Sleep and Healthy Aging Symposium

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Disclosures

Officer of the ATS (2012-2017)

ResMed gave philanthropic donation to UCSD

MedXCloud no personal income

Equillium, Livanova, Corvus

NIH funds my lab

Outline

- 1. Sleep Deprivation
- 2. Obstructive Sleep Apnea

An Official American Thoracic Society Statement: The Importance o
Healthy Sleep
Recommendations and Future Priorities

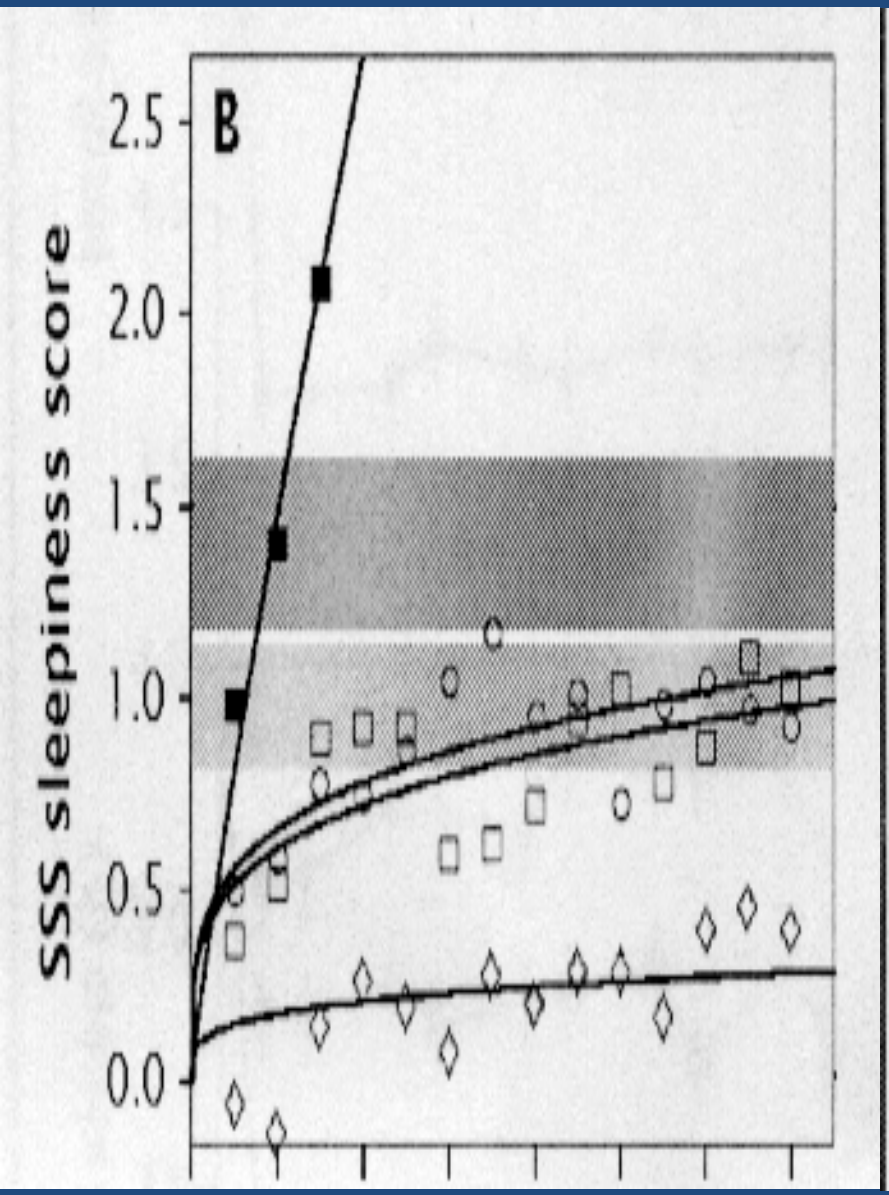
Sutapa Mukherjee, Sanjay R. Patel, Stefanos N. Kales, Najib T. Ayas, Kingman P. Strohl, David Gozal, and Atul Malhotra; on behalf of the American Thoracic Society *ad hoc* Committee on Healthy Sleep

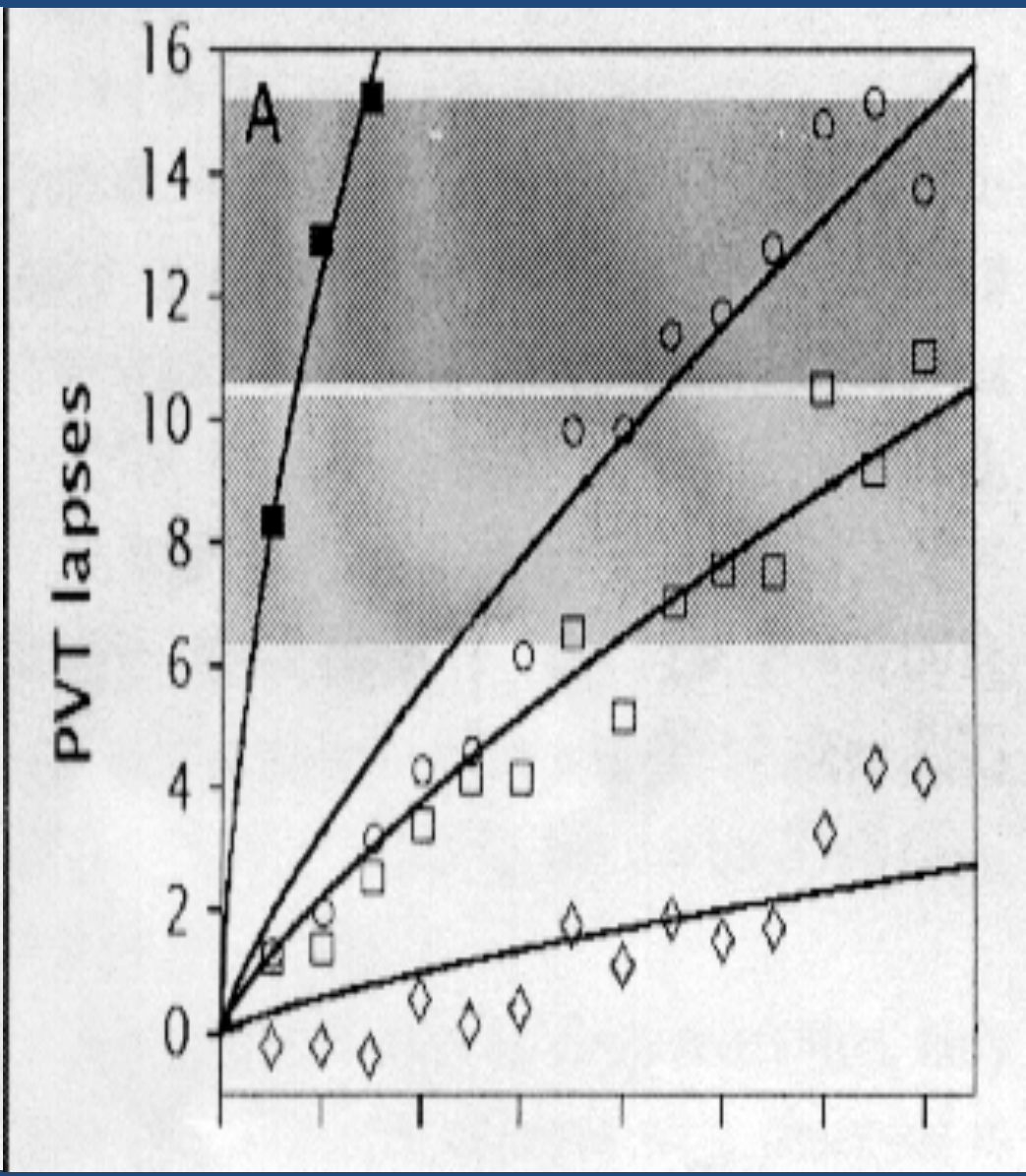
THIS OFFICIAL POLICY STATEMENT OF THE AMERICAN THORACIC SOCIETY (ATS) WAS APPROVED BY THE ATS BOARD OF DIRECTORS, APRIL 2015

- **Dinges et al.**
- **Almost all require 7-9 hrs sleep/nt**
- **Measurable decline in cognitive performance after 18hrs: 1 drink**
- **At 24hrs: legally drunk**
- **Optimal neurocognitive function may require 9 hours per 24hr period**

AJRCCM 2015; Dawson Nature 1997

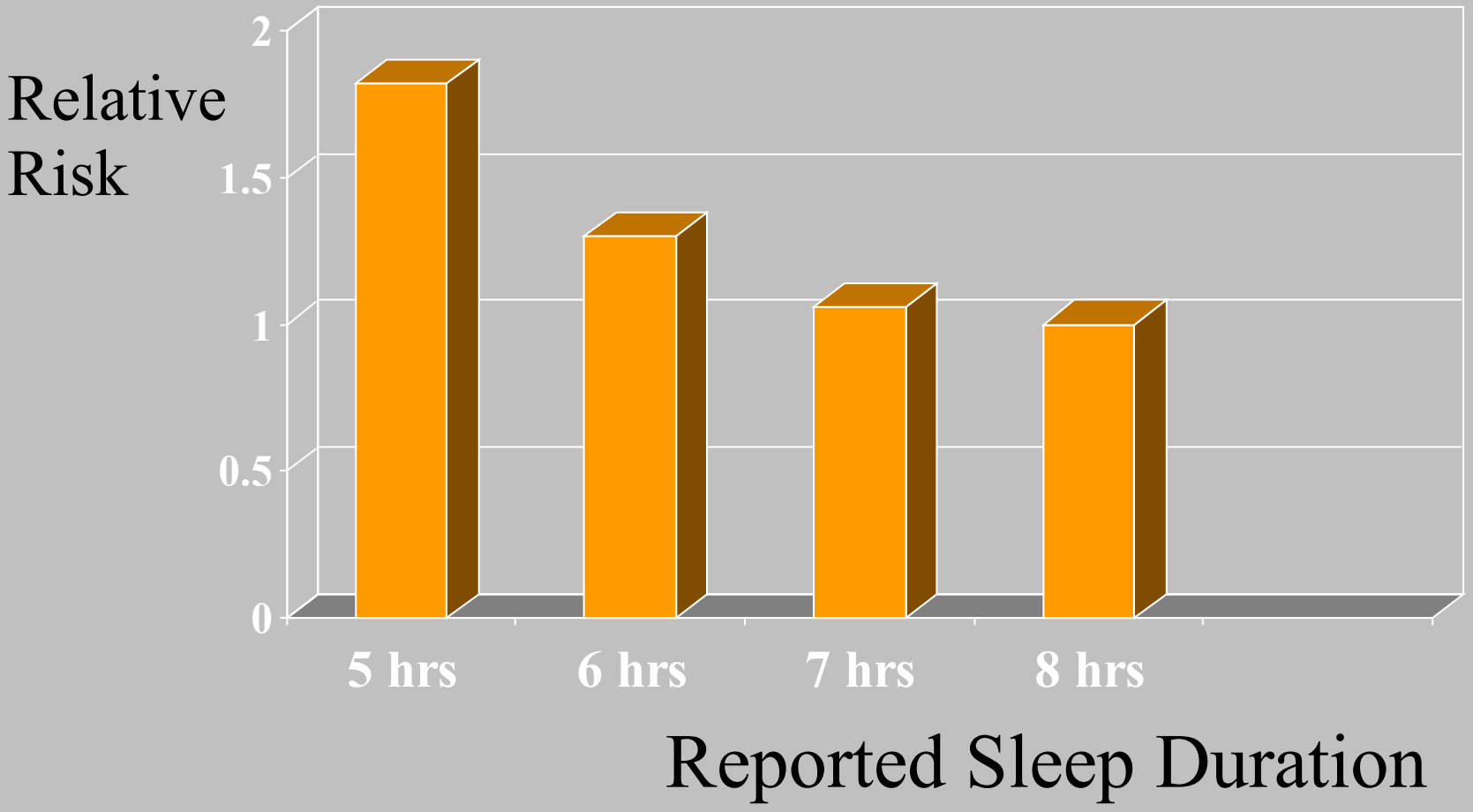
Van Dongen et al. SLEEP 2003





Age-adjusted Relative Risks of Incident Coronary Heart Disease (n=71,617)

Archives Int. Med. 2003



Sleep Issues in COVID

- 1. Sleep Duration improved ~1hr

Is Increased Sleep Responsible for Reductions in Myocardial Infarction During the COVID-19 Pandemic?

The COVID-19 pandemic caused by the highly contagious SARS-CoV-2 virus has had dev-

Am. J. Cardiol. 2020

- 2. OSA as a possible risk factor

OSA as a probable risk factor for severe COVID-19

Response to Salles C, Mascarenhas Barbosa H. COVID-19 and obstructive sleep apnea. *J Clin Sleep Med*. 2020(XX):XXX–XXX. doi:10.5664/jcsm.8606

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[1]Acute Medicine, Transplant and Pulmonary Departments, Mater Misericordiae University Hospital and University College Dublin, Ireland
[2]UC San Diego School of Medicine, San Diego, California

Potential influences of obstructive sleep apnea and obesity on COVID-19 severity

David McSharry, MD[1]; Atul Malhotra, MD[2]

[1]Acute Medicine and Pulmonary Department, Mater Misericordiae University Hospital and University College Dublin, Ireland
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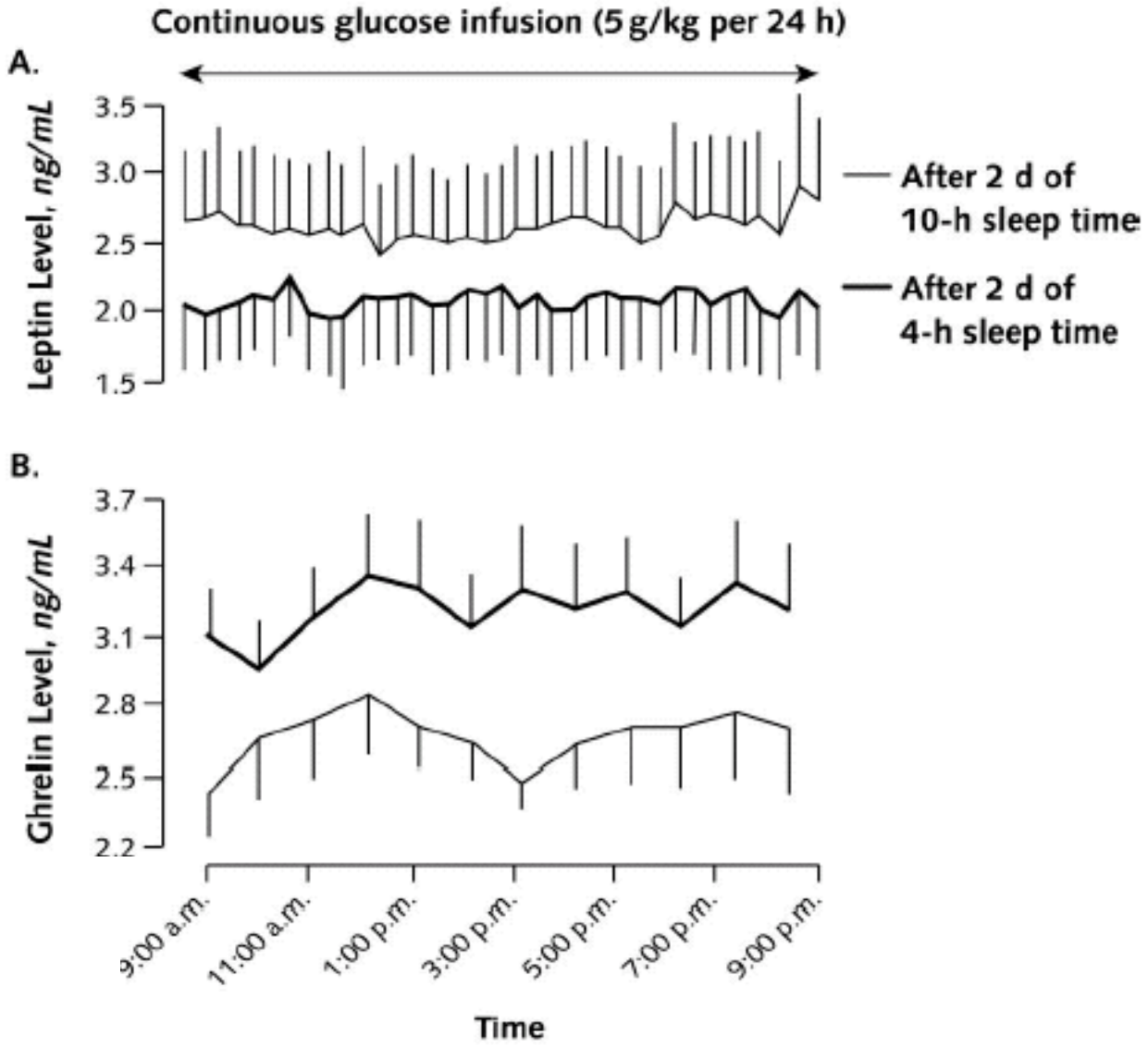
2 June 2020
15 June 2020

Spiegel et al. Lancet 1999
Tasali et al. PNAS 2008

- Induced sleep deprivation in normals
- Measured impaired glucose tolerance
- Elevated sympathetic activity
- Increased cortisol levels

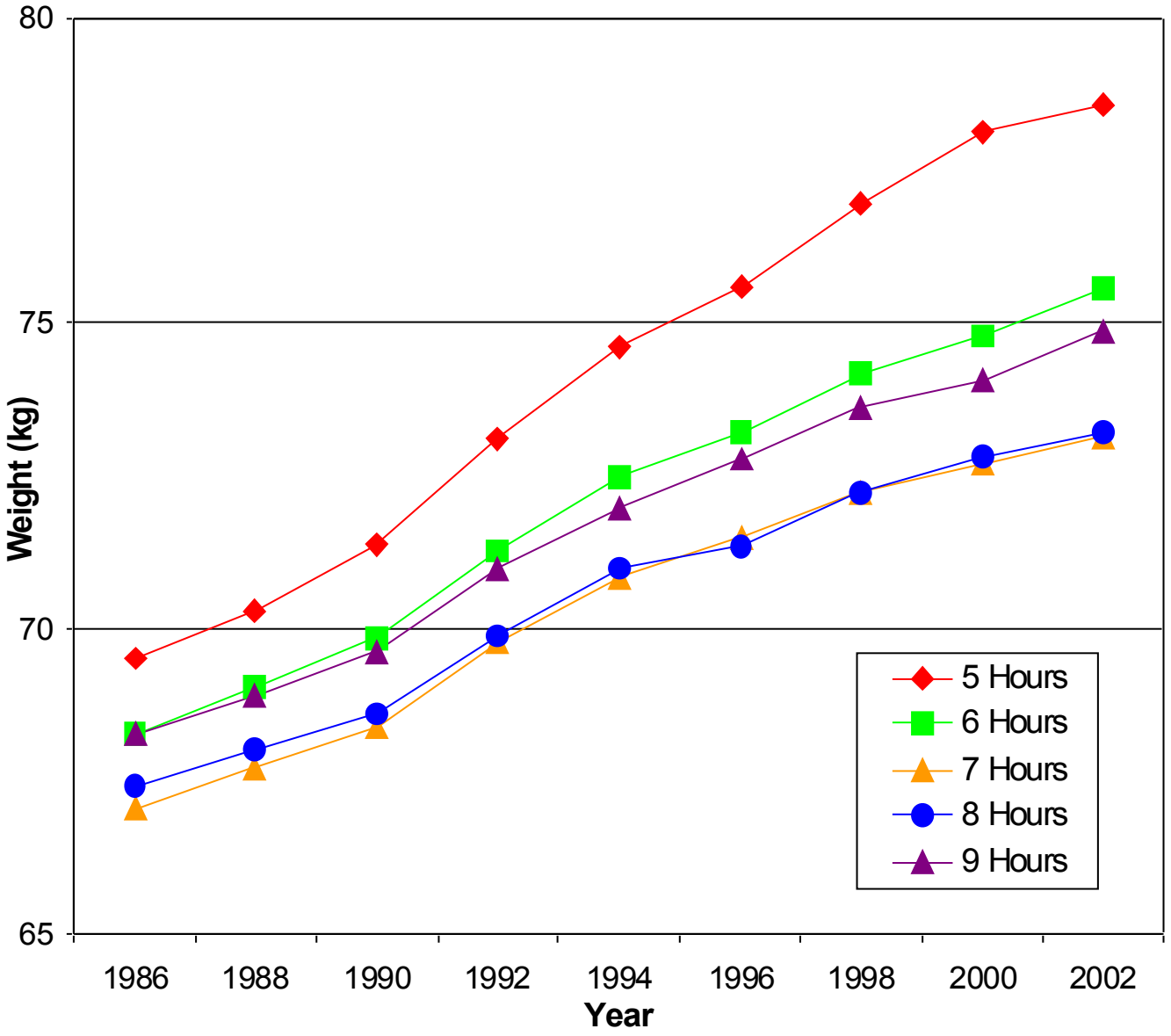
- Slow wave sleep seems critical

Effect of sleep restriction on leptin and ghrelin



Spiegel et al.;
Annals Intern Med 2004

Age Adjusted Weight Trends



AJE 2006

Annals of Internal Medicine | ORIGINAL RESEARCH

Insufficient Sleep Undermines Dietary Efforts to Reduce Adiposity

Arlet V. Nedeltcheva, MD; Jennifer M. Kilkus, MS; Jacqueline Imperial, RN; Dale A. Schoeller, PhD; and Plamen D. Penev, MD, PhD

Results: Sleep curtailment decreased the proportion of weight lost as fat by 55% (1.4 vs. 0.6 kg with 8.5 vs. 5.5 hours of sleep opportunity, respectively; $P = 0.043$) and increased the loss of fat-free body mass by 60% (1.5 vs. 2.4 kg; $P = 0.002$). This was accompanied by markers of enhanced neuroendocrine adaptation to caloric restriction, increased hunger, and a shift in relative substrate utilization toward oxidation of less fat.

Conclusion: The amount of human sleep contributes to the maintenance of fat-free body mass at times of decreased energy intake. Lack of sufficient sleep may compromise the efficacy of typical dietary interventions for weight loss and related metabolic risk reduction.

Annals 10/2010

Short sleep duration and incident coronary artery calcification

Christopher Ryan King, BS[1], **Kristen L Knutson, PhD**[1], **Paul J Rathouz, PhD**[1], **Steve Sidney, MD, MPH**[2], **Kiang Liu, PhD**[3], and **Diane S Lauderdale, PhD**[1]

1 *Department of Health Studies, University of Chicago, Chicago, Illinois*

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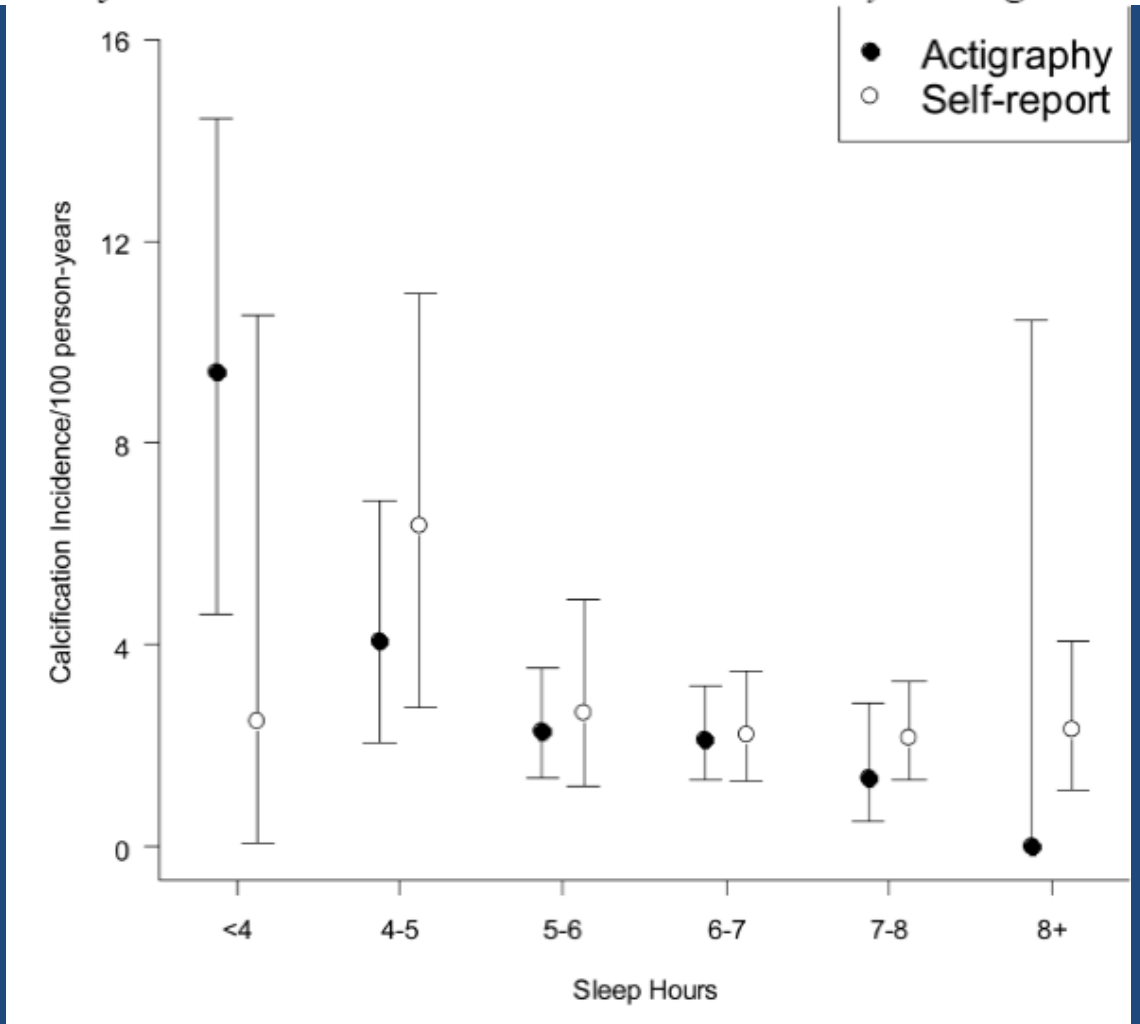

JAMA Dec 2008

Summary Sleep Deprivation

- Inadequate sleep has health consequences
- Impaired brain function not surprising
- Increased metabolic and cardiovascular complications also present
- Data are rapidly evolving

Outline

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- 2. Obstructive Sleep Apnea

Sleep Apnea Background

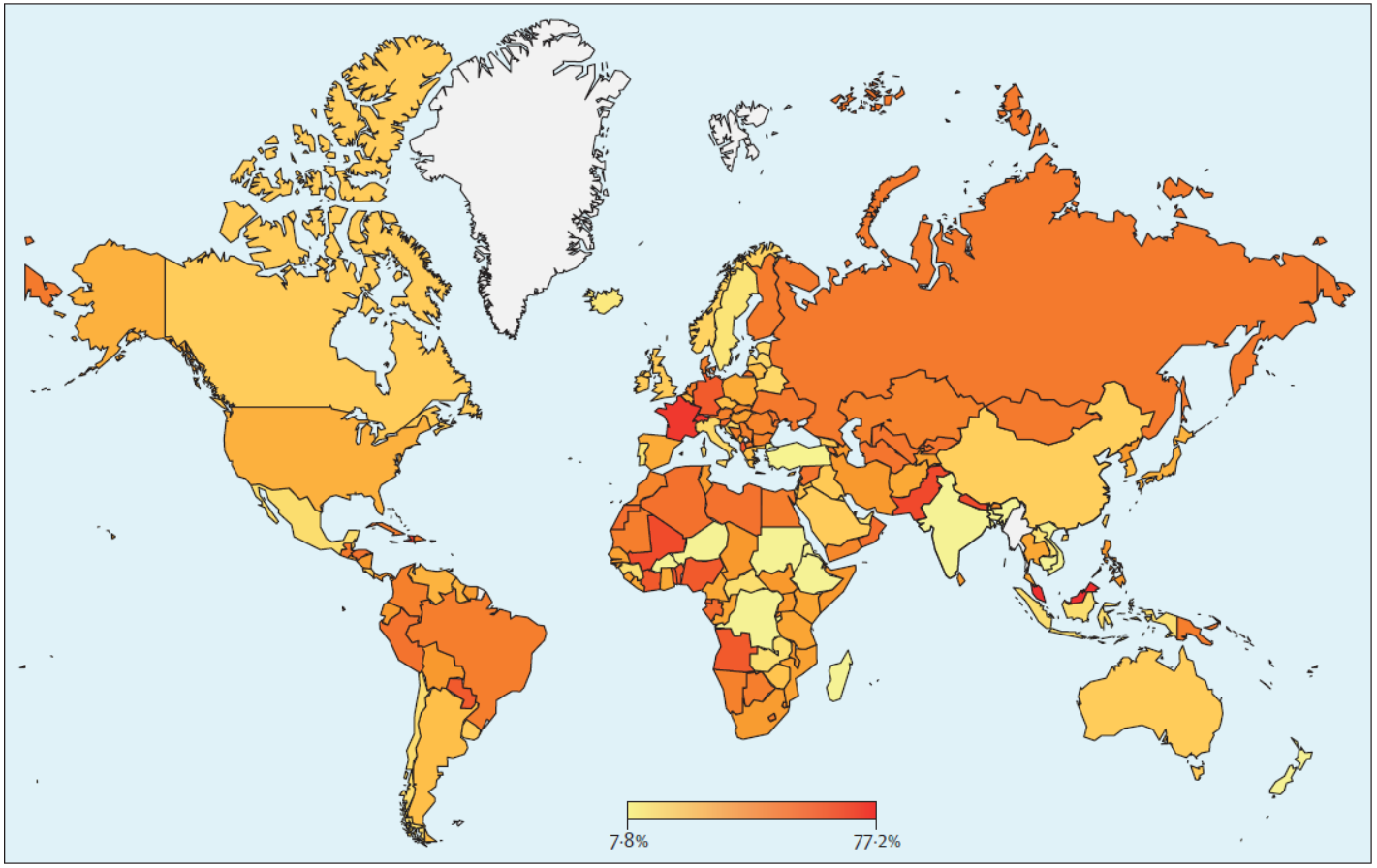
- Stoppages in breathing during sleep
- Associated with neurocognitive and cardiovascular sequelae
- Risk factors including aging, obesity, male gender

Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis

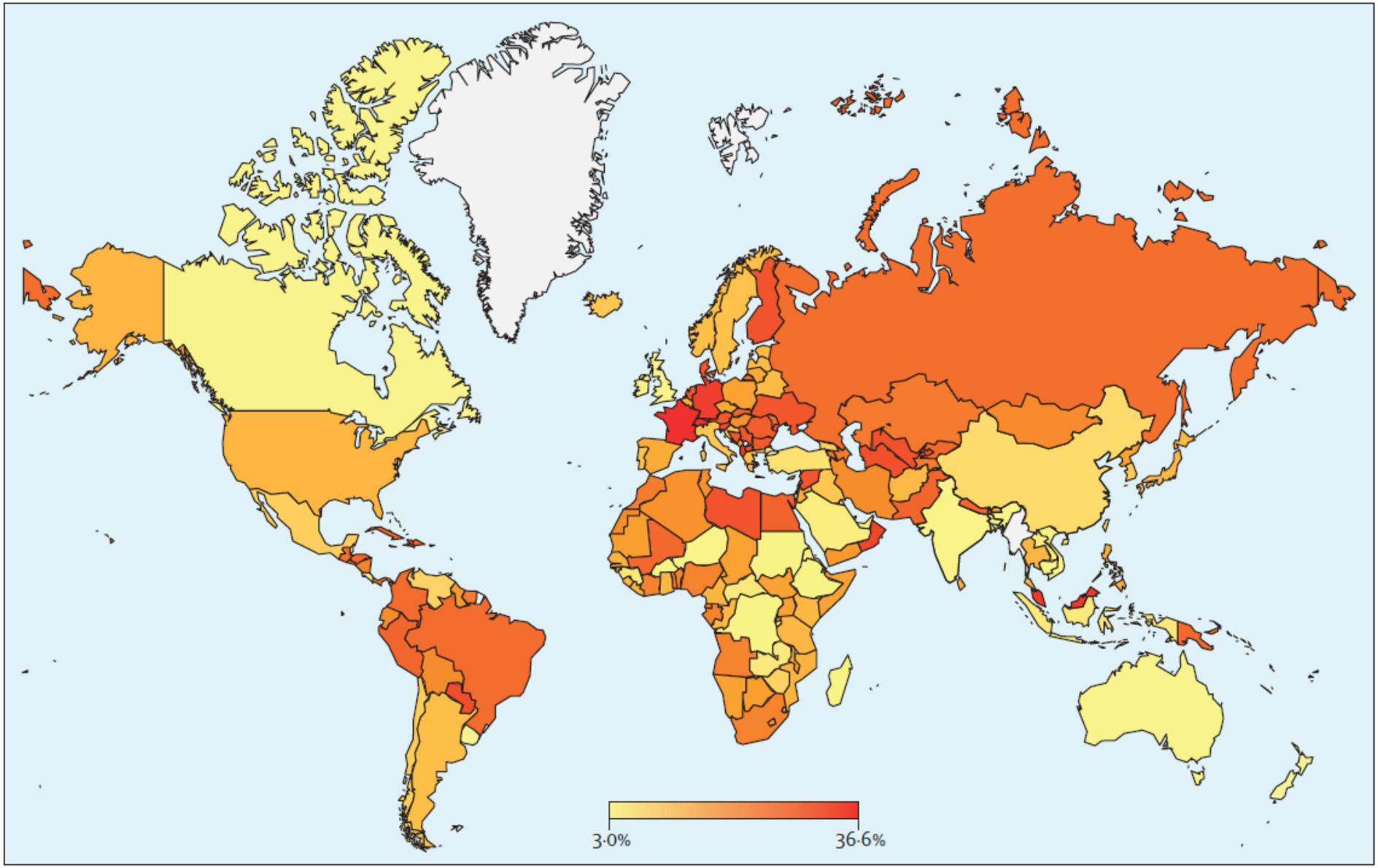
Adam V Benjafield, Najib T Ayas, Peter R Eastwood, Raphael Heinzer, Mary S M Ip, Mary J Morrell, Carlos M Nunez, Sanjay R Patel, Thomas Penzel, Jean-Louis D Pépin, Paul E Peppard, Sanjeev Sinha, Sergio Tufik, Kate Valentine, Atul Malhotra

AHI ≥ 5

936,360,689



Lancet Respiratory Medicine 2019

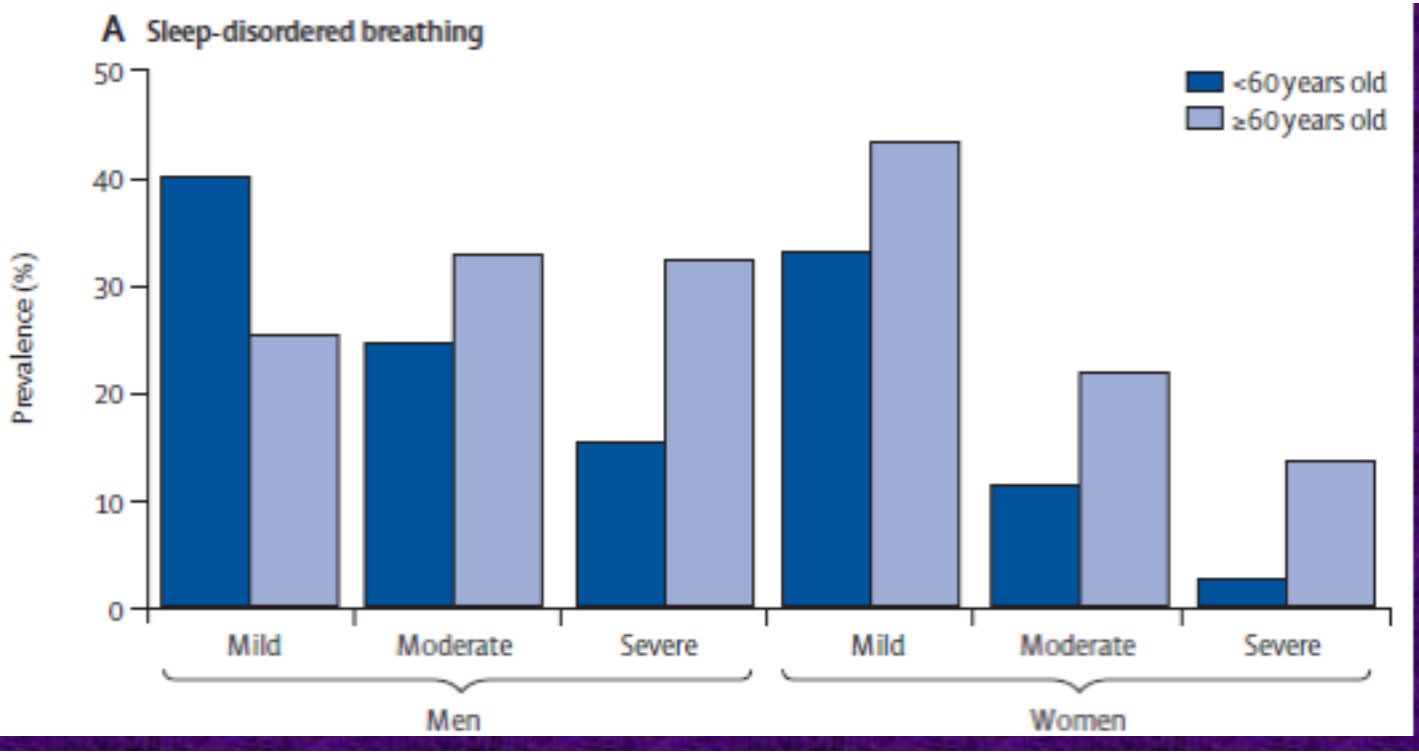


AHI ≥ 15

424,630,028

Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study

R Heinzer, S Vat, P Marques-Vidal, H Marti-Soler, D Andries, N Tobback, V Mooser, M Preisig, A Malhotra, G Waeber, P Vollenweider, M Tafti,* I Haba-Rubio*



LRM 2015

(7·2–27·1) in men. The prevalence of moderate-to-severe sleep-disordered breathing (≥15 events per h) was 23·4% (95% CI 20·9–26·0) in women and 49·7% (46·6–52·8) in men. After multivariable adjustment, the upper quartile

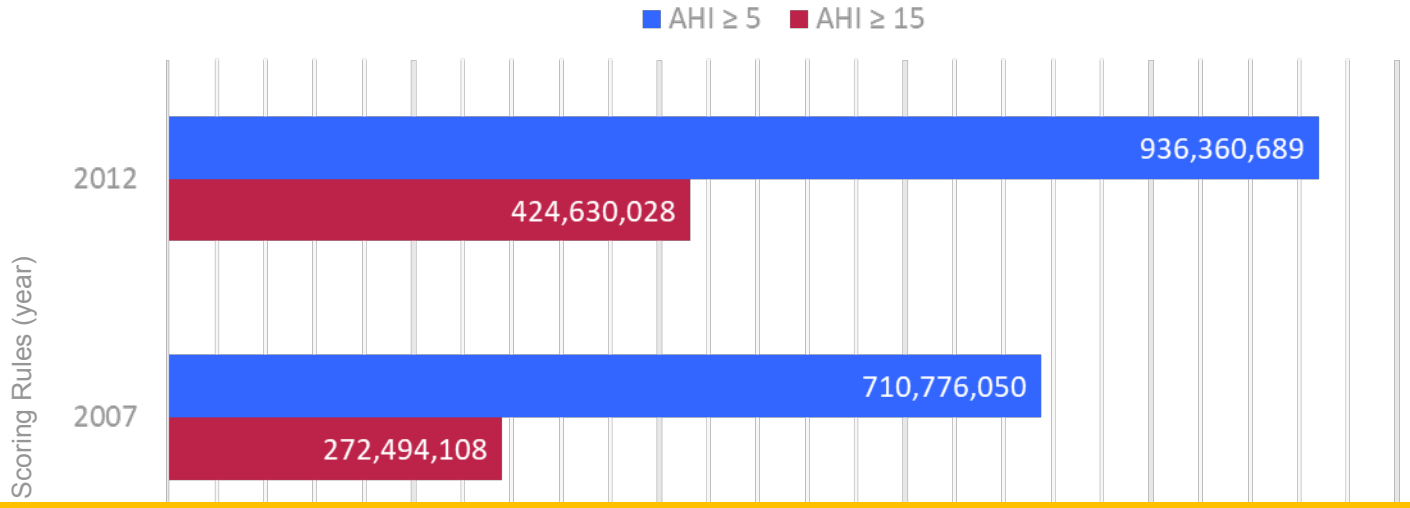
Multivariate: AHI predicts HTN, DM, depression

Concept: OSA is highly prevalent, but not all are likely to get cardiovascular benefit from CPAP

Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis

Adam V Benjafield, Najib T Ayas, Peter R Eastwood, Raphael Heinzer, Mary S M Ip, Mary J Morrell, Carlos M Nunez, Sanjay R Patel, Thomas Penzel, Jean-Louis D Pépin, Paul E Peppard, Sanjeev Sinha, Sergio Tufik, Kate Valentine, Atul Malhotra

Results – Scoring Rule Impact



Take Home:

OSA affects up to 1 billion people. Numbers vary with scoring criteria and equipment but we need to think how to address this global burden

ORIGINAL ARTICLE

CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea

R. Doug McEvoy, M.D., Nick A. Antic, M.D., Ph.D., Emma Heeley, Ph.D., Yuanming Luo, M.D., Qiong Ou, M.D., Xilong Zhang, M.D., Olga Mediano, M.D., Rui Chen, M.D., Luciano F. Drager, M.D., Ph.D., Zhihong Liu, M.D., Ph.D., Guofang Chen, M.D., Baoliang Du, M.D., Nigel McArdle, M.D., Sutapa Mukherjee, M.D., Ph.D., Manjari Tripathi, M.D., Laurent Billot, M.Sc., Qiang Li, M.Biostat., Geraldo Lorenzi-Filho, M.D., Ferran Barbe, M.D., Susan Redline, M.D., M.P.H., Jiguang Wang, M.D., Ph.D., Hisatomi Arima, M.D., Ph.D., Bruce Neal, M.D., Ph.D., David P. White, M.D., Ron R. Grunstein, M.D., Ph.D., Nanshan Zhong, M.D., and Craig S. Anderson, M.D., Ph.D., for the SAVE Investigators and Coordinators*

Therapy with CPAP plus usual care, as compared with usual care alone, did not prevent cardiovascular events in patients with moderate-to-severe obstructive sleep apnea and established cardiovascular disease. (Funded by the National Health and Medical Re-

NEJM 2016

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Need better therapies/adherence
Need to identify high risk patients better
Need more basic research re: mechanisms

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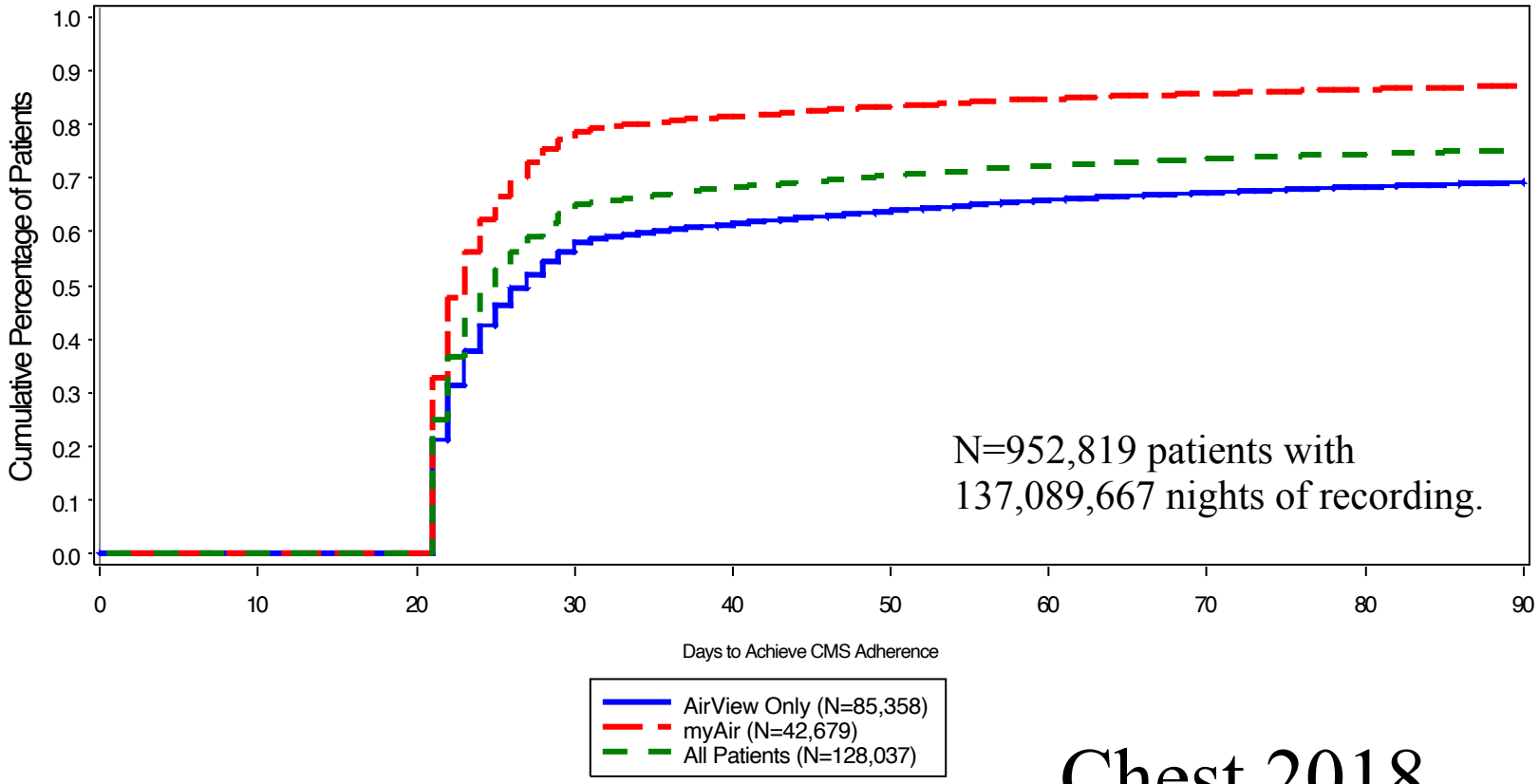
NEJM 2016

Patient Engagement Using New Technology to Improve Adherence to Positive Airway Pressure Therapy

A Retrospective Analysis

Atul Malhotra, MD; Maureen E. Crocker, BS; Leslee Willes, MS; Colleen Kelly, PhD; Sue Lynch, RN; and Adam V. Benjafield, PhD



Chest 2018

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medXcloud

Chest 2018

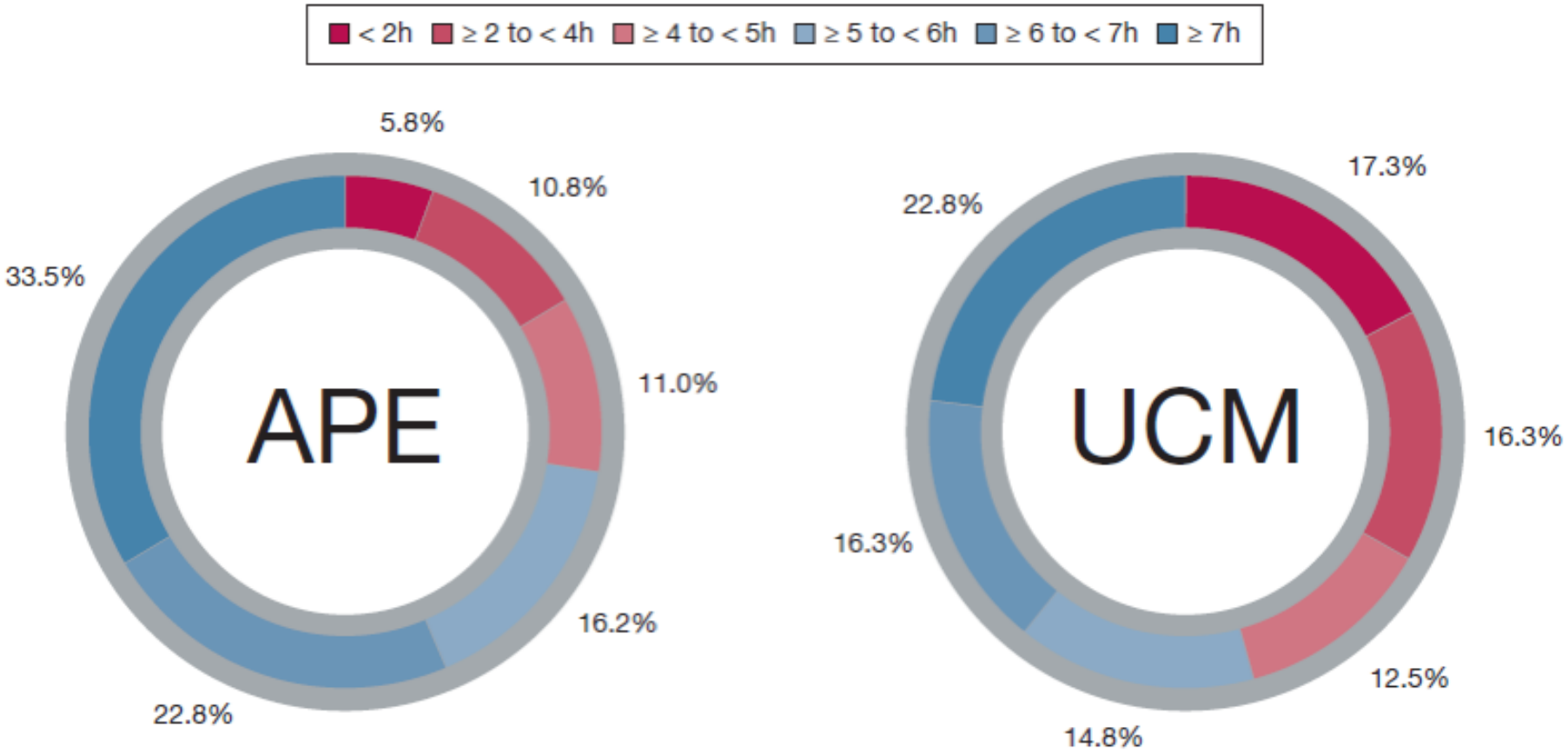

Figure 2 – *Distribution of mean nightly positive airway pressure usage. See Figure 1 legend for expansion of abbreviations.*

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Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Brief Communication

Short-term CPAP adherence in obstructive sleep apnea: a big data analysis using real world data

Peter A. Cistulli [a, g, *], Jeff Armitstead [b, g], Jean-Louis Pepin [c, g], Holger Woehrle [d, g], Carlos M. Nunez [e, g], Adam Benjafield [e, g], Atul Malhotra [f, g]

Table 1
Adherence data from the first 90 days of therapy.

Adherence measures	Values (n = 2,621,182) Median (IQR)[a]
CMS compliance in first 90 days, n (%)	1,955,961 (74.6)
Time to achieve CMS compliance, days	23.00 (21.00, 27.00)
Device usage, h/session	6.18 (4.79, 7.35)
Daily usage (all days), h/night	5.54 (3.42, 7.64)
Proportion of days with non-zero usage, %	93.3 (72.2, 98.9)
Proportion of days compliant (usage ≥ 4 h/night), %	80.0 (46.7, 95.6)

CMS, Center for Medicare and Medicaid Services; IQR, interquartile range; SD, standard deviation. CMS Compliance definition: ≥4 hours' PAP use on 70% of nights in a consecutive 30-day period in the first 90 days of therapy.

Nasal CPAP is the Treatment of Choice

- Improves symptoms
- Improves blood pressure
- Transformative for some patients
- A defeatist attitude towards CPAP is not justified

- Need new therapies based on ongoing research