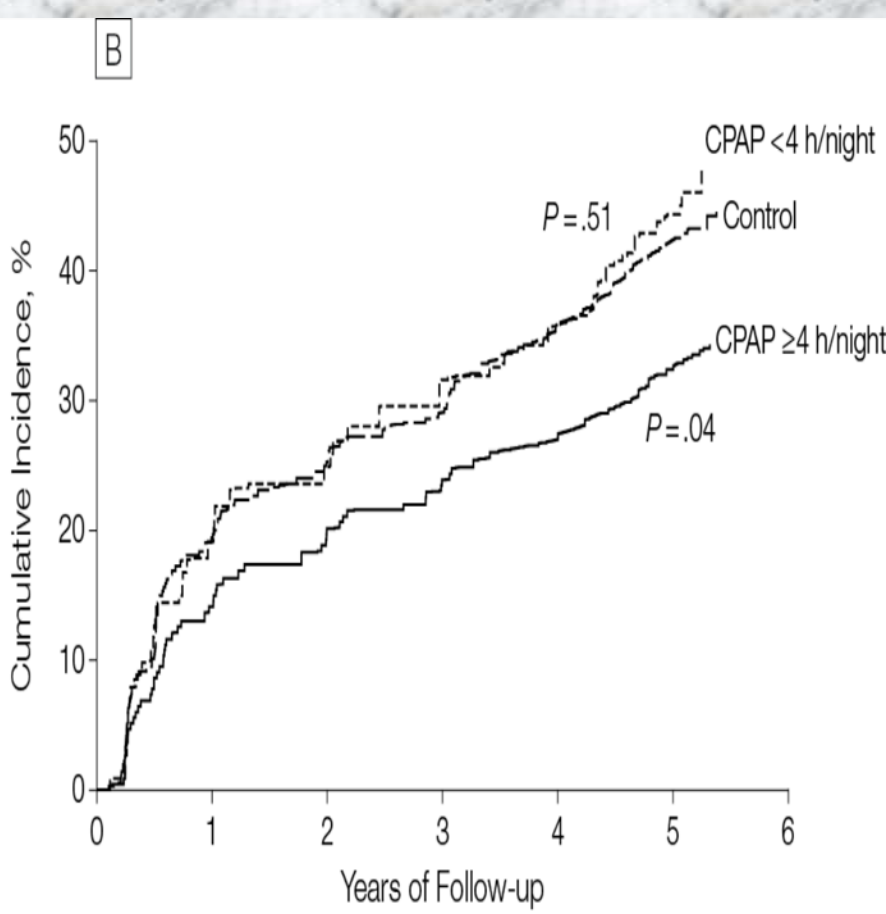
Incident Hypertension in Non-sleepy Patients

(Barbe F, JAMA 2012, n=723) Mean age ~ 51



No. at risk

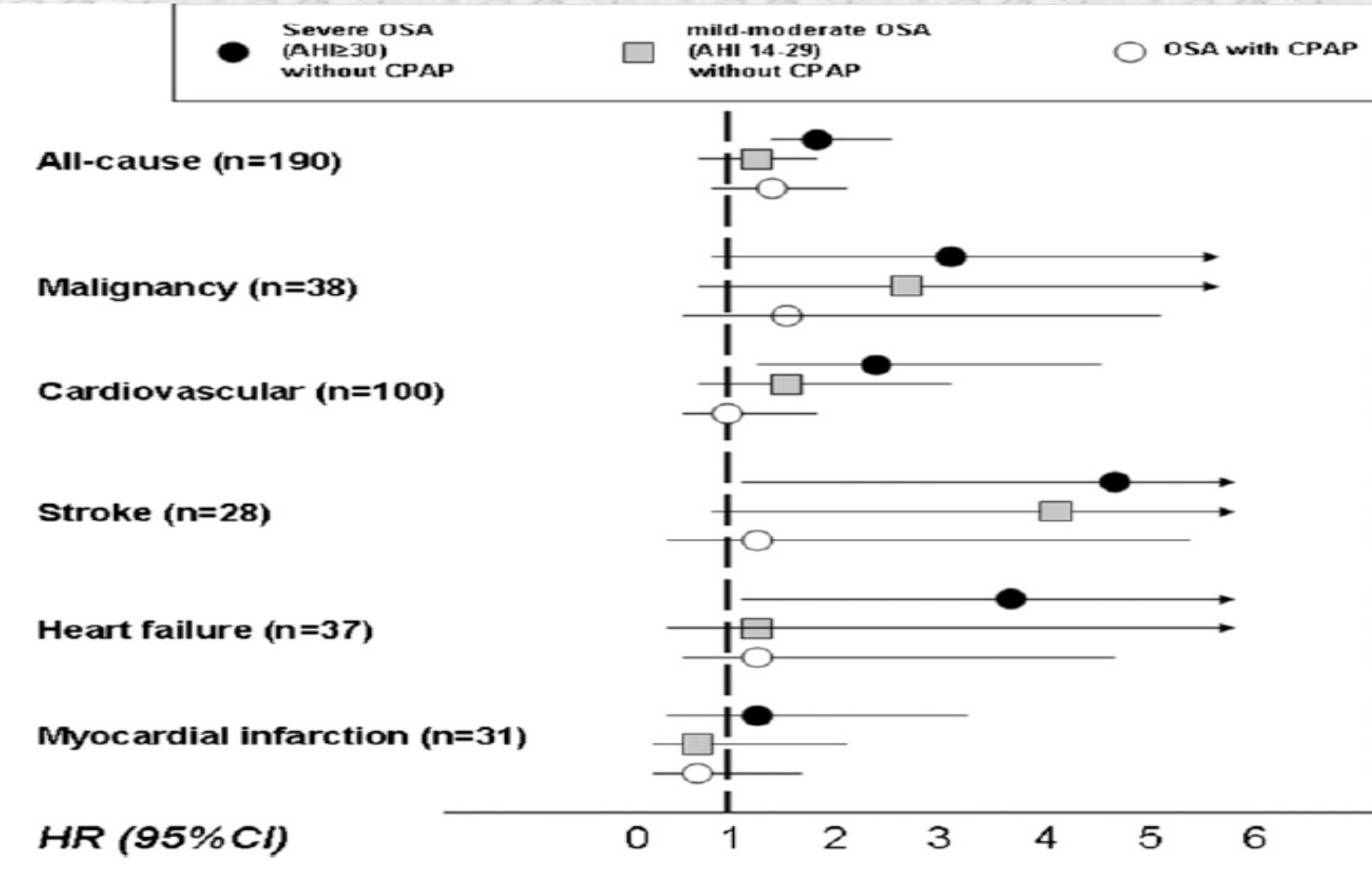
Control	366	264	234	206	134	10
CPAP	357	271	247	217	148	16



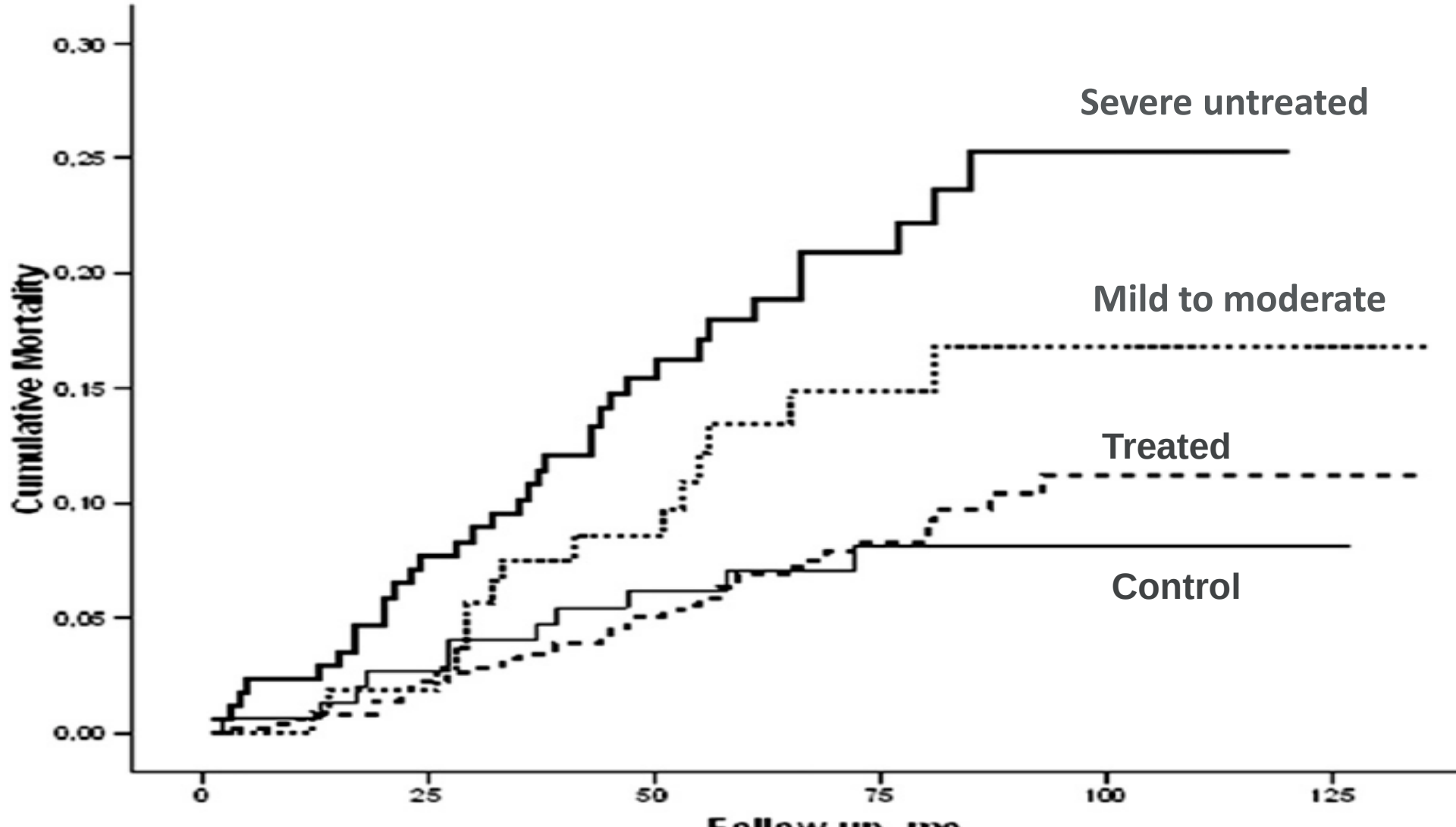
No. at risk

Control	366	264	234	206	134	10
CPAP <4 h/night	127	79	72	56	41	3
CPAP ≥4 h/night	230	192	175	161	107	13

Death in Seniors with OSA
(Martinez Garcia MA, AJRCCM 2012) Mean age 71

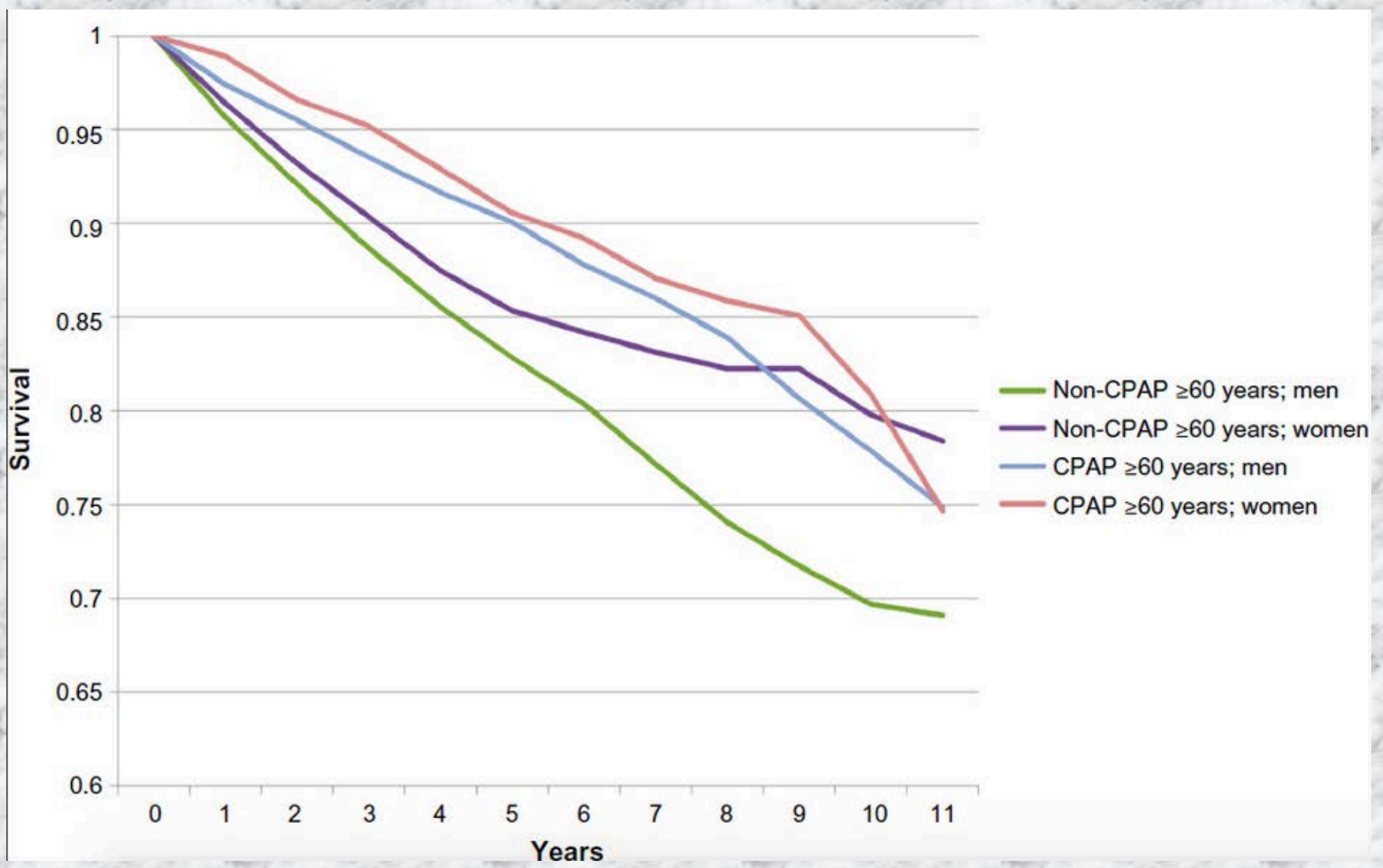


CPAP Treatment and 6-Year Mortality in the Elderly (~ 71 yrs) (Martinez Garcia MA, AJRCCM 2012)



Sleep Apnea, CPAP and Death (OSA not defined)

Jennum P, Nat Sci Sleep 2015, n=25,389



Overview

Significance

State-of-the-art knowledge

Knowledge gaps

Research opportunities

Cognitive Function and OSA

Rosenzweig I Lancet Respir Med 2015

Cognitive deficits most strongly associated with OSA:

- Attention/vigilance
- Visuospatial and constructional abilities
- Executive function
- Delayed visual and verbal memory

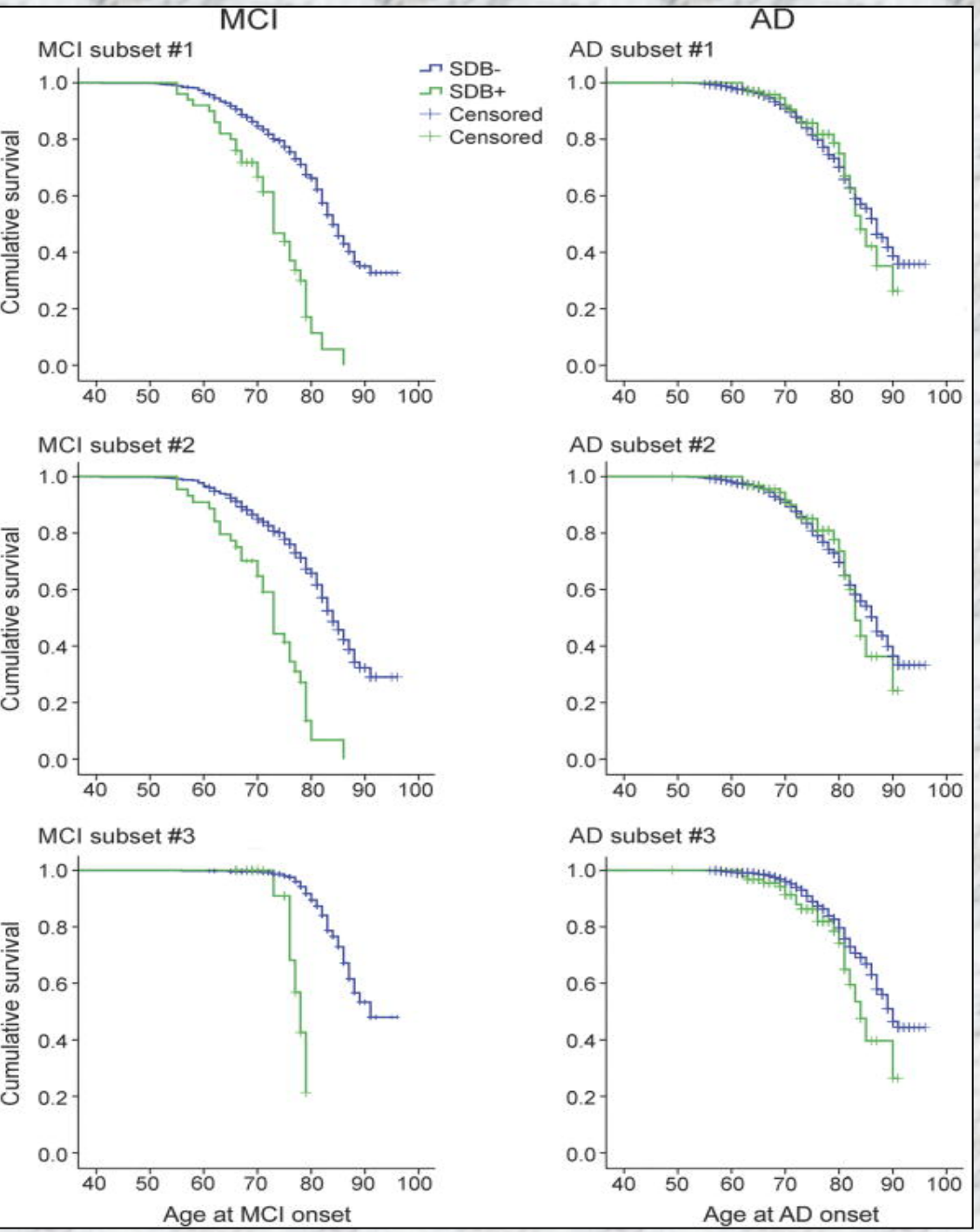
Cognitive dysfunction correlate with severity of hypoxemia; but attention/vigilance correlates with sleep fragmentation (Buck R Respirology 2013).

Patients with severe OSA had impressive recovery of white matter and improvement in memory, attention and executive functioning at 2 years (Castronovo V Sleep 201).

Patients with OSA had improved cognition and increased grey matter after 3 months of CPAP (Kohler, Expert Opin Investig Drugs 2009).

Patients with **severe** OSA and AD who used CPAP had slower decline over 3 years than those untreated (Troussiere AC J Neurol Neurosurg Psychiatry 2014).

Questions remain about duration/timing of treatment, which deficits are causal and reversible.



Patients with OSA were significantly younger at MCI and AD-dementia onset.

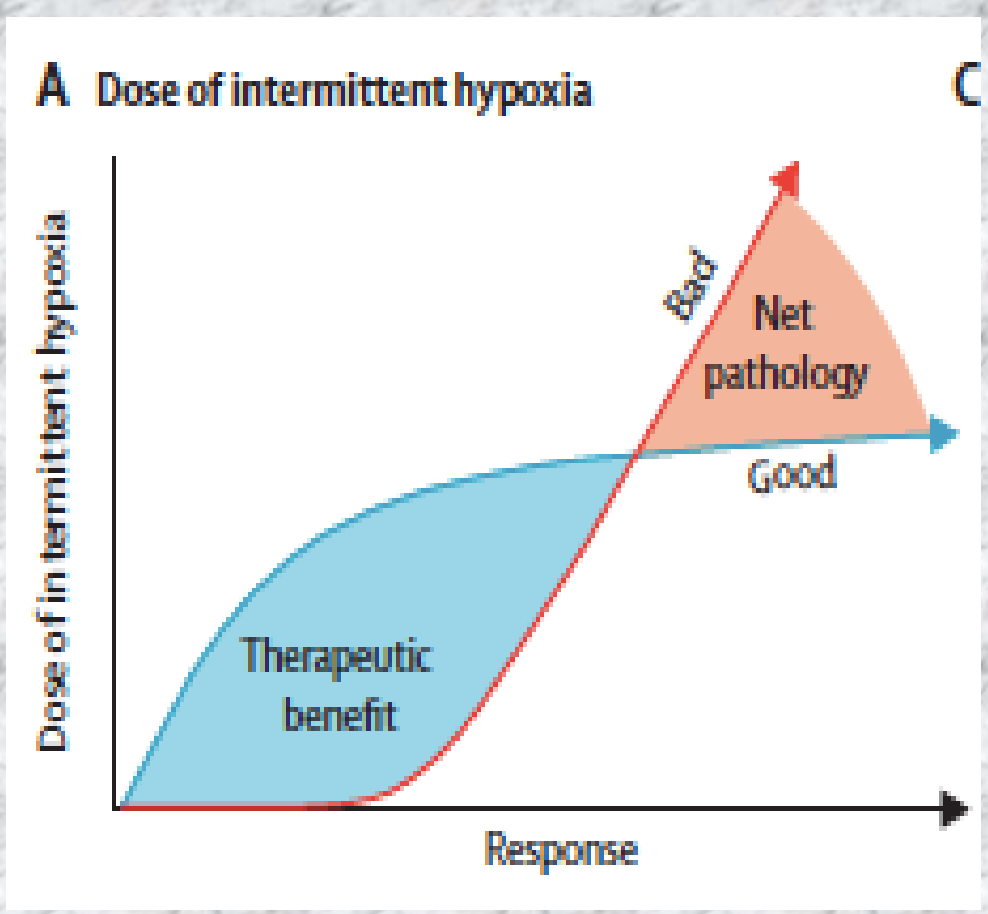
CPAP treatment reduced this effect.

(N=767
"OSA" self-reported)

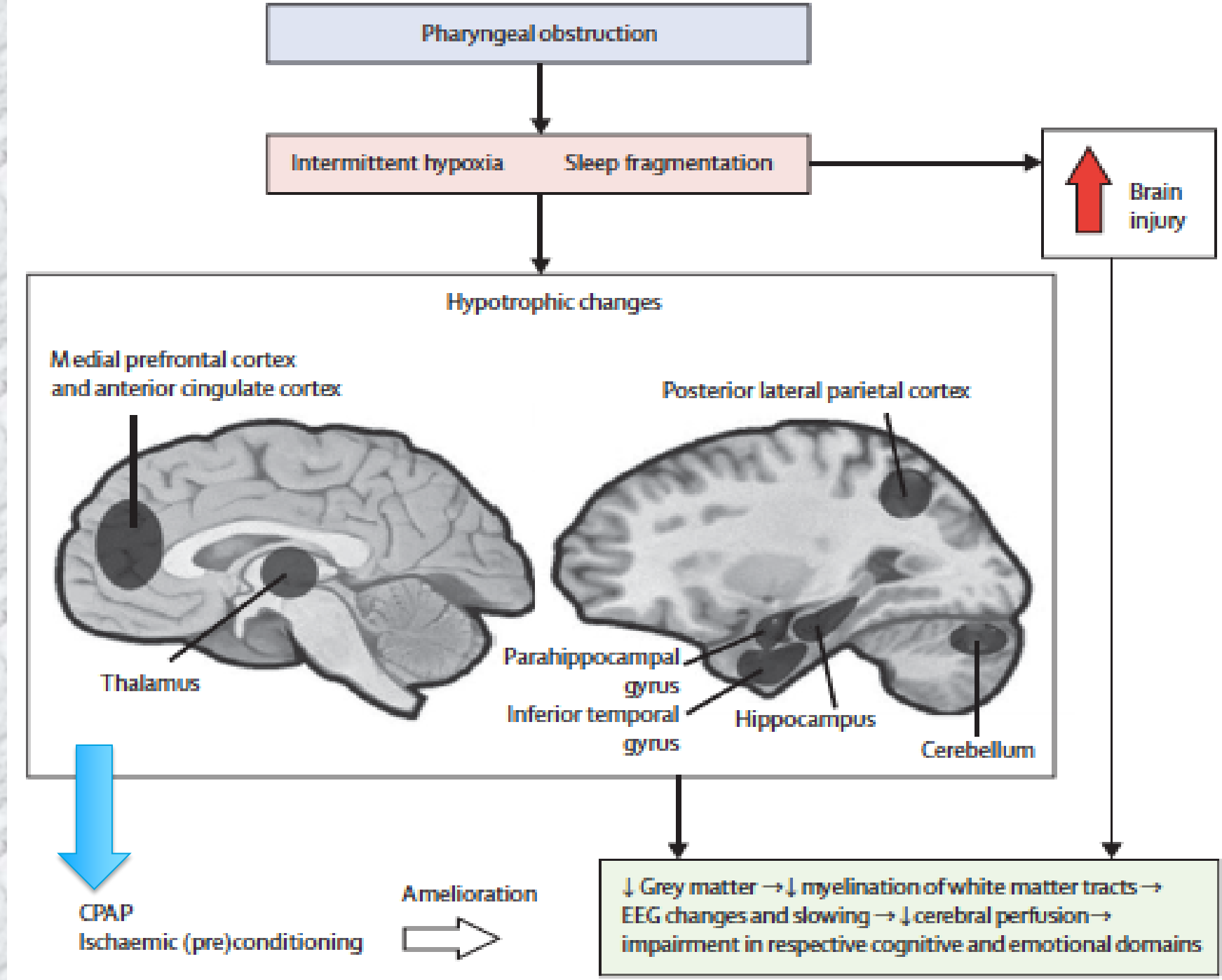
Osoria R Neurology 2015

Intermittent Hypoxia (IH)

Rosenzweig I Lancet Respir Med 2015



- **Short, mild, lower cycle frequency IH is believed to generate adaptive responses in the brain, ie *ischemic preconditioning.***
- **Chronic severe high frequency IH results in disruption of homeostatic mechanisms and inflammation.**


Pharyngeal obstruction
Intermittent hypoxia
Sleep fragmentation
Brain injury
Hypotrophic changes
Medial prefrontal cortex and anterior cingulate cortex
Posterior lateral parietal cortex
Thalamus
Parahippocampal gyrus
Inferior temporal gyrus
Hippocampus
Cerebellum
CPAP
Ischaemic (pre)conditioning
Amelioration
↓ Grey matter → ↓ myelination of white matter tracts →
EEG changes and slowing → ↓ cerebral perfusion →
impairment in respective cognitive and emotional domains

APPLES (Apnea Positive Pressure Long Term Efficacy Study)

Kushida C Sleep 2012

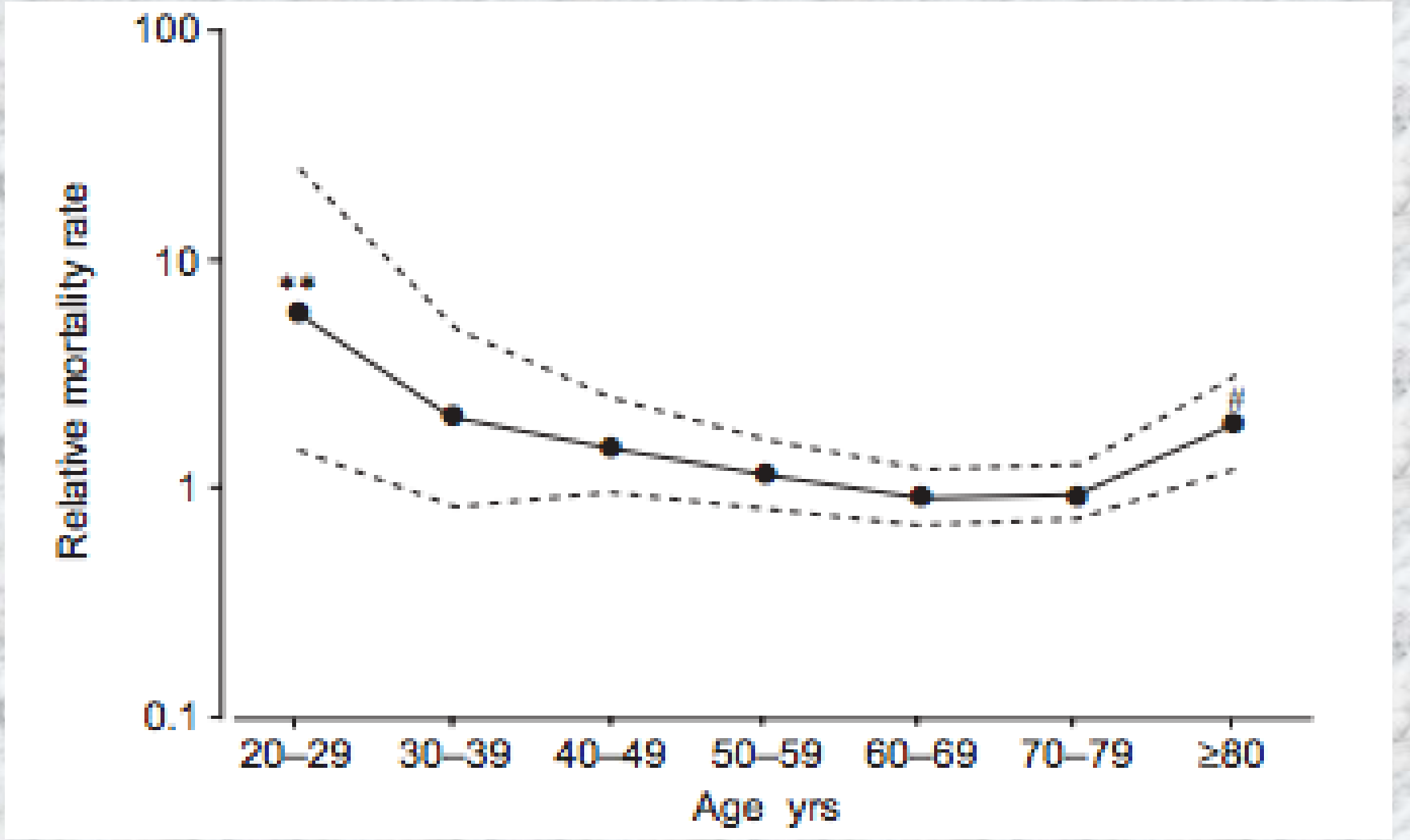
- RCT of CPAP and cognitive function in OSA.
- “OSA” defined as AHI > 10, but apnea and hypopnea not defined in primary article.
- 1098 participants, about 2/3s male, mean age about 52, mean BMI about 32. **Severely hypoxemic patients were excluded.**
- NO difference in primary outcomes at 6 months, tho CPAP treated patients were less sleepy.
- Editorial argues that this suggests that cognitive impairment is irreversible, but preventable. (Schwartz SW Sleep 2012)

Cardiac Disease and OSA

Lavie, L Sleep Med Rev 2015

- OSA is associated with cardiovascular risk factors and comorbidities, BUT
- Mild to moderate intermittent hypoxemia appears to result in ischemic preconditioning in both animals and humans.
- Ischemic preconditioning likely the cells' ability to maintain homeostatic redox balance by upregulation of cytoprotective genes responsible for promoting the cells' antioxidant capacity.
- Conflicting/paradoxical data from mortality endpoint studies, particularly in the elderly, may be the result of ischemic preconditioning.

"Sleep Apnea" was RDI (AHI not defined) > 10, in men with symptoms. Lavie P Eur Respir J 2005, n=14589



Overview

Significance

State-of-the-art knowledge

Knowledge gaps

Research opportunities

Knowledge Gap #1: Do We Need to Treat Mild/Moderate Sleep Apnea in Older People?

Knowledge Gap #2: What IS sleep apnea?

CMS's Definition of Obstructive Sleep Apnea (OSA)

CPAP will be covered for adults with sleep-disordered breathing if:

AHI $\geq$ 15 *OR*

AHI $\geq$ 5 with

- Hypertension
- Stroke
- Sleepiness
- Ischemic heart disease
- Insomnia
- Mood disorders

Sleep Heart Health Study: Apneas and Hypopneas

Decrease in airflow *or* chest wall movement to an amplitude smaller than approximately 25% (*apnea*) or 70% (*hypopnea*) of baseline for at least 10 seconds

PLUS

oxyhemoglobin desaturation of 4% or greater as compared with baseline.

Why? Impossible to get inter-scorer reliability otherwise.

SHHS's AHI is really an ODI 4

All events (apneas and hypopneas) required a 4% oxygen desaturation to be counted because

It was not otherwise possible to achieve acceptable inter-rater reliability based on flow rate or arousals.

Scoring Apneas and Hypopneas According to the AASM Scoring Manual (Iber C, AASM, 2007)

- Apneas are measured with a thermistor
  - Signal drops by 90% of baseline
  - For at least 10 seconds
  - No requirement for desaturation
- Hypopneas are measured with a pressure transducer
  - Signal drops by $\geq$ 30% of baseline with a $\geq$ 4% desat OR
  - Signal drops by $\geq$ 50% of baseline with a $\geq$ 3% desat *or the event is associated with an arousal.*

What IS Sleep Apnea in Older People?

1/3 of seniors have AHI > 5, and most have symptoms (Phillips B Chest 1992, Ancoli-Israel Sleep, 1991)

Latest, Greatest Scoring Rules
(JCSM 2012)

Apnea=signal drop ≥ 90% of pre-event baseline using an oronasal thermal sensor, PAP device flow or an alternative apnea sensor for ≥ 10 seconds.

Hypopnea = signal drop by ≥ 30% of pre-event baseline for ≥ 10 seconds in association with either ≥ 3% arterial oxygen desaturation **or an arousal.**

Severity Criteria Based on PSG From the American Academy of Sleep Medicine (Sleep, 1999)

"Mild" sleep apnea is 5-15 events/hr

"Moderate" sleep apnea is 15-30 events/hr

"Severe" sleep apnea is over 30 events/hr

("Events" includes apneas, hypopneas, and RERA's)

This give no importance to symptoms, hypoxemia, sleep disturbance.

Which Patient Has “Mild” OSA?

	Patient 1	Patient 2
AHI (events/hr)	40	10
Apnea duration (secs)	10-22	10-90
Lowest Sa02 (%)	90	71
% REM on study	18	0
Arousals/hr	8	80
Cardiac arrhythmias	none	v tach

Do Symptoms and Definitions Matter? (Sforza E, Sleep Med 2015, n=825, mean age 68 yrs)

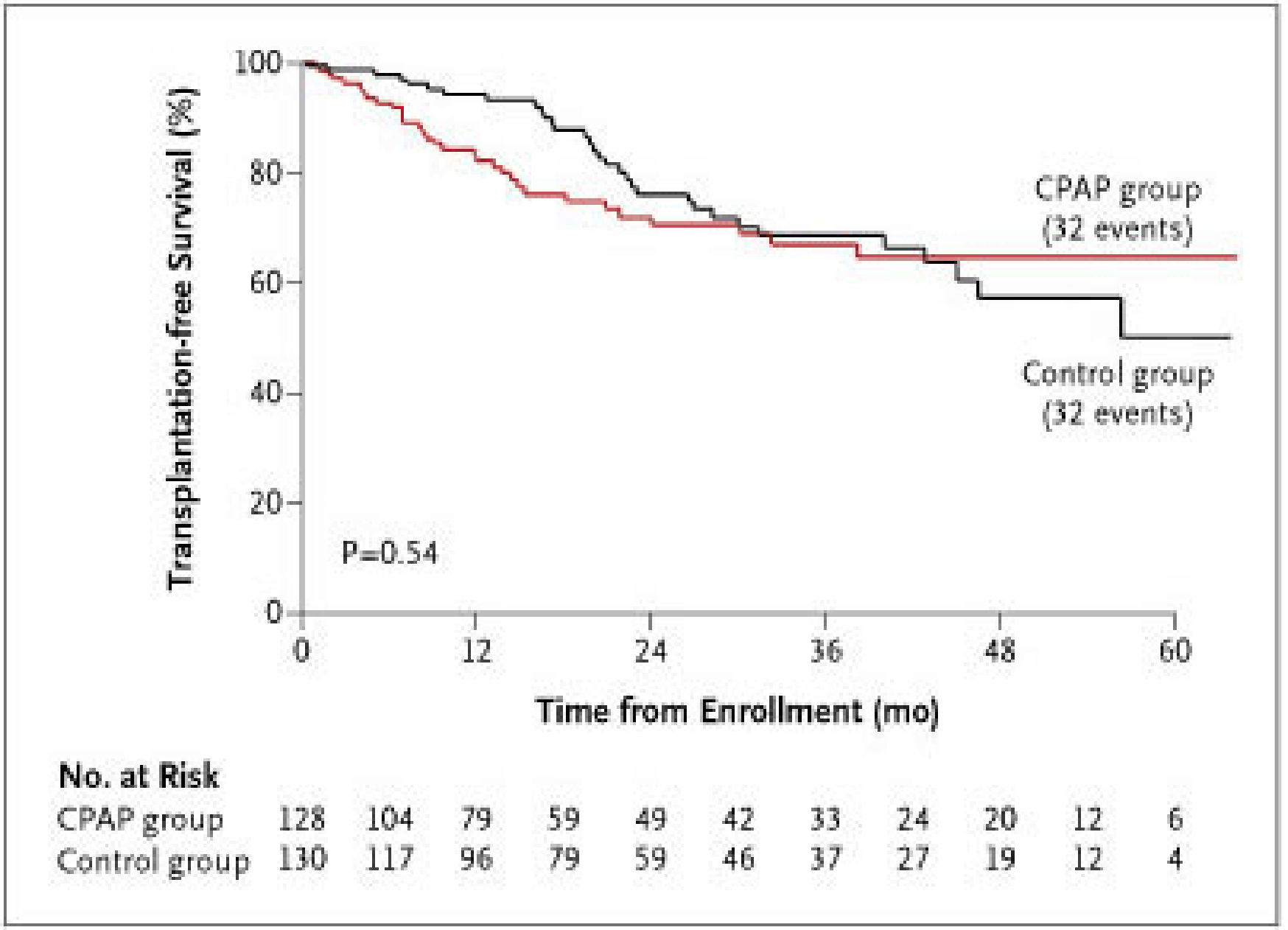
- Population-based cohort study (PROOF) in France
- "Sleepiness" defined by ESS ≥ 10
- "Apnea" defined as ≥10 secs no flow
- "Hypopnea" ≥ 10 secs 50% reduced flow, + 3% desat
- "Sleep apnea" defined *solely on basis of AHI*
  - < 5 normal
  - 5-15 mild
  - 15-30 moderate
  - >30 severe
- Mean ESS< 10 in all categories, ranging 5.7-6.6
- Desaturation was mostly mild (high 80s)
- Sleepiness correlated with AHI, ODI, min Sa02, T<90%, but male gender, depression and obesity were STRONGER predictors (confirmed by Lopes JM Rev Bras Epidemiol 2013, n=168 mean age 72)
- The authors propose two key concepts:
  - Older patients with OSA are a different phenotype
  - Identification/management of OSA in older patients is not clear cut

Knowledge Gap #3: How (And When) Should We Treat CENTRAL Apnea?

CANPAP

CANADIAN POSITIVE AIRWAY PRESSURE TRIAL FOR TREATMENT OF CENTRAL SLEEP APNEA IN HEART FAILURE

- 5 Year, multi-center RCT to examine effects of treating CSA by CPAP in patients with CHF
- Jointly funded by the CIHR, Respironics, ResMed and Tyco



No. at Risk

CPAP group	128	104	79	59	49	42	33	24	20	12	6
Control group	130	117	96	79	59	46	37	27	19	12	4

“Adaptive servo-ventilation had no significant effect on the primary end point inpatients who had heart failure with reduced ejection fraction and predominantly central sleep apnea, but all-cause and cardiovascular mortality were both increased with this therapy.”

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 SEPTEMBER 17, 2015 VOL. 373 NO. 12

Adaptive Servo-Ventilation for Central Sleep Apnea in Systolic Heart Failure

Martin R. Cowie, M.D., Holger Woehrle, M.D., Karl Wegscheider, Ph.D., Christiane Angermann, M.D., Marie-Pia d'Ortho, M.D., Ph.D., Erland Erdmann, M.D., Patrick Levy, M.D., Ph.D., Anita K. Simonds, M.D., Virend K. Somers, M.D., Ph.D., Faiez Zannad, M.D., Ph.D., and Helmut Teschler, M.D.

Overview

Significance

State-of-the-art knowledge

Knowledge gaps

Research opportunities

Knowledge Gaps

- What IS sleep apnea (OSA) in the elderly?
  - Is it different than OSA in younger people? How?
  - How is it best defined:
    - AHI, RDI, ODI, T<90%?
    - Symptoms?
- Is intermittent hypoxia a threat or a menace? And…
  - Are some older people better off not being treated?
- What treatments are most effective for central sleep apnea?
  - Or when does it need to be treated?

Summary/Key Questions

What IS sleep apnea in the the older person, and how should it best be defined and measured?

Is intermittent hypoxemia a friend or a foe?

HOW (and WHEN) do we treat central sleep apnea?