How To Reduce CPAP With Better Results

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HOMELESS
WITH 2 YEAR

Disclosures

- None

My Challenge

- Have you worn CPAP???

Masque
GRAVITY
HATFIELDS
RONIN

Technion-Israel Institute of Technology President Prof. Peretz Lavie – a psychologist and one of the country's leading sleep medicine experts – and his wife and fellow researcher cell biologist, Dr. Lena Lavie, have found that in elderly people, moderate apnea may in fact extend their lives rather than shorten it.

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Decreased inspired oxygen stimulates *de novo* formation of coronary collaterals in adult heart

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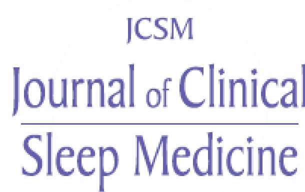
Relation of Obstructive Sleep Apnea in Patients With a Coronary Chronic Total Occlusion to Coronary Collaterals and Mortality

Usaid K. Allahwala, MBBS[a,b,*], Peter A. Cistulli, MBBS, PhD[c,d], Avedis Ekmejian, MBBS[a], Nadeem Mughal, B App Sci Med Rad[a], Hasthi U. Dissanayake, PhD[d], Michael Ward, MBBS, PhD[a], James C Weaver, MBBS, PhD[b,e], and Ravinay Bhindi, MBBS, PhD[a,b]

A chronic total occlusion (CTO) is frequently identified in patients undergoing coronary angiography. The prognostic implications of intermittent hypoxia from obstructive sleep apnea (OSA) on patients with a CTO, and effects on collateral recruitment are unknown. The aim of this study was to determine the prevalence, vascular effects, and prognostic implications of the presence of OSA in patients with a CTO. Patients with a CTO between July 2010 and December 2019 were reviewed. Electronic medical records were accessed to determine documented patient history of OSA, demographics, and clinical course. Patients with robust collateral recruitment were defined as Rentrop grade 2 or 3. A total of 948 patients were included in the study, of which 127 (13.4%) had a documented history of OSA. These patients were younger (67.0 years vs 70.6 years, $p < 0.01$), had a higher body mass index (29.6 kg/m^2 vs 26.7 kg/m^2, $p < 0.0001$), higher rates of hypertension (91.3% vs 83.2%, $p < 0.05$), higher rates of smokers (63.3% vs 49.0%, $p < 0.01$) and more use of β-blockers (79% vs 68.5%, $p < 0.05$) and statins (92.7% vs 82.1%, $p < 0.01$). A documented history of OSA was independently associated with robust collaterals (OR 3.0 95%CI 1.5 to 5.8, $p < 0.01$) and lower mortality (HR 0.3 95% CI 0.1 to 0.7, $p < 0.01$) with a mean survival of 10.8 years, as compared to 8.1 years (log rank $p < 0.0001$). In conclusion, in patients with a CTO, documented OSA is independently associated with more robust coronary collaterals and lower mortality. The possible cardioprotective implications of intermittent hypoxia in OSA, as well as treatment effect requires further investigation. **© 2021 Published by Elsevier Inc.** **(Am J Cardiol 2021;148:30−35)**



SCIENTIFIC INVESTIGATIONS

Sleep Apnea in Patients Hospitalized With Acute Ischemic Stroke: Underrecognition and Associated Clinical Outcomes

Nura Festic, MD; David Alejos, MD; Vikas Bansal, MBBS, MPH; Lesia Mooney, MSN; Paul A. Fredrickson, MD; Pablo R. Castillo, MD; Emir Festic, MD, MSc

Mayo Clinic, Jacksonville, Florida

Study Objectives: To evaluate clinical recognition of sleep apnea and related outcomes in patients hospitalized with acute ischemic stroke.

Methods: A retrospective study of all patients hospitalized with acute ischemic stroke from April 2008 to December 2014. The primary predictor and outcome variables were sleep apnea and hospital mortality, respectively. Secondary outcomes were mechanical ventilation, hospital length of stay, and the survivor's functional level by the modified Rankin scale. A sensitivity multivariate regression analysis included the propensity score for cardiovascular comorbidities and sleep apnea.

Results: Of 989 patients, 190 (19%) were considered to have sleep apnea. Only 42 patients (22%) received any treatment for sleep apnea during the hospital stay. Despite higher prevalence of cardiovascular comorbidities, the patients with sleep apnea had lower hospital mortality, 1% versus 5.6% in patients without sleep apnea (odds ratio [OR] 0.18; 95% confidence interval [CI], 0.03–0.58, $P = .002$). Only the National Institutes of Health Stroke Scale (NIHSS) and the Glasgow coma scale (GCS) were significant predictors of adjusted hospital mortality (OR 1.06, 95% CI 1.01–1.11, $P = .01$ and OR 0.61, 95% CI 0.51–0.69, $P \leq .001$, respectively). A composite clinical propensity score for sleep apnea and cardiovascular comorbidities was significantly associated with decreased mortality, independent to either NIHSS (OR 0.11, 95% CI 0.017–0.71; $P = .02$) or GCS (OR 0.07, 95% CI 0.01–0.52; $P = .01$).

Conclusions: Prevalence of sleep apnea in our study was low, likely because of clinical underrecognition. Despite having more cardiovascular disease, the patients with acute stroke and sleep apnea had less severe neurological injury and lower unadjusted mortality than those without a history of sleep apnea.

Keywords: acute ischemic stroke, ischemic preconditioning, mortality, obstructive sleep apnea

Citation: Festic N, Alejos D, Bansal V, Mooney L, Fredrickson PA, Castillo PR, Festic E. Sleep apnea in patients hospitalized with acute ischemic stroke: underrecognition and associated clinical outcomes. *J Clin Sleep Med.* 2018;14(1):75–80.

Original work | Published: 31 March 2022

Effect of Obstructive Sleep Apnea on Outcomes After Traumatic Brain Injury: A Retrospective Cohort Analysis

Talha Mubashir, Hunza S. Ahmad, Hongyin Lai, Rabail Chaudhry, Vahed Maroufy, Julius Balogh, Biai Dominique, Ray Hwong, Frances Chung & George W. Williams

Neurocritical Care **37**, 228–235 (2022) | Cite this article

363 Accesses | Metrics

Conclusions

Patients with TBI with underlying OSA diagnosis were older and had higher comorbidity burden; however, hospital mortality was lower. Pre-existing OSA may result in protective physiologic changes such as hypoxic-ischemic preconditioning especially to cardiac and neural tissues, which can provide protection following neurological trauma, which may lead to a reduction in mortality.

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Increasing the Adaptive Potential, Endurance and Working Capacity of the Brain

Elena A. Rybnikova[1], Natalia N. Nalivaeva[1,2], Mikhail Y. Zenko[1] and Ksenia A. Baranova[1]*

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This review is devoted to the phenomenon of intermittent hypoxic training and is aimed at drawing the attention of researchers to the necessity of studying the mechanisms mediating the positive, particularly neuroprotective, effects of hypoxic training at the molecular level. The review briefly describes the historical aspects of studying the beneficial effects of mild hypoxia, as well as the use of hypoxic training in medicine and sports. The physiological mechanisms of hypoxic adaptation, models of hypoxic training and their effectiveness are summarized, giving examples of their beneficial effects in various organs including the brain. The review emphasizes a high, far from being realized at present, potential of hypoxic training in preventive and clinical medicine especially in the area of neurodegeneration and age-related cognitive decline.

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CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea

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Sleep for Stroke Management and Recovery Trial (Sleep SMART): Rationale and methods.

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Obtaining Valid Estimates of the Effect of CPAP Therapy

Reducing Healthy Adherer and Other Biases in Observational Studies

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Bruce M. Psaty, MD, PhD
Seattle, WA

Randomized controlled trials (RCTs) treating OSA with CPAP have demonstrated improvements for outcomes that can be assessed over the short-term, including improved quality of life and sleepiness despite moderate CPAP adherence.[1] Short-term RCTs have also demonstrated that CPAP therapy reduces BP, especially in patients with elevated BP, with severe OSA, and with good adherence to CPAP therapy.[2] In contrast, RCTs have failed to demonstrate improvements in long-term cardiovascular outcomes, including incident hypertension, coronary artery disease, heart failure, stroke, and cardiovascular mortality.[1] Because of ethical concerns about randomizing patients with severe symptomatic OSA and the difficulty in achieving optimal long-term CPAP adherence, these health outcome trials, which excluded patients most likely to benefit, represent an incomplete test of the efficacy and safety of CPAP. To provide evidence about major health outcomes, investigators have advocated for carefully designed observational studies in clinical populations that include more symptomatic and highly adherent CPAP users.[1] The challenge is to identify a comparison group and a set of methods that provide valid and unbiased estimates of association.

FOR RELATED ARTICLE, SEE PAGE 1657

AFFILIATIONS: From the Department of Medicine (V. K. Kapur and B. M. Psaty); the Division of Pulmonary, Critical Care and Sleep Medicine (V. K. Kapur); and the Cardiovascular Health Research Unit, Departments of Epidemiology and Health Systems and Population Health (B. M. Psaty), University of Washington.

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In this issue of *CHEST*, Pepin and colleagues[3] report the association between CPAP termination in the first year of therapy and all-cause mortality over 3 years. Patients with OSA who terminated therapy were identified from a French national insurance reimbursement system database and propensity score matched to 88,007 patients with OSA who continued therapy. Continuation of CPAP therapy was associated with a lower risk of death (hazard ratio [HR], 0.61); incident heart failure (HR, 0.77) and hypertension (HR, 0.75) were also less common in this group. These results mirror the findings from prior observational studies that have shown large beneficial impacts on incident cardiovascular events and death. A strength of the current study is the huge number of patients included across France, not only providing excellent statistical power but also bolstering generalizability of findings. As acknowledged by the authors, potentially important confounding factors were not measured and adjusted for. Among these are clinically important factors related to OSA, such as physiologic severity, symptoms (sleepiness), the level of systolic BP, and BMI, some of which have been considered in some prior studies.[4-7]

Observational designs that include comparison groups that receive active therapies with similar indications and use patterns show better agreement with RCT findings.[8] In contrast, comparing a treatment of interest with non-users or nonadherent participants is fraught with difficulty. In observational studies, differences between study groups can confound the association with the outcome. A particularly vexing form of bias, termed the healthy adherer bias, is particularly relevant to comparisons between patients with OSA who are adherent and those who are nonadherent to CPAP therapy. Individuals who choose to use or adhere to CPAP therapy are more likely to use other preventative behaviors (eg, diet or exercise) or to be more adherent to other interventions (eg, medications), which might lead to beneficial effects independent of CPAP effect. This bias, which has typically not been addressed in observational studies of CPAP, is likely to appreciably influence their results. Observational study comparisons

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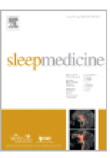
Sleep Medicine
Volume 96, August 2022, Pages 119-121



Effect of positive airway pressure therapy of obstructive sleep apnea on circulating Angiopoietin-2

Daniel J. Gottlieb [a b], David J. Lederer [c], John S. Kim [d], Russell P. Tracy [e], Su Gao [f], Susan Redline [b], Sanja Jelic [f]

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Highlights

- Obstructive sleep apnea is associated with biomarkers of systemic inflammation.
- CPAP did not reduce biomarkers of alveolar epithelial and endothelial injury.
- Angiopoietin-2, a marker of endothelial injury and CVD risk, increased with CPAP.
- Increased lung stretch due to CPAP may be associated with vascular inflammation.
- This unexpected effect may limit the cardiovascular benefit of CPAP.

CPAP may promote an endothelial inflammatory milieu in sleep apnoea after coronary revascularization

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Summary

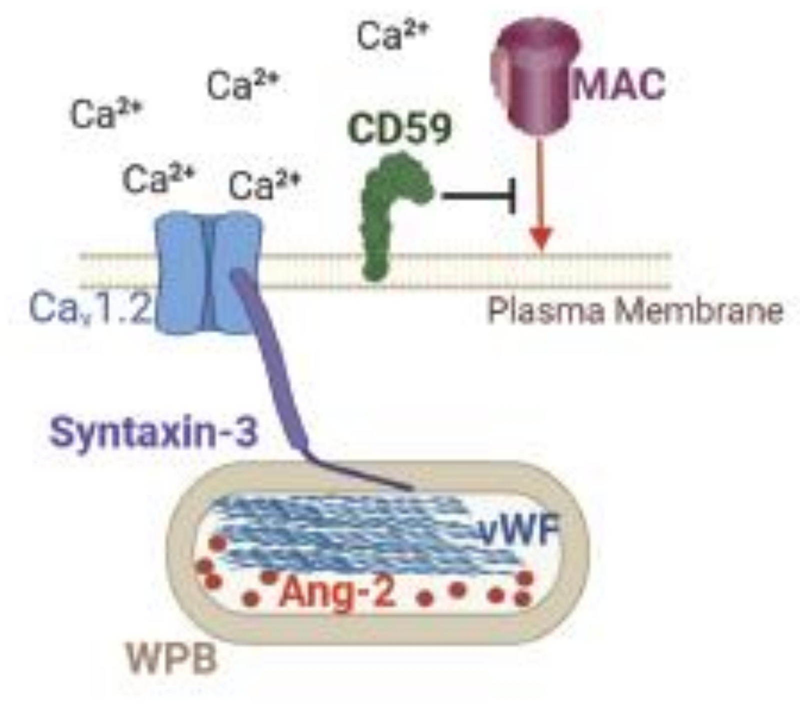
Background Continuous positive airway pressure (CPAP) has failed to reduce cardiovascular risk in obstructive sleep apnoea (OSA) in randomized trials. CPAP increases angiopoietin-2, a lung distension-responsive endothelial proinflammatory marker associated with increased cardiovascular risk. We investigated whether CPAP has unanticipated proinflammatory effects in patients with OSA and cardiovascular disease.

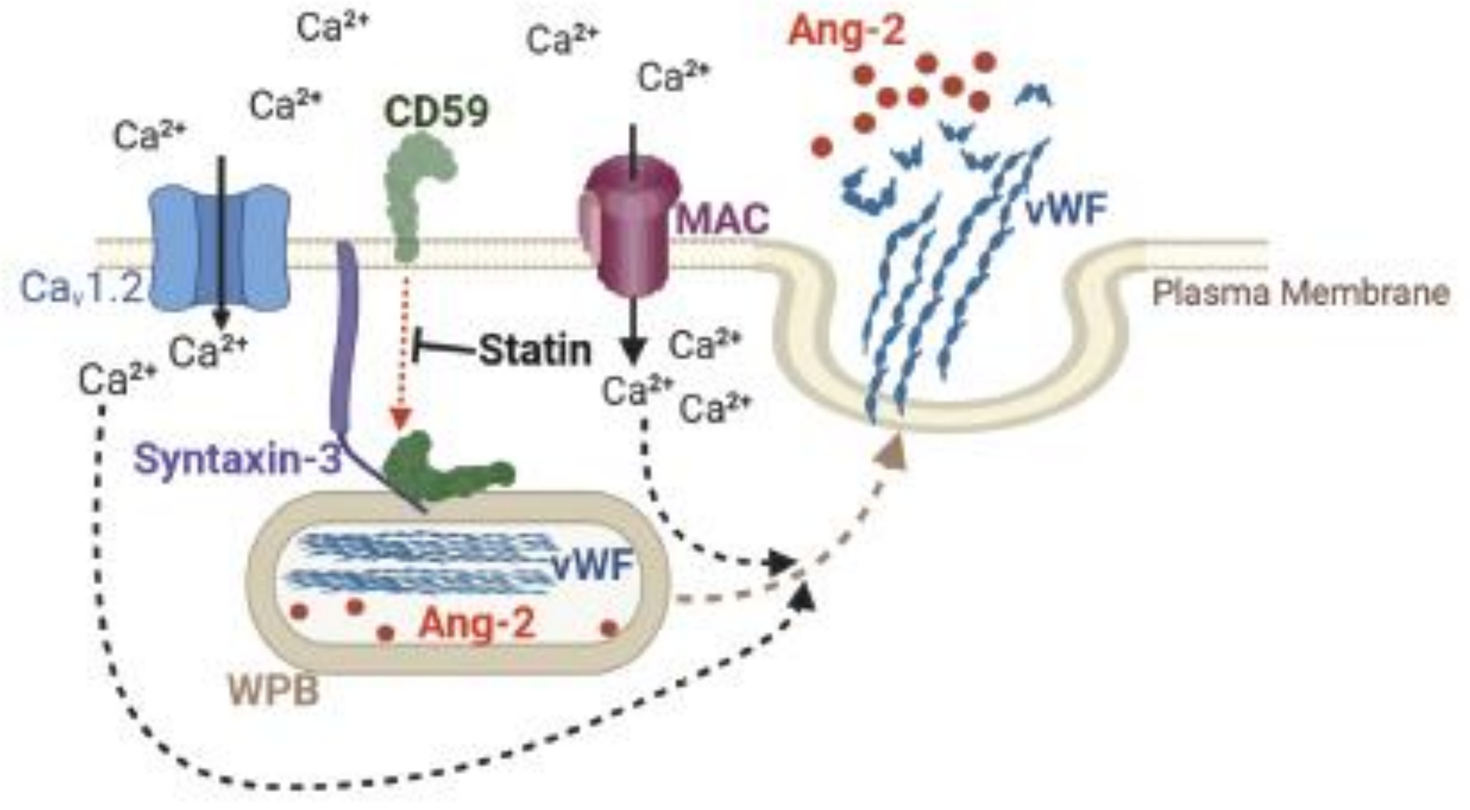
eBioMedicine
2024;101: 105015
Published Online 24 February 2024
https://doi.org/10.1016/j.ebiom.2024.105015

Conclusions: This finding raises concern for a possible adverse impact of PAP therapy on vascular endothelium.

Keywords: Angiopoietin-2; Lung injury; Obstructive sleep apnea; Positive airway pressure.

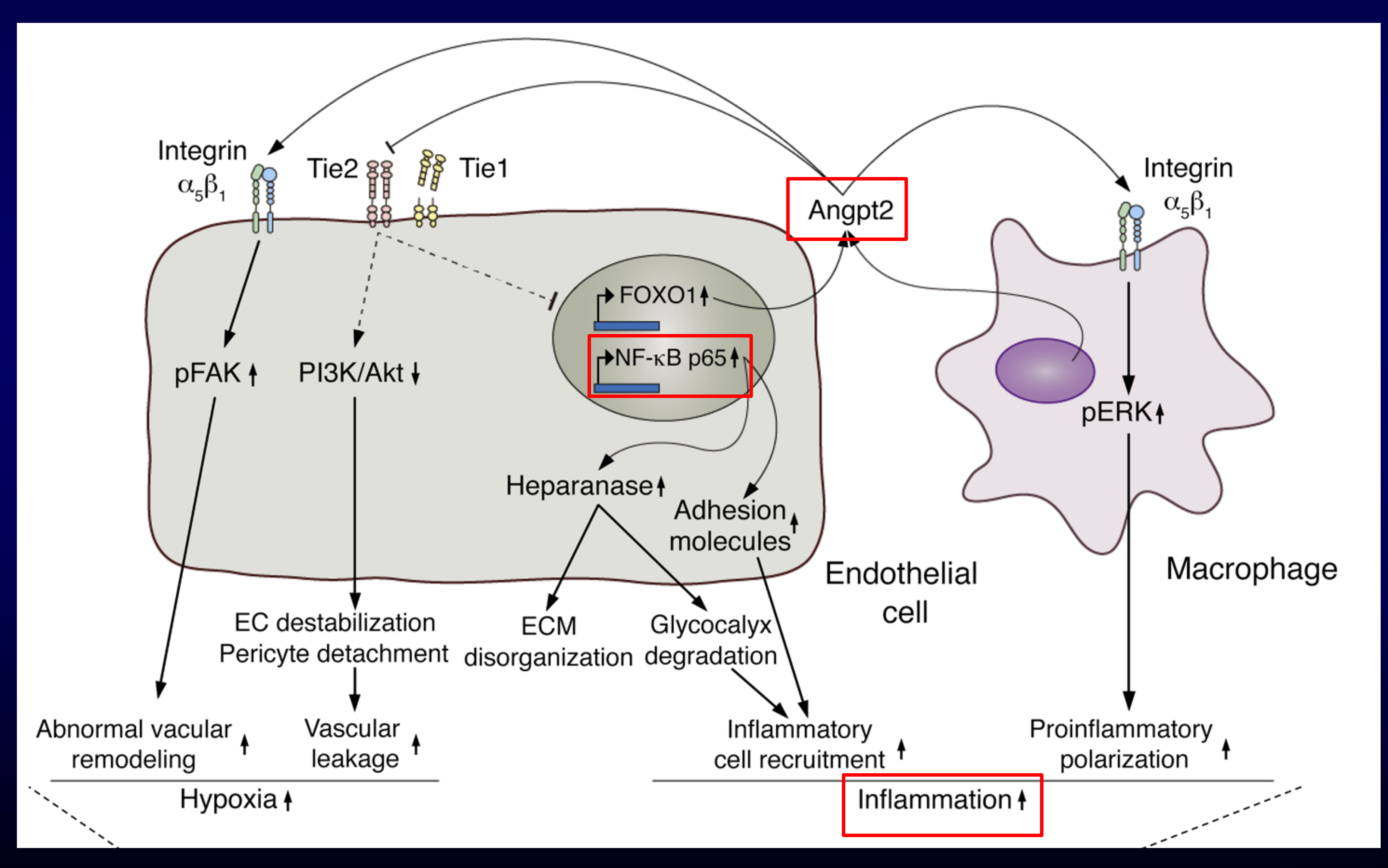
Angiopoietin-2 is stored in Weibel-Palade bodies of endothelial cells and released in response to hypoxemia





Gao, Sleep 2021;44:zsaa286

Angiopoietin-2 is a mediator of endothelial inflammation



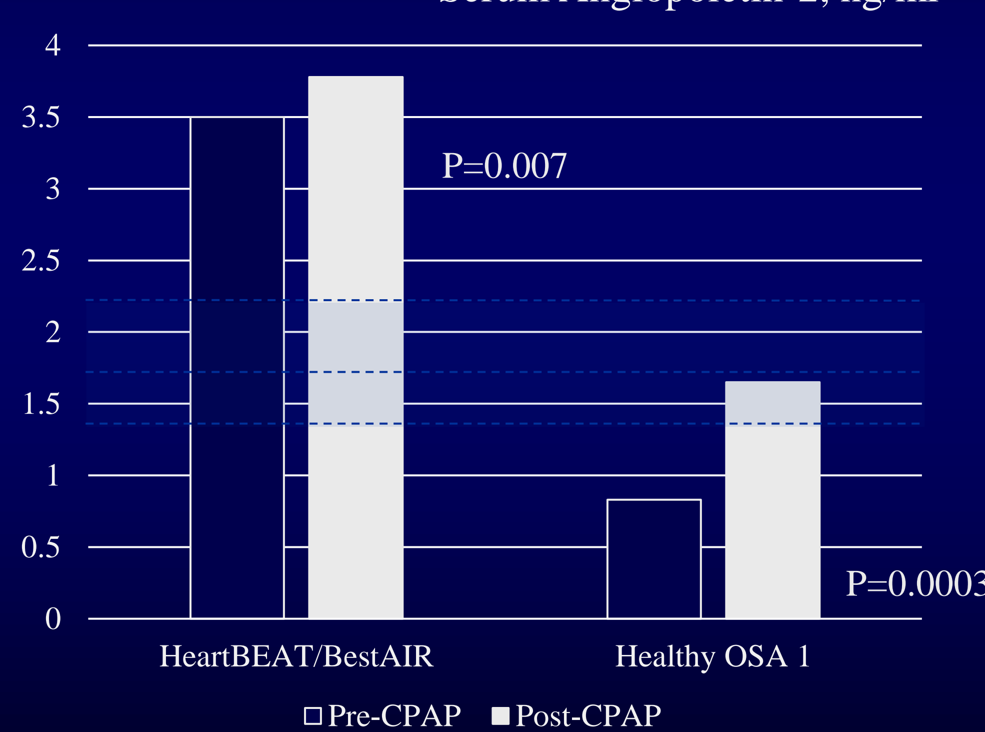
Lee, J Clin Invest, 2018;128:5-18

Angiopoietin-2 level is associated with cardiovascular mortality

- In a population study, 1 SD higher serum concentration of Ang-2 was associated with a HR of 1.32 (1.18-1.49) for cardiovascular mortality
- In 2 clinical cohorts of patients with acute coronary syndrome, 1 SD higher plasma concentration of Ang-2 was associated with HR 1.19 (1.05-1.35) and 1.56 (1.30-1.88) for 5-year mortality

Hypoxia-related increases in Ang-2 release might contribute to OSA-related cardiovascular risk

CPAP eliminates OSA-related hypoxemia – but paradoxically increases circulating level of angiopoietin-2



<u>HeartBEAT/BestAIR Discovery Cohort</u>

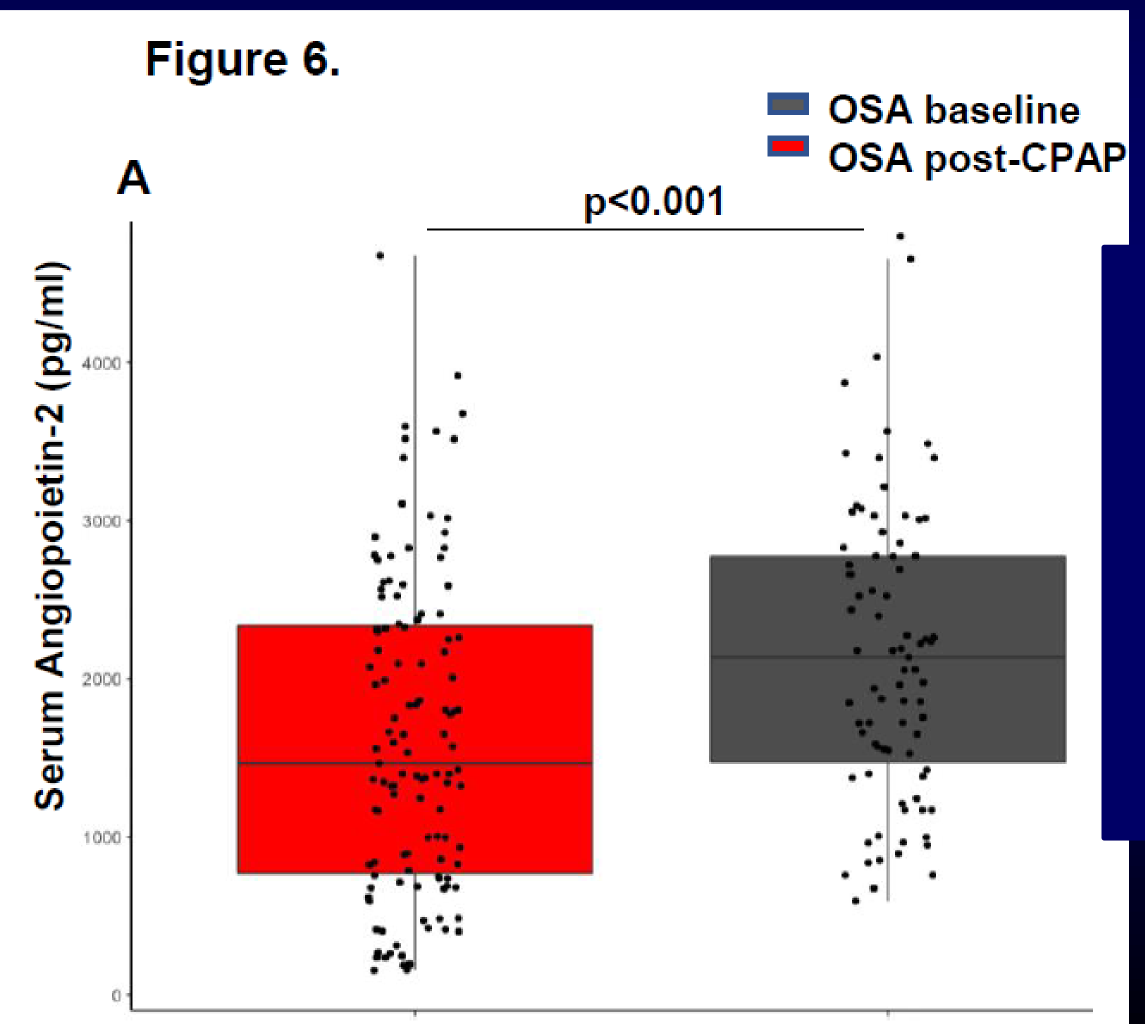
- 77 participants with OSA and CVD or multiple CVD risk factors from HeartBEAT and BestAIR trials
- AHI-3% 30.2 (SD 11.4) on HSAT
- Treatment with CPAP for 3 or 6 months
- CPAP adherence 5.9 (SD 1.4) hours/night

<u>Healthy OSA Replication Cohort</u>

- 11 health-screened patients, no chronic illness except HTN
- AHI-3% 24.5 (SD 29.4) on PSG
- Treatment with CPAP for 4 weeks
- CPAP adherence 5.5 (SD 1.3) hours/night

Gottlieb, Sleep Med 2022;96:119

CPAP eliminates OSA-related hypoxemia – but paradoxically increases circulating level of angiopoietin-2



Replication Cohort 2

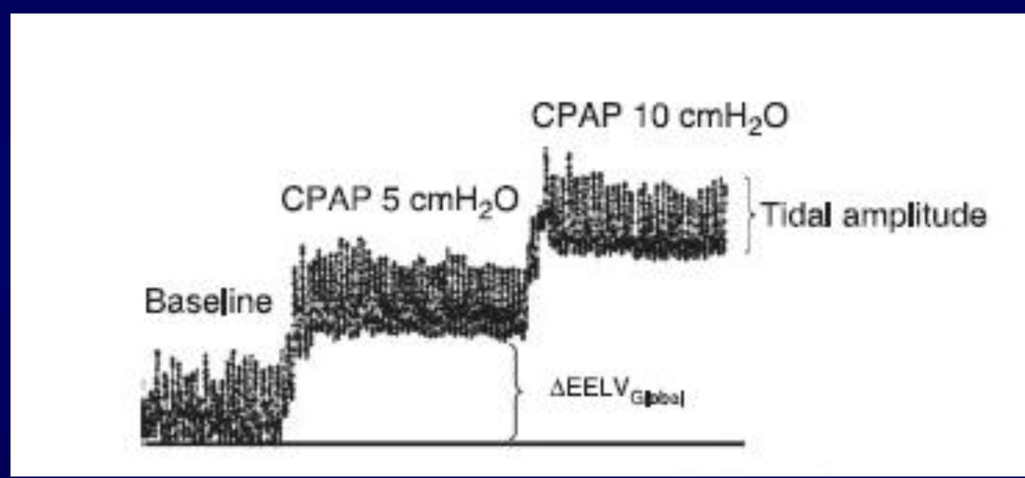
- 83 newly diagnosed OSA patients
- AHI-3% 29.8 (SD 28) on PSG
- Treatment with CPAP for 4 weeks
- CPAP adherence 3.0 (SD 3.1) hours/night

- Increase in Ang-2 driven by the adherent participants

Shah, Annals ATS 2023;20:1029

Why does CPAP increase levels of circulating angiopoietin-2?

- CPAP causes a large increase in lung volume
  - 10 cm PAP increases FRC by >1L



- Endothelial cells stretched by 20% rapidly increase Ang-2 secretion by 2.7-fold

Craig, Anesthesiology 1972;36:540
Abboud, Anesthesiology 1975;42:138
Andersson, Acta Anesthesiol Scand 2010;55:157
Chang, Clin Sci 2003;104:421

Hypothesis

CPAP-induced lung inflation causes pulmonary vascular inflammation, analogous to ventilator-induced lung injury, with release of angiopoietin-2

The systemic effects of this inflammation may counter the expected benefits of CPAP in reducing intermittent hypoxemia, resulting in null findings of randomized clinical trials of CPAP for prevention of MACCE

Effect of CPAP on Biomarkers of Vascular Inflammation - RICCADSA

- Patients screened for OSA (AHI >15) following coronary revascularization, excluded if ESS >10, randomized to CPAP or usual care
- 190 patients (160 men, 30 women)
  - Age 66 (SD 8), BMI 28.4 (SD 3.5), AHI 29.2 (SD 13.4)
  - CPAP adherence 3.2 (SD 2.9) hours
- Biomarkers measured at baseline and after 12 months of therapy
  - Angiopoietin-2 (endothelial inflammation, angiogenesis)
  - VEGF-A (angiogenesis)

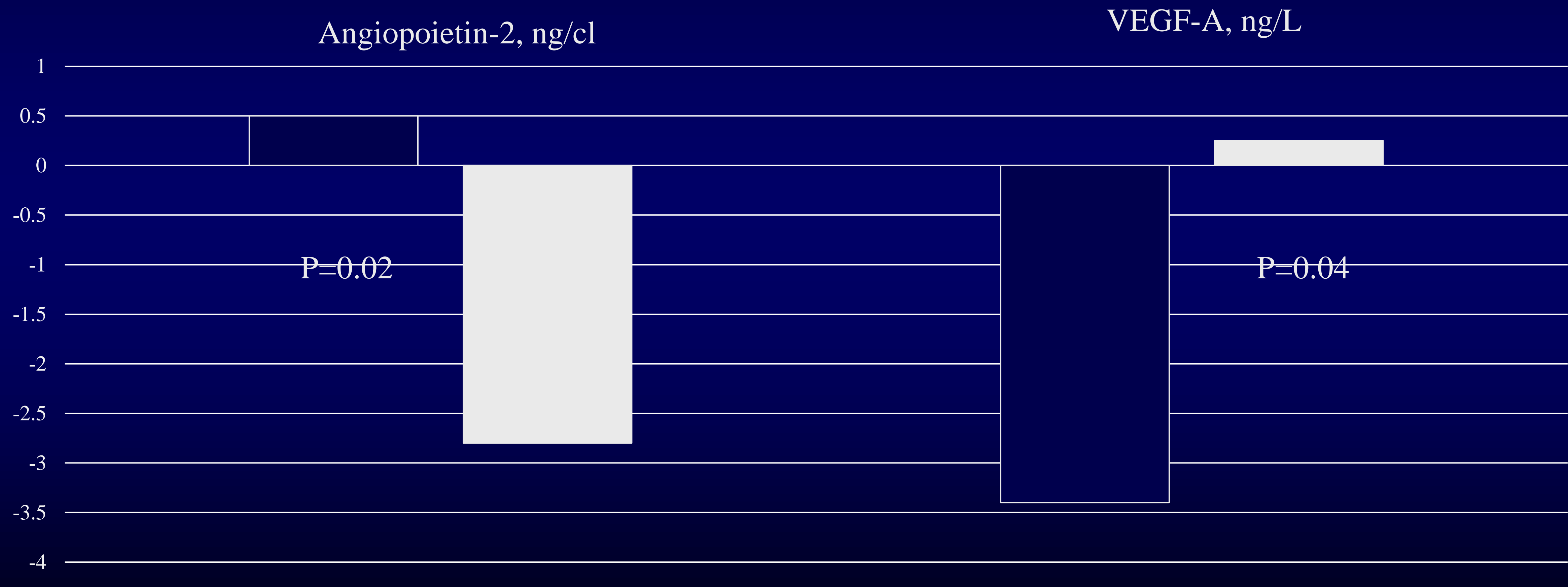
Ang-2 → High VEGF → Angiogenesis

Ang-2 → Low VEGF → Inflammation

Peker, EBioMedicine 2024; doi.org/10.1016/j.ebiom.2024.105015

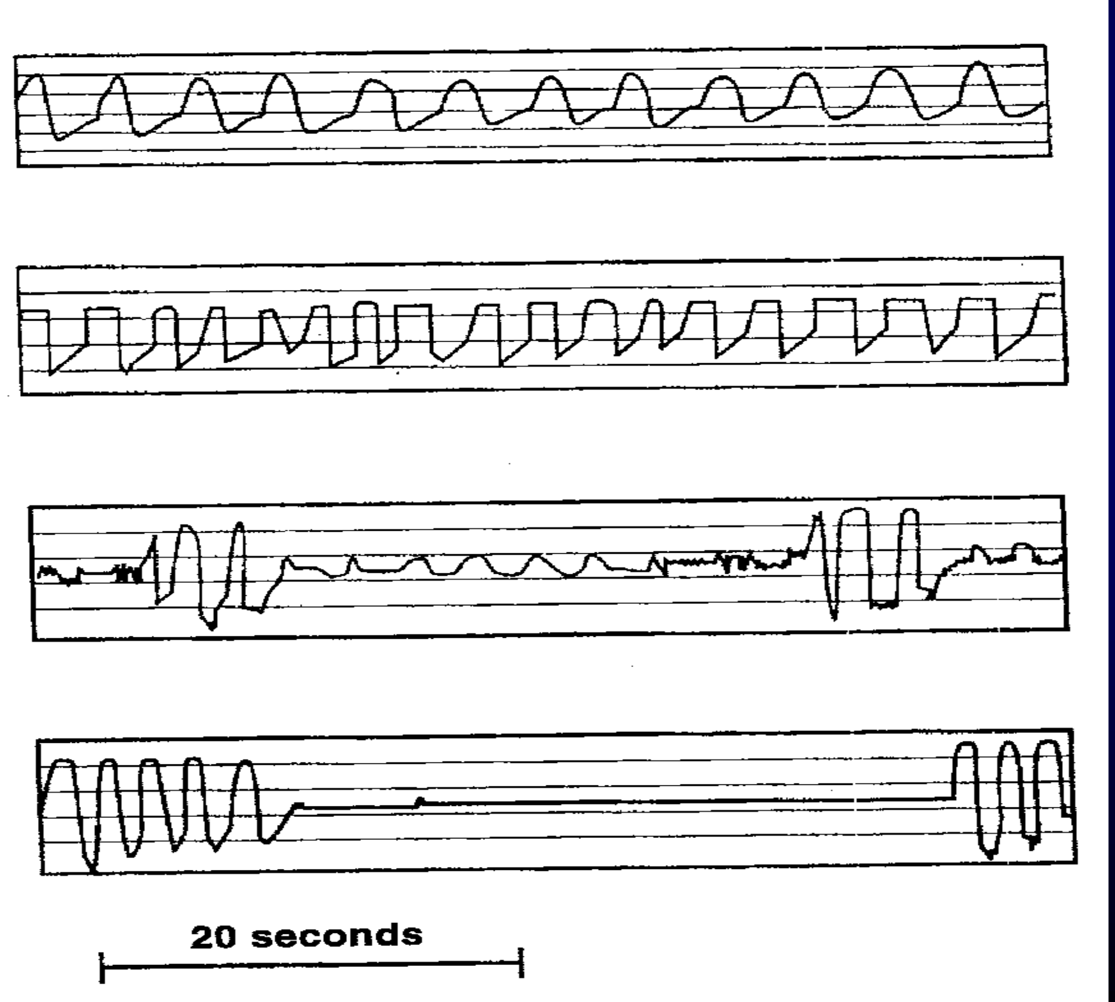
Effect of CPAP on Biomarkers of Vascular Inflammation - RICCADSA

Change in Biomarker Level over 12 months



Peker, EBioMedicine 2024; doi.org/10.1016/j.ebiom.2024.105015

What is OSA?



ORIGINAL INVESTIGATION

Predictors of Sleep-Disordered Breathing in Community-Dwelling Adults

The Sleep Heart Health Study

Terry Young, PhD; Eyal Shahar, MD, MPH; F. Javier Nieto, MD, PhD; Susan Redline, MD, MPH; Anne B. Newman, MD, MPH; Daniel J. Gottlieb, MD, MPH; Joyce A. Walsleben, PhD; Laurel Finn, MS; Paul Enright, MD; Jonathan M. Samet, MD, MS; for the Sleep Heart Health Study Research Group

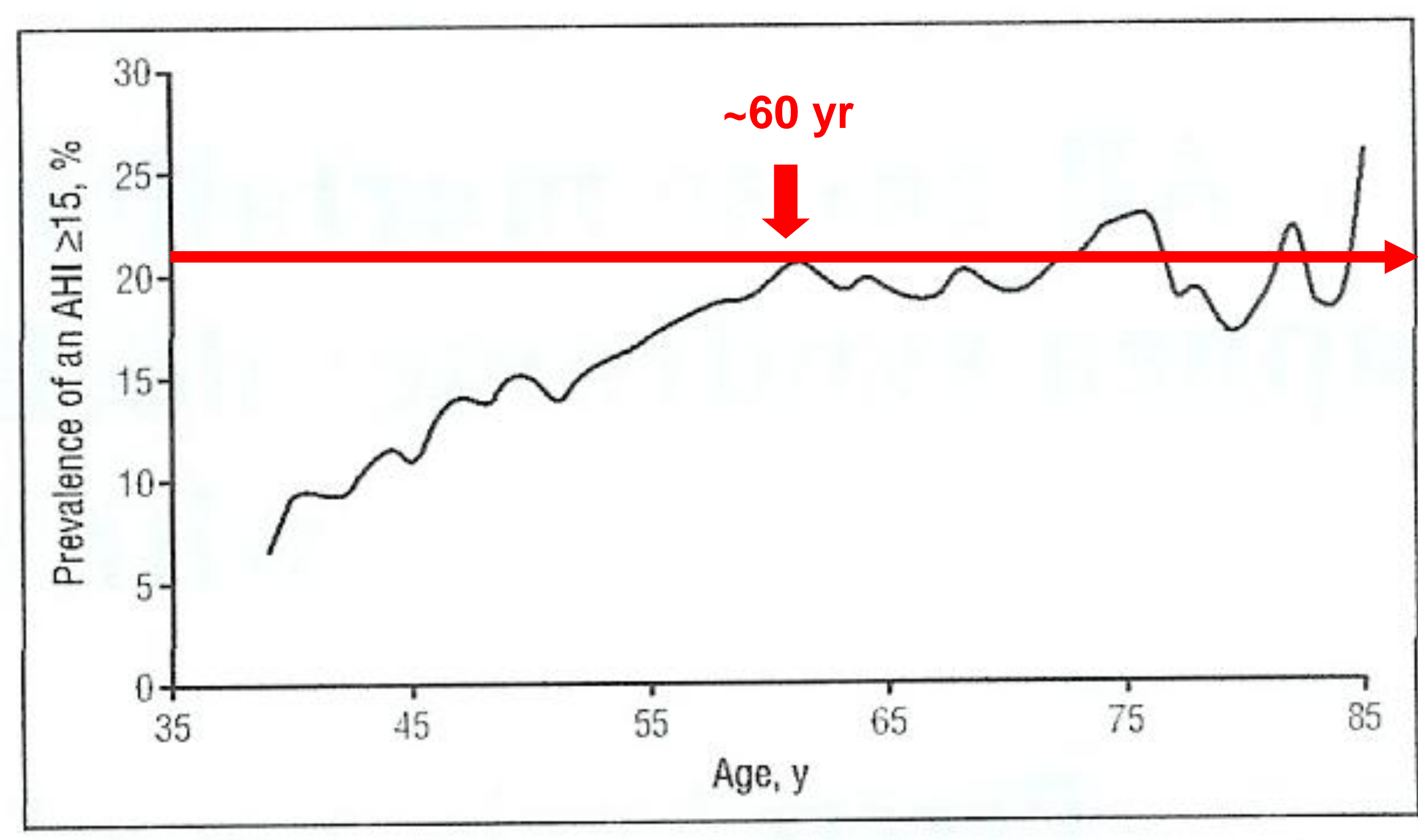
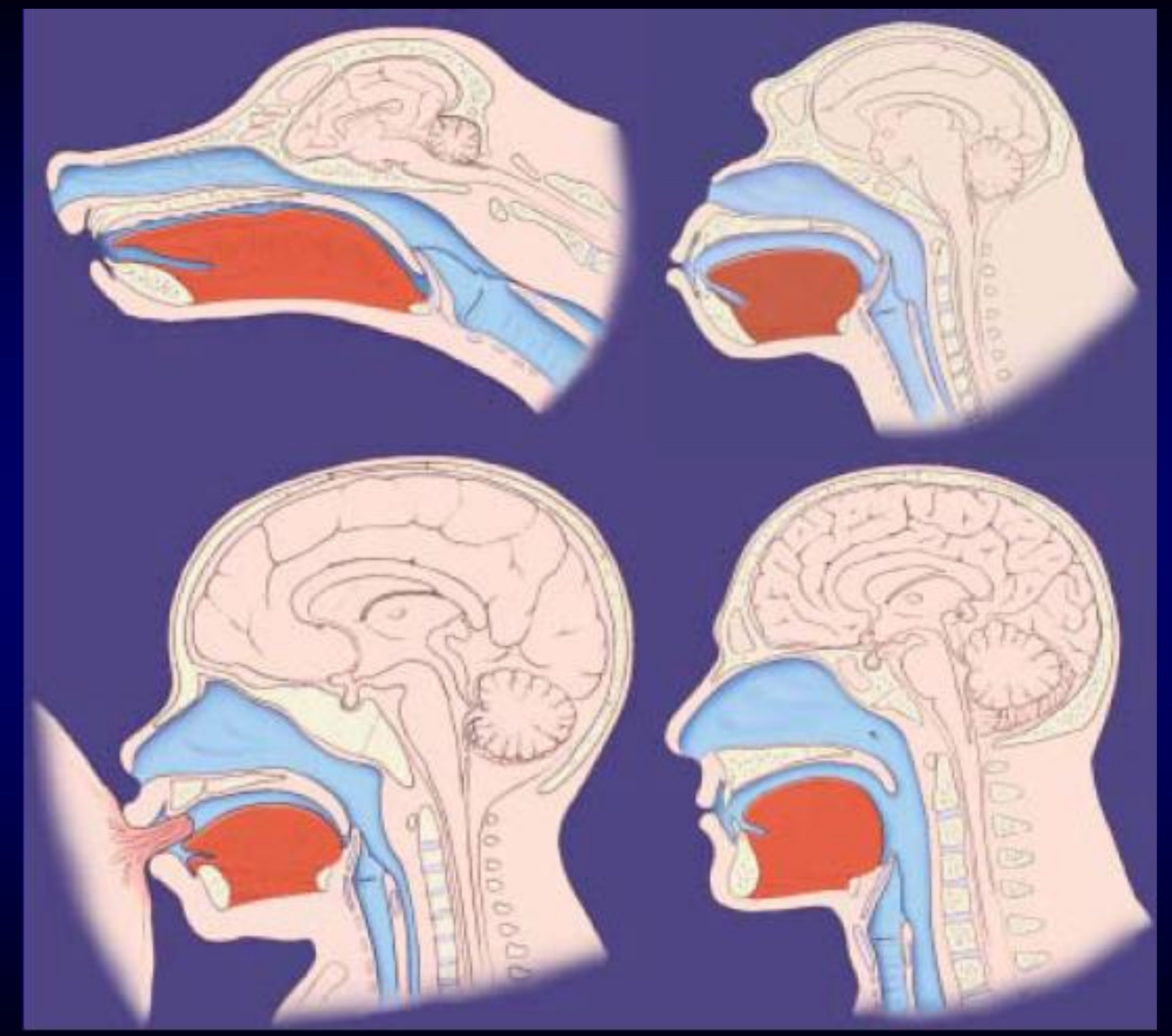


Figure 1. Smoothed plot (5-year moving average) of the prevalence of an apnea-hypopnea index (AHI) of 15 or greater by age.

Why Is Sleep Apnea So Common?

- Bipedalism
- Vocal language

- Poor olfaction
- Fewer teeth
- Smaller teeth
- Aspiration
- Collapsible segment



OSA Phenotypes

- Obstructive sleep apnea
  - No prominent sleepiness
- Obstructive sleep apnea syndrome
  - Significant excessive sleepiness
- Comorbid insomnia with OSA (COMISA)

OSA Endophenotypes

- Hypoxemic burden
- Other factors that enhance susceptibility to hypoxia, sympathetic activity, and sleep fragmentation

AHI

- Each event counts as one
- Duration, desaturation, recovery between
- Individual sensitivities
- Oxygen cycling
- Hypoxia burden
- Diet and TMAO
- Second-hand snoring
- Fragmentation
- Sympathetic tone

Potential Goals In OSA Treatment

- Eliminate snoring
- Reduce hypoxic burden
- Improve sleep continuity and reduce arousals
- Increase daytime alertness

The Agency for Healthcare Research and Quality (AHRQ)

Technology Assessment Program

Long-Term Health Outcomes in Obstructive Sleep Apnea: A Systematic Review of Comparative Studies Evaluating Positive Airway Pressure and the Validity of Breathing Measures as Surrogate Outcomes

Final
Technology Assessment
Project ID: SLPT0919
12/01/2022

- 31 RCTs and NRCTs January 2010 through March 22, 2021
- Inconsistent respiratory event tracking and AHI

low SoE of an association between CPAP use and lower risk of death. Data from the NRCSs did not change other conclusions. Both RCTs and NRCSs provide insufficient evidence regarding the effect of CPAP on the risk of transient ischemic attack, angina, coronary artery revascularization, congestive heart failure, and atrial fibrillation.

RCTs also did not provide evidence that CPAP affects the risk of driving accidents or the risk of incident diabetes (both low SoE), or that CPAP results in clinically significant changes in depression or anxiety scores, executive cognitive function measures, or nonspecific quality of life measures (all low SoE). RCTs provide insufficient evidence regarding the effect of CPAP on incident hypertension, functional status measures, male or female sexual function, or days of work missed. Data from the NRCSs did not change these conclusions.

AMERICAN THORACIC SOCIETY DOCUMENTS

The Great Controversy of Obstructive Sleep Apnea Treatment for Cardiovascular Risk Benefit: Advancing the Science through Expert Consensus

An Official American Thoracic Society Workshop Report

Oren Cohen*, Vaishnavi Kundel*, Ferran Barbé, Yüksel Peker, Doug McEvoy, Manuel Sánchez-de-la-Torre, Daniel J. Gottlieb, T. Douglas Bradley, Mayte Suárez-Fariñas, Andrey Zinchuk, Ali Azarbarzin, Atul Malhotra, Helena Schotland, David Gozal, Sanja Jelic, Alberto R. Ramos, Jennifer L. Martin, Sushmita Pamidi, Dayna A. Johnson, Reena Mehra, Virend K. Somers, Camilla M. Hoyos, Chandra L. Jackson, Carmela Alcantara, Martha E. Billings, Deepak L. Bhatt, Sanjay R. Patel, Susan Redline, Henry K. Yaggi*, and Neomi A. Shah*; on behalf of the American Thoracic Society Assembly on Sleep and Respiratory Neurobiology

THIS OFFICIAL WORKSHOP REPORT OF THE AMERICAN THORACIC SOCIETY WAS APPROVED SEPTEMBER 2024

Abstract

The prevalence of obstructive sleep apnea (OSA) is on the rise, driven by various factors, including more sensitive diagnostic criteria, increased awareness, enhanced technology through at-home testing enabling easy and cost-effective diagnosis, and a growing incidence of comorbid conditions such as obesity. Treating symptomatic patients with OSA syndrome to enhance quality of life remains a cornerstone approach. However, there is a lack of consensus regarding treatment to improve cardiovascular disease (CVD) outcomes, particularly in light of overall negative results from several randomized controlled trials indicating no benefit of positive airway pressure therapy on primary and secondary CVD events. These randomized controlled trials were limited by suboptimal positive airway pressure adherence, use of composite CVD outcomes, and limited diversity and generalizability to sleep clinic patients. As such, this workshop assembled clinical experts, as well as researchers in basic and translational science, epidemiology, clinical trials, and population health, to discuss the current state and future research directions to guide personalized therapeutic strategies and future research directions in OSA. There was overall consensus among workshop participants that OSA represents a heterogeneous disease with variable endotypes and phenotypes and heterogeneous responses to treatment. Future research should prioritize using multimodal therapeutic approaches within innovative and adaptive trial designs, focusing on specific subgroups of patients with OSA hypothesized to benefit from a CVD perspective. Future work should also be inclusive of diverse populations and consider the life course of OSA to better comprehend treatment strategies that can address the disproportionate impact of OSA on racially minoritized groups. Furthermore, a more holistic approach to sleep must be adopted to include broader assessments of symptoms, sleep duration, and comorbid sleep and circadian disorders. Finally, it is imperative to establish a sleep research consortium dedicated to collecting raw data and biospecimens categorized by OSA subtypes. This will facilitate mechanistic determinations, foster collaborative research, and help bolster the pipeline of early-career researchers.

Keywords: obstructive sleep apnea; positive airway pressure therapy; cardiovascular disease outcomes; health equity

Adherence Metrics Variables

- 4 hours per night, 70% of nights
- Part of the 4 hours is awake
- Second half of night AHIs have more apneas and last longer
- Is this 4 out of 4 hours or 4 out of 8 hours?

Colin M. Shapiro
Meenakshi Gupta
Dora Zalai
Editors

CPAP Adherence

Factors and Perspectives

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What Is Our Mission?

- Years of life and life in the years
  - Longevity and health

> Sleep. 2020 Aug 12;43(8):zsaa010. doi: 10.1093/sleep/zsaa010.

Association between weekend catch-up sleep and high-sensitivity C-reactive protein levels in adults: a population-based study

Kyu-Man Han [1], Heon-Jeong Lee [1], Leen Kim [1], Ho-Kyoung Yoon [1]

Affiliations + expand

PMID: 32006432 DOI: 10.1093/sleep/zsaa010

Abstract

Study objectives: To investigate the association between weekend catch-up sleep (WCS) and the levels of high-sensitivity C-reactive protein (hsCRP)-a serum inflammatory maker-in adults.

Methods: Data of 5,506 adults aged 19 years or older were obtained from the nationwide cross-sectional Korea National Health and Nutrition Examination Surveys conducted in 2016. Serum hsCRP level, weekday and weekend sleep durations, and sociodemographic and health-related characteristics were assessed. Participants whose weekend sleep duration was more than 1 h longer than their weekday sleep duration were included in the WCS group. hsCRP level was categorized into quartiles (i.e. highest, middle-high, middle-low, and lowest). Obesity was defined by body mass index ≥ 25.0 kg/m2.

Results: The WCS group included 1,901 participants (34.5%). In the logistic regression analysis controlling for all variables, adults in the WCS group were significantly less likely to show the highest hsCRP level (versus the lowest level) compared with those without WCS in the complete sample (adjusted odds ratio = 0.795, 95% confidence interval [CI] = 0.662 to 0.955). In a subgroup analysis, this association was significant only for those with weekday sleep duration of 6 h or lower. Longer WCS (≥3 h) was not associated with hsCRP levels. Non-obese people with WCS demonstrated a lower risk for high hsCRP levels, while there was no significant difference in obese people with WCS.

Conclusions: Our findings indicate that WCS may be beneficial for low-grade systemic inflammation in adults, particularly among those with shorter weekday sleep durations. WCS may also interact with obesity.

Microgravity Reduces Sleep-disordered Breathing in Humans

ANN. R. ELLIOTT, STEVEN A. SHEA, DERK-JAN DIJK, JAMES K. WYATT, EYMARD RIEL, DAVID F. NERI, CHARLES A. CZEISLER, JOHN B. WEST, and G. KIM PRISK

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To understand the factors that alter sleep quality in space, we studied the effect of spaceflight on sleep-disordered breathing. We analyzed 77 8-h, full polysomnographic recordings (PSGs) from five healthy subjects before spaceflight, on four occasions per subject during either a 16- or 9-d space shuttle mission and shortly after return to earth. Microgravity was associated with a 55% reduction in the apnea–hypopnea index (AHI), which decreased from a preflight value of 8.3 ± 1.6 to 3.4 ± 0.8 events/h inflight. This reduction in AHI was accompanied by a virtual elimination of snoring, which fell from 16.5 ± 3.0% of total sleep time preflight to 0.7 ± 0.5% inflight. Electroencephalogram (EEG) arousals also decreased in microgravity (by 19%), and this decrease was almost entirely a consequence of the reduction in respiratory-related arousals, which fell from 5.5 ± 1.2 arousals/h preflight to 1.8 ± 0.6 inflight. Postflight there was a return to near or slightly above preflight levels in these variables. We conclude that sleep quality during spaceflight is not degraded by sleep-disordered breathing. This is the first direct demonstration that gravity plays a dominant role in the generation of apneas, hypopneas, and snoring in healthy subjects.

tures is believed to be responsible for positional sleep-disordered breathing and is probably one of the primary factors in the upper airway resistance syndrome in humans (7).

On the other hand, the removal of gravity might be expected to increase any sleep-related respiratory disturbances and sleep disturbance because microgravity causes a headward shift in blood and body fluids (8) that could affect both respiratory mechanics and chemoreceptor function. For instance, increased fluid volume in the head and neck could passively reduce upper airway caliber, thereby increasing the propensity for obstructive events. Microgravity reduces the hypoxic ventilatory response by about 50% compared with the upright posture, so that the response is comparable to that measured in the supine position on the ground (6). Chemoreceptor function has been strongly implicated in the initiation of both obstructive and central periodic breathing (9) as well as the ultimate arousal from sleep caused by blood gas derangement during apneas (10, 11).

To date, only one other spaceflight experiment has attempted to examine the respiratory system during sleep. A

5 astronauts and 77 PSGs
Before, during and after space flight

- Mandibular neutrality
- No gravitation effects on tongue
- No gravitation effects on viscera
- No fluids shifts

TABLE 1. APNEAS, HYPOPNEAS, SNORING, AND AROUSALS DURING SLEEP

Period	AHI_{TST} (*number/h*)	AHI_{NREM} (*number/h*)	AHI_{REM} (*number/h*)	Snoring (*%TST*)*	$Arousals_{RE}$ (*number/h*)
Preflight	8.3 ± 1.6	7.9 ± 1.7	9.7 ± 1.7	16.5 ± 3.0	5.5 ± 1.2
μG	3.4 ± 0.8†	2.7 ± 0.8†	6.1 ± 1.3†	0.7 ± 0.5†	1.8 ± 0.6†
Postflight	9.5 ± 2.2‡	8.0 ± 2.3‡	12.9 ± 2.5†,‡	18.2 ± 3.0‡	6.0 ± 1.9‡

Definition of abbreviations: AHI = apnea–hypopnea index; $arousals_{RE}$ = arousals associated with a respiratory event (see text for details); NREM = non-rapid eye movement sleep; μG = microgravity; REM = rapid eye movement sleep; Snoring = snoring above a predefined threshold as a percentage of TST (*see* text for details); TST = total sleep time.

* As a percentage of the preflight average (control) for that subject.

† Signficantly different from preflight value.

‡ Signficantly different from inflight value.

Mandibular Movement

- Protrusion and retraction
- Opening

Simple Mechanics

- Limit salt and fluids three hours before bed
- Prop up legs half hour
- Walk or exercise legs before sleep
- Sidelying position with reinforcement
  - Supine to lateral, the retroglossal space increased by about 50%
- Head of the bed up about 4 inches

Lung Volume and Continuous Positive Airway Pressure Requirements in Obstructive Sleep Apnea

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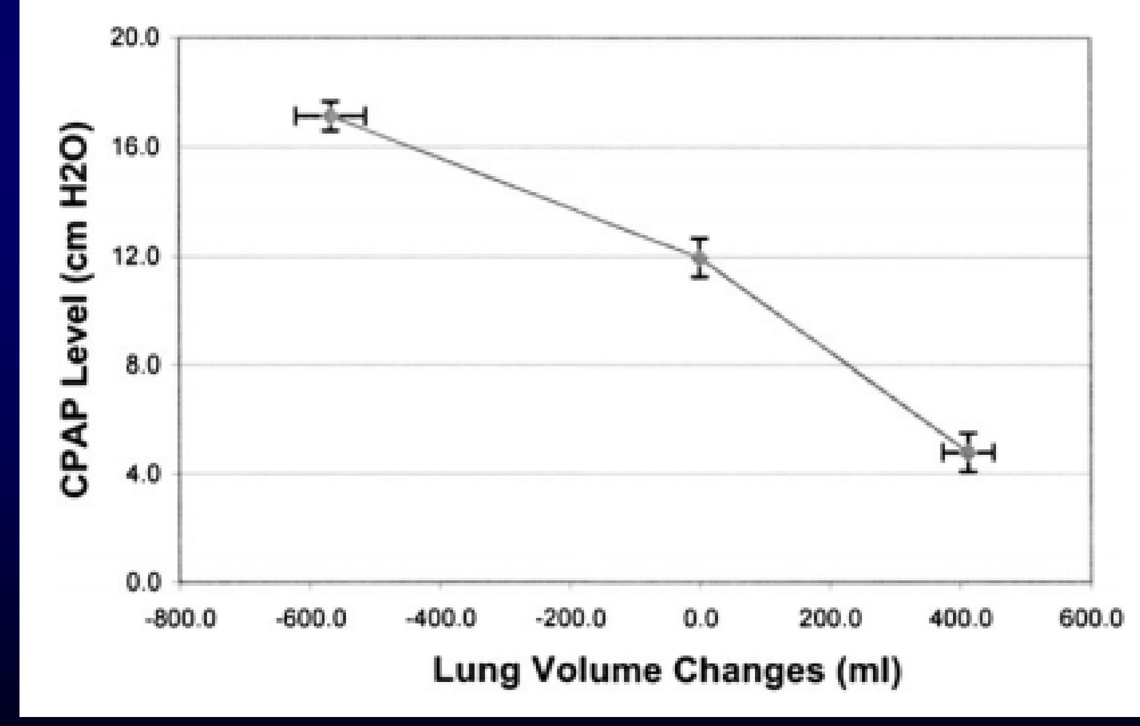
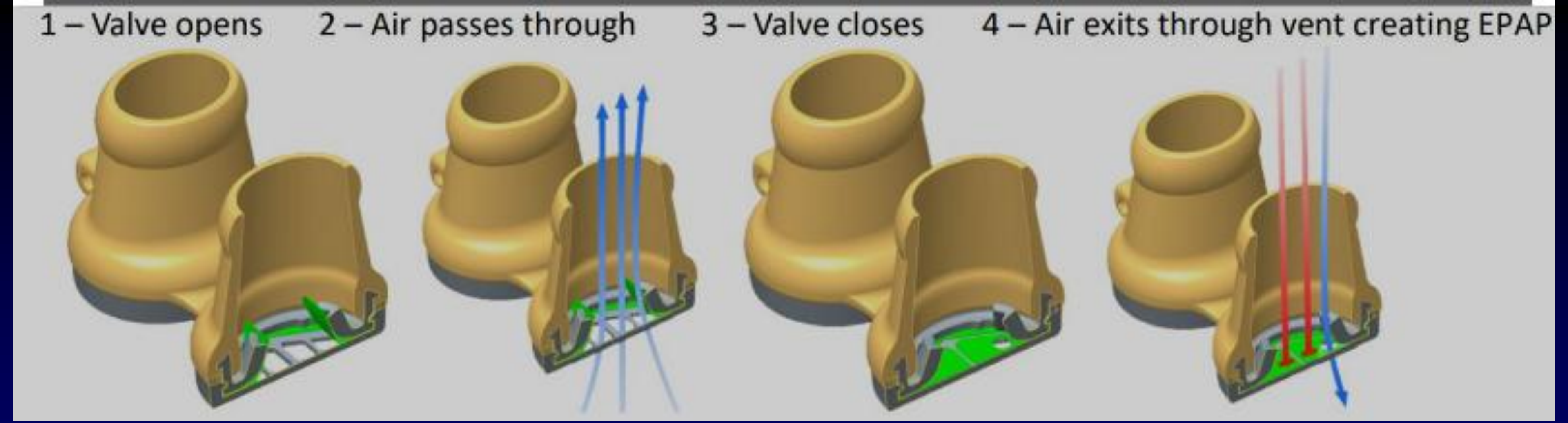


Medicare Now Reimburses Positional Obstructive Sleep Apnea Therapy

Jan 4, 2024 | Positional Therapies for Supine Sleep Avoidance | 0 |



PSG Results Baseline vs Month 12 (n = 34)

110
100
90
80
70
60
50
40
30
20
10
0

P < 0.001
15.7
4.7
P = 0.008
12.6
7.6
P = 0.009
23.9
19.0

Baseline Nasal EPAP Baseline Nasal EPAP Baseline Nasal EPAP

AHI ODI Arousal Index

Three Pharmacologic Treatments For OSA

- Atomoxetine-Oxybutynin
- Etanercept
- Tirzepatide

ORIGINAL ARTICLE

The Combination of Atomoxetine and Oxybutynin Greatly Reduces Obstructive Sleep Apnea Severity

A Randomized, Placebo-controlled, Double-Blind Crossover Trial

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Abstract

Rationale: There is currently no effective pharmacological treatment for obstructive sleep apnea (OSA). Recent investigations indicate that drugs with noradrenergic and antimuscarinic effects improve genioglossus muscle activity and upper airway patency during sleep.

Objectives: We aimed to determine the effects of the combination of a norepinephrine reuptake inhibitor (atomoxetine) and an antimuscarinic (oxybutynin) on OSA severity (apnea–hypopnea index [AHI]; primary outcome) and genioglossus responsiveness (secondary outcome) in people with OSA.

Methods: A total of 20 people completed a randomized, placebo-controlled, double-blind, crossover trial comparing 1 night of 80 mg atomoxetine plus 5 mg oxybutynin (ato–oxy) to placebo administered before sleep. The AHI and genioglossus muscle responsiveness to negative esophageal pressure swings were measured via in-laboratory polysomnography. In a subgroup of nine patients, the AHI was also measured when the drugs were administered separately.

Measurements and Main Results: The participants' median (interquartile range) age was 53 (46–58) years and body mass index was 34.8 (30.0–40.2) kg/m^2. ato–oxy lowered AHI by 63% (34–86%), from 28.5 (10.9–51.6) events/h to 7.5 (2.4–18.6) events/h ($P < 0.001$). Of the 15/20 patients with OSA on placebo (AHI > 10 events/hr), AHI was lowered by 74% (62–88%) ($P < 0.001$) and all 15 patients exhibited a ⩾50% reduction. Genioglossus responsiveness increased approximately threefold, from 2.2 (1.1–4.7)%/cm H_2O on placebo to 6.3 (3.0 to 18.3)%/cm H_2O on ato–oxy ($P < 0.001$). Neither atomoxetine nor oxybutynin reduced the AHI when administered separately.

Conclusions: A combination of noradrenergic and antimuscarinic agents administered orally before bedtime on 1 night greatly reduced OSA severity. These findings open new possibilities for the pharmacologic treatment of OSA.

Clinical trial registered with www.clinicaltrials.gov (NCT02908529).

Keywords: pharmacologic treatment; antimuscarinic; norepinephrine reuptake inhibitors; upper airway

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Marked Decrease in Sleepiness in Patients with Sleep Apnea by Etanercept, a Tumor Necrosis Factor-α Antagonist

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The proinflammatory cytokines, TNFα and IL-6, are elevated in obstructive sleep apnea (OSA) and have been proposed as mediators of excessive daytime sleepiness in humans. We tested the effects of etanercept, a medication that neutralizes TNFα and is approved by the FDA for the treatment of rheumatoid arthritis, in eight obese male apneics. These patients participated in a pilot, placebo-controlled, double-blind study during which nighttime polysomnography, multiple sleep latency test, and fasting blood glucose and plasma levels of IL-6, C-reactive protein, insulin, and adiponectin were obtained. There was a significant and marked decrease in sleepiness by etanercept, which increased sleep latency during the multiple sleep latency test by 3.1 ± 1.0 min ($P < 0.05$) compared with placebo. Also, the number of apneas/hypopneas per hour was reduced significantly by the drug compared with placebo (52.8 ± 9.1 *vs.* 44.3 ± 10.3; adjusted difference, −8.4 ± 2.3; $P < 0.05$). Furthermore, IL-6 levels were significantly decreased after etanercept administration compared with placebo (3.8 ± 0.9 *vs.* 1.9 ± 0.4 pg/ml; adjusted difference, −1.9 ± 0.5; $P < 0.01$). However, no differences were observed in etanercept *vs.* placebo in the levels of fasting blood glucose and plasma C-reactive protein, insulin, and adiponectin. We conclude that neutralizing TNFα activity is associated with a significant reduction of objective sleepiness in obese patients with OSA. This effect, which is about 3-fold higher than the reported effects of continuous positive airway pressure on objective sleepiness in patients with OSA (0.9 *vs.* 3.1 min), suggests that proinflammatory cytokines contribute to the pathogenesis of OSA/sleepiness. (*J Clin Endocrinol Metab* 89: 4409–4413, 2004)

Association of Tumor Necrosis Factor-Alpha, Interleukin-1β, Interleukin-8, and Interferon-γ with Obstructive Sleep Apnea in Both Children and Adults: A Meta-Analysis of 102 Articles

by **Amin Golshah** [1], **Edris Sadeghi** [2] and **Masoud Sadeghi** [2,*]

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Conclusions: The levels of proinflammatory cytokines of TNF-α, IL-8, and IL-1β in adults, and TNF-α, IL-8, and IFN-γ in children with OSA, are significantly higher than those in controls.

JOURNAL ARTICLE CORRECTED PROOF

Habitual Coffee, Tea, and Caffeine Consumption, Circulating Metabolites, and the Risk of Cardiometabolic Multimorbidity

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Xujia Lu, Xiaohong Zhu, Guochen Li, Luying Wu, Liping Shao, Yulong Fan, Chen-Wei Pan, Ying Wu, Yan Borné, Chaofu Ke ✉

The Journal of Clinical Endocrinology & Metabolism, dgae552,
https://doi.org/10.1210/clinem/dgae552
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Abstract

Context

Cardiometabolic multimorbidity (CM) is an increasing public health concern. Previous observational studies have suggested inverse associations between coffee, tea, and caffeine intake and risks of individual cardiometabolic diseases; however, their associations with CM and related biological markers are unknown.

Methods

This prospective study involved 172 315 (for caffeine analysis) and 188 091 (tea and coffee analysis) participants free of any cardiometabolic diseases at baseline from the UK Biobank; 168 metabolites were measured among 88 204 and 96 393 participants. CM was defined as the coexistence of at least 2 of the following conditions: type 2 diabetes, coronary heart disease, and stroke.

Results

Nonlinear inverse associations of coffee, tea, and caffeine intake with the risk of new-onset CM were observed. Compared with nonconsumers or consumers of less than 100 mg caffeine per day, consumers of moderate amount of coffee (3 drinks/d) or caffeine (200-300 mg/d) had the lowest risk for new-onset CM, with respective hazard ratios (95% CIs) of 0.519 (0.417-0.647) and 0.593 (0.499-0.704). Multistate models revealed that moderate coffee or caffeine intake was inversely associated with risks of almost all developmental stages of CM, including transitions from a disease-free state to single cardiometabolic diseases and subsequently to CM. A total of 80 to 97 metabolites, such as lipid components within very low-density lipoprotein, histidine, and glycoprotein acetyls, were identified to be associated with both coffee, tea, or caffeine intake and incident CM.

Conclusion

Habitual coffee or caffeine intake, especially at a moderate level, was associated with a lower risk of new-onset CM and could play important roles in almost all transition phases of CM development. Future studies are warranted to validate the implicated metabolic biomarkers underlying the relation between coffee, tea, and caffeine intake and CM.

The Effects of Long-term CPAP on Weight Change in Patients With Comorbid OSA and Cardiovascular Disease

Data From the SAVE Trial

Qiong Ou, MD; Baixin Chen, MMed; Kelly A. Loffler, PhD; Yuanming Luo, MD, PhD; Xilong Zhang, PhD; Rui Chen, PhD; Qian Wang, MMed; Luciano F. Drager, MD, PhD; Geraldo Lorenzi-Filho, MD, PhD; Michael Hlavac, PhD; Nigel McArdle, MD; Sutapa Mukherjee, MD, PhD; Olga Mediano, MD; Ferran Barbe, MD; Craig S. Anderson, MD, PhD; R. Doug McEvoy, MD; Richard J. Woodman, PhD; on behalf of the SAVE investigators[*]

BACKGROUND: Although recent evidence suggests that OSA treatment may cause weight gain, the long-term effects of CPAP on weight are not well established.

METHODS: This study was a post hoc analysis of the Sleep Apnea Cardiovascular Endpoints (SAVE) study, a multicenter, randomized trial of CPAP plus standard care vs standard care alone in adults with a history of cardiac or cerebrovascular events and moderate to severe OSA. Participants with weight, BMI, and neck and waist circumferences measured at baseline and during follow-up were included. Linear mixed models were used to examine sex-specific temporal differences, and a sensitivity analysis compared high CPAP adherers (≥ 4 h per night) with propensity-matched control participants.

RESULTS: A total of 2,483 adults (1,248 in the CPAP group and 1,235 in the control group) were included (mean 6.1 ± 1.5 measures of weight available). After a mean follow-up of 3.78 years, there was no difference in weight change between the CPAP and control groups, for male subjects (mean [95% CI] between-group difference, 0.07 kg [–0.40 to 0.54]; *P* = .773) or female subjects (mean [95% CI] between-group difference, –0.14 kg [–0.37 to 0.09]; *P* = .233). Similarly, there were no significant differences in BMI or other anthropometric measures. Although male participants who used CPAP ≥ 4 h per night gained slightly more weight than matched male control subjects without CPAP (mean difference, 0.38 kg [95% CI, 0.04 to 0.73]; *P* = .031), there were no between-group differences in other anthropometric variables, nor were there any differences between female high CPAP adherers and matched control subjects.

CONCLUSIONS: Long-term CPAP use in patients with comorbid OSA and cardiovascular disease does not result in clinically significant weight change.

TRIAL REGISTRY: ClinicalTrials.gov; No.: NCT00738179; URL: www.clinicaltrials.gov.

CHEST 2019; 155(4):720-729

KEY WORDS: CPAP; long-term; OSA; weight

FOR EDITORIAL COMMENT, SEE PAGE 657

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2011

[1] Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

<20%
20%-<25%
25%-<30%
30%-<35%
35%-<40%
40%-<45%
45%-<50%
50% +
Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2012

† Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

- <20%
- 20%-<25%
- 25%-<30%
- 30%-<35%
- 35%-<40%
- 40%-<45%
- 45%-<50%
- 50% +
- Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2013

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<20%
20%-<25%
25%-<30%
30%-<35%
35%-<40%
40%-<45%
45%-<50%
50% +
Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2014

† Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

<20%
20%-<25%
25%-<30%
30%-<35%
35%-<40%
40%-<45%
45%-<50%
50% +
Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2015

† Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

<20%
20%-<25%
25%-<30%
30%-<35%
35%-<40%
40%-<45%
45%-<50%
50% +
Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2016

† Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

- <20%
- 20%-<25%
- 25%-<30%
- 30%-<35%
- 35%-<40%
- 40%-<45%
- 45%-<50%
- 50% +
- Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2017

* Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

<20%
20%-<25%
25%-<30%
30%-<35%
35%-<40%
40%-<45%
45%-<50%
50% +
Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2018

* Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

<20%
20%-<25%
25%-<30%
30%-<35%
35%-<40%
40%-<45%
45%-<50%
50% +
Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2019

* Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

- <20%
- 20%-<25%
- 25%-<30%
- 30%-<35%
- 35%-<40%
- 40%-<45%
- 45%-<50%
- 50% +
- Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥ 30%, or no data in a specific year.

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2020

* Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

WA MT ND MN ME OR ID WY SD WI MI VT NH NY MA RI CT NJ PA NV UT CO NE IA IL IN OH MD DE DC WV VA CA KS MO KY NC TN AZ NM OK AR SC GA AL MS TX LA FL AK HI GU PR

<20%
20%-<25%
25%-<30%
30%-<35%
35%-<40%
40%-<45%
45%-<50%
50% +
Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Self-Reported Obesity Among U.S. Adults by State and Territory, BRFSS, 2021

* Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

WA OR CA NV ID MT WY UT AZ CO NM ND SD NE KS OK TX MN IA MO AR LA WI IL MI IN OH KY TN MS AL GA FL SC NC VA WV PA NY VT NH ME MA RI CT NJ DE MD DC AK HI GU PR VI

- <20%
- 20%-<25%
- 25%-<30%
- 30%-<35%
- 35%-<40%
- 40%-<45%
- 45%-<50%
- 50% +
- Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Obesity Based on Self-Reported Weight and Height Among US Adults by State and Territory, BRFSS, 2022

† Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

WA OR CA NV ID MT WY UT AZ CO NM ND SD NE KS OK TX MN IA MO AR LA WI IL MI IN OH KY TN MS AL GA FL SC NC VA WV PA NY VT NH ME MA CT RI NJ DE MD DC AK HI GU VI PR

- <20%
- 20%-<25%
- 25%-<30%
- 30%-<35%
- 35%-<40%
- 40%-<45%
- 45%-<50%
- 50%+
- Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Prevalence of Obesity Based on Self-Reported Weight and Height Among US Adults by State and Territory, BRFSS, 2023

¶ Prevalence estimates reflect BRFSS methodological changes started in 2011. These estimates should not be compared to prevalence estimates before 2011.

- <20%
- 20%-<25%
- 25%-<30%
- 30%-<35%
- 35%-<40%
- 40%-<45%
- 45%-<50%
- 50%+
- Insufficient data*

*Sample size <50, the relative standard error (dividing the standard error by the prevalence) ≥30%, or no data in a specific year.

Original Investigation | Pulmonary Medicine

Effect of an Interdisciplinary Weight Loss and Lifestyle Intervention on Obstructive Sleep Apnea Severity

The INTERAPNEA Randomized Clinical Trial

Almudena Carneiro-Barrera, PhD; Francisco J. Amaro-Gahete, PhD; Alejandro Guillén-Riquelme, PhD; Lucas Jurado-Fasoli, MSc; Germán Sáez-Roca, MD; Carlos Martín-Carrasco, MD; Gualberto Buela-Casal, PhD; Jonatan R. Ruiz, PhD

CONCLUSIONS AND RELEVANCE In this study, an interdisciplinary weight loss and lifestyle intervention involving Spanish men with moderate to severe OSA and had overweight or obesity and were receiving CPAP therapy resulted in clinically meaningful and sustainable improvements in OSA severity and comorbidities as well as health-related quality of life. This approach may therefore be considered as a central strategy to address the substantial impact of this increasingly common sleep-disordered breathing condition.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03851653

JAMA Network Open. 2022;5(4):e228212. doi:10.1001/jamanetworkopen.2022.8212

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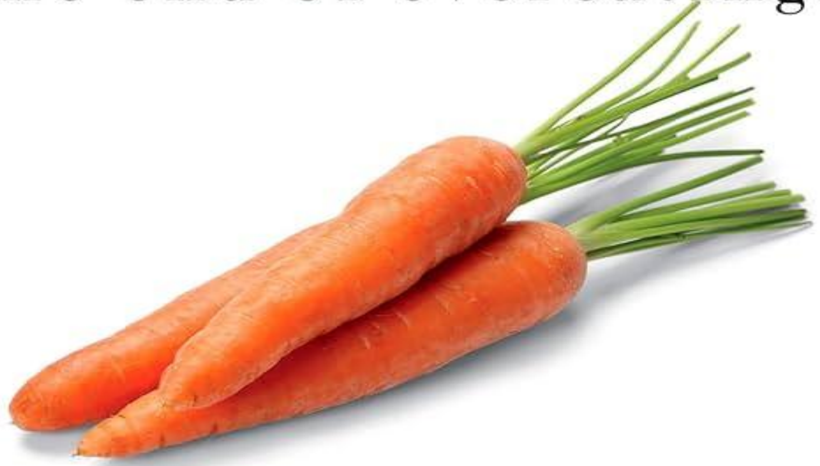


TAKING CONTROL OF THE INSATIABLE AMERICAN APPETITE

DAVID A. KESSLER, MD

HUMAN PLANET

International Food Addiction Consensus (IFAC) 2024

The Development of an International Consensus on Addiction-like Symptoms related to Food

An International Workshops Programme reviewing perspectives and experience of addiction-like symptoms related to food amongst academics, researchers and clinicians.

The project, using a modified Delphi methodology, took a year, involving 40 clinicians, researchers and academics, spanning 10 countries around the world and working with a team of 4 facilitators. Consensus was achieved with 37 out of the 40 participants, as seen in Appendix A.

(*)Ultra Processed Food Addiction (UPFA) is a chronic disease involving complex interactions among brain circuits, genetics, the environment and an individual's life experiences. People with UPFA use food in a way similar to drugs of abuse, obsess about food, and/or engage in eating behaviours that become compulsive and often continue despite harmful medical and biopsychosocial consequences.

Ultra-processed Foods Have Addiction Impact on our Bodies

Ashley Gearhardt

Dr. Gearhardt Identified as One of World's Top 2% of Scientists

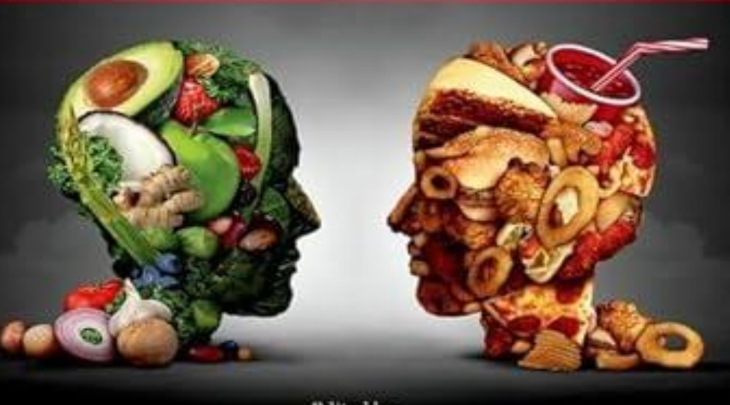
By worthin / February 5, 2024

Dr. Gearhardt identified as one of world's top 2% of scientists based on citation metrics.

FOOD & ADDICTION

A Comprehensive Handbook

SECOND EDITION



Edited by

ASHLEY N. GEARHARDT, KELLY D. BROWNELL, MARK S. GOLD, AND MARC N. POTENZA

Ashley Gearhardt

Clinical Science Area Chair; Professor of Psychology

Food and Addiction Science & Treatment Lab

Professor Ashley Gearhardt has found compelling biological and behavioral evidence that some ultraprocessed foods are addictive like cigarettes or alcohol.

Chapter

The Badly Behaving Brain: How Ultra-Processed Food Addiction Thwarts Sustained Weight Loss

IntechOpen

Susan Peirce Thompson and Andrew Kurt Thaw

Abstract

Global obesity rates continue to rise, despite billions spent annually on weight loss. Sustained success is rare; recidivism is the most common feature of weight loss attempts. According to the DSM-5 criteria for substance use disorders, the pattern of ultra-processed food (UPF) overconsumption is best characterized as an addiction. There is significant overlap in how UPF and drugs of abuse impact many brain systems. Over time, neurological changes result in overpowering cravings, insatiable hunger, and a willpower gap. The Yale Food Addiction Scale 2.0 is a validated and widely used tool for the diagnosis of UPF addiction. Research on treatment is nascent, but two weight loss approaches that directly target addiction, GLP-1 agonists and Bright Line Eating, both decrease hunger and cravings and result in significantly greater sustained weight loss than other methods. Addressing addiction is an avenue to weight loss that warrants further study.

NIH News in Health

A monthly newsletter from the National Institutes of Health, part of the U.S. Department of Health and Human Services

- ***NIHNiH:*** *How do ultra-processed foods resemble addictive drugs?*
- A lot of times, people are motivated to consume ultra-processed foods excessively not because they need calories, but because they're looking to change their mood, get a hit of pleasure, feel less stressed, or reduce their feelings of boredom. And the ingredients that are elevated in ultra-processed foods—refined carbs like sugar, added fats—activate reward centers of the brain in ways that appear to be similar to something like nicotine or alcohol.
- ***NIHNiH:*** What about ultra-processed foods makes you think they might be addictive, like drugs?
- When you look at highly addictive drugs, they're nearly all human-made or at least human-refined. There is no cigarette tree, there is no wine river. We take a leaf, we take a plant, we take a potato, and we alter it, process it, and refine it in a way that rapidly delivers these reinforcing ingredients into the brain.
- ***NIHNiH:*** What would your advice be to people who are trying to eat better?
- Right now, we're kind of like, "just eat these foods in moderation." And for the people for whom consumption of these foods has become compulsive, it's like telling people with alcohol use disorder to just find a way to drink in moderation. Especially in a food environment like ours, where you're constantly being triggered and cued.

JOURNAL ARTICLE CORRECTED PROOF

Overall diet quality and proinflammatory diet in relation to risk of obstructive sleep apnea in 3 prospective US cohorts

Get access >

Yue Liu, Fred K Tabung, Meir J Stampfer, Susan Redline, Tianyi Huang

The American Journal of Clinical Nutrition, nqac257,
https://doi.org/10.1093/ajcn/nqac257
Published: 16 September 2022 **Article history** ▾

Review

The Impact of Glucagon-like Peptide 1 Receptor Agonists on Obstructive Sleep Apnoea: A Scoping Review

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Abstract: Background: Obstructive sleep apnoea (OSA) and associated hypopnoea syndromes are chronic conditions of sleep-disordered breathing with significant sequelae if poorly managed, including hypertension, cardiovascular disease, metabolic syndrome and increased mortality. Glucagon-like peptide 1 receptor agonists (GLP-1RA) have recently garnered significant interest as a potential therapeutic, attributed to their durable effects in weight loss and glycaemic control in metabolic syndromes, such as obesity and type 2 diabetes mellitus. This has led to significant investment into companies that produce these medications and divestment from traditional gold standard methods of OSA management such as continuous positive airway pressure machines. Despite these sentiments, the impacts of these medications on OSA outcomes are poorly characterised, with no high-quality evidence at this stage to support this hypothesis. This scoping review therefore aims to address the research question of whether GLP-1RAs lead to a direct improvement in OSA and associated hypopnoea syndromes. Methods: A scoping review was performed following a computer-assisted search of Medline, Embase and Cochrane Central databases. Papers that evaluated the use of GLP-1RA medications related to sleep-disordered breathing, OSA or other sleep-related apnoeic or hypopnoeic syndromes were included. Results: Literature search and evaluation identified 9 articles that were eligible for inclusion. Of these, 1 was a study protocol, 1 was a case report, 1 was an abstract of a randomised controlled trial (RCT), 1 was a non-randomised clinical trial and the remaining 5 were randomised clinical trials of variable rigour. All studies evaluated the outcomes of GLP-1RAs in patients with diagnosed OSA or symptoms suggestive of this condition. Conclusion: This scoping review identified early evidence to suggest that GLP-1RAs may improve OSA as defined by reduction in apnoea-hypopnoea index (AHI). This evidence is however conflicting due to contradicting results demonstrated from other studies. Overall, these medications were tolerated well, with minor gastrointestinal side-effects reported in some cases. Of all included studies, the quality of evidence was low, with short lengths of follow-up to identify durable effects of these medications on OSA outcomes and identify adverse events. More rigorous, RCTs with sufficient length of follow-up are required before consideration of formalising these medications into OSA treatment guidelines, frameworks and policies are warranted.

Keywords: glucagon-like peptide 1 receptor agonists (GLP-1RA); GLP-1 agonists; semaglutide; liraglutide; exenatide; Ozempic; obstructive sleep apnoea (OSA); sleep disordered breathing; obesity

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1. Introduction

Obstructive sleep apnoea (OSA) is a chronic condition of sleep-disordered breathing with important health outcomes including hypertension, atherosclerotic cardiovascular

ORIGINAL ARTICLE

Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity

Atul Malhotra, M.D., Ronald R. Grunstein, M.D., Ph.D., Ingo Fietze, M.D., Terri E. Weaver, Ph.D., Susan Redline, M.D., M.P.H., Ali Azarbarzin, Ph.D., Scott A. Sands, Ph.D., Richard J. Schwab, M.D., Julia P. Dunn, M.D., Sujatro Chakladar, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Josef Bednarik, M.D., for the SURMOUNT-OSA Investigators*

ABSTRACT

BACKGROUND

Obstructive sleep apnea is characterized by disordered breathing during sleep and is associated with major cardiovascular complications; excess adiposity is an etiologic risk factor. Tirzepatide may be a potential treatment.

METHODS

We conducted two phase 3, double-blind, randomized, controlled trials involving adults with moderate-to-severe obstructive sleep apnea and obesity. Participants who were not receiving treatment with positive airway pressure (PAP) at baseline were enrolled in trial 1, and those who were receiving PAP therapy at baseline were enrolled in trial 2. The participants were assigned in a 1:1 ratio to receive either the maximum tolerated dose of tirzepatide (10 mg or 15 mg) or placebo for 52 weeks. The primary end point was the change in the apnea–hypopnea index (AHI, the number of apneas and hypopneas during an hour of sleep) from baseline. Key multiplicity-controlled secondary end points included the percent change in AHI and body weight and changes in hypoxic burden, patient-reported sleep impairment and disturbance, high-sensitivity C-reactive protein (hsCRP) concentration, and systolic blood pressure.

RESULTS

At baseline, the mean AHI was 51.5 events per hour in trial 1 and 49.5 events per hour in trial 2, and the mean body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) was 39.1 and 38.7, respectively. In trial 1, the mean change in AHI at week 52 was −25.3 events per hour (95% confidence interval [CI], −29.3 to −21.2) with tirzepatide and −5.3 events per hour (95% CI, −9.4 to −1.1) with placebo, for an estimated treatment difference of −20.0 events per hour (95% CI, −25.8 to −14.2) (P<0.001). In trial 2, the mean change in AHI at week 52 was −29.3 events per hour (95% CI, −33.2 to −25.4) with tirzepatide and −5.5 events per hour (95% CI, −9.9 to −1.2) with placebo, for an estimated treatment difference of −23.8 events per hour (95% CI, −29.6 to −17.9) (P<0.001). Significant improvements in the measurements for all prespecified key secondary end points were observed with tirzepatide as compared with placebo. The most frequently reported adverse events with tirzepatide were gastrointestinal in nature and mostly mild to moderate in severity.

CONCLUSIONS

Among persons with moderate-to-severe obstructive sleep apnea and obesity, tirzepatide reduced the AHI, body weight, hypoxic burden, hsCRP concentration, and systolic blood pressure and improved sleep-related patient-reported outcomes. (Funded by Eli Lilly; SURMOUNT-OSA ClinicalTrials.gov number, NCT05412004.)

From the University of California, San Diego, La Jolla (A.M.); Woolcock Institute of Medical Research, Macquarie University, Royal Prince Alfred Hospital, and the University of Sydney — all in Sydney (R.R.G.); the Center of Sleep Medicine, Charité University Hospital Berlin, Berlin (I.F.); the College of Nursing, University of Illinois Chicago, Chicago (T.E.W.); the School of Nursing (T.E.W.) and Perelman School of Medicine (R.J.S.), University of Pennsylvania, Philadelphia; the Division of Sleep and Circadian Disorders, Brigham and Women's Hospital, and Harvard Medical School — both in Boston (S.R., A.A., S.A.S.); and Eli Lilly, Indianapolis (J.P.D., S.C., M.C.B., J.B.). Dr. Malhotra can be contacted at amalhotra@health.ucsd.edu or at the University of California, San Diego, 9500 Gilman Dr., La Jolla, CA 92037.

*A complete list of the SURMOUNT-OSA trial investigators is provided in the Supplementary Appendix, available at NEJM.org.

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Dual glucose-dependent insulinotropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1) receptor agonist

Downside of Care Fragmentation

- Cost
- Hassle
- Delay in care due to appointment delays
- Cross communication
- Misinformation and contradiction

- Opportunity for sleep or health coaches lifestyle medicine collaboration

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Tirzepatide for the Treatment of Obstructive Sleep Apnea and Obesity

Atul Malhotra, M.D., Ronald R. Grunstein, M.D., Ph.D., Ingo Fietze, M.D., Terri E. Weaver, Ph.D., Susan Redline, M.D., M.P.H., Ali Azarbarzin, Ph.D., Scott A. Sands, Ph.D., Richard J. Schwab, M.D., Julia P. Dunn, M.D., Sujatro Chakladar, Ph.D., Mathijs C. Bunck, M.D., Ph.D., and Josef Bednarik, M.D., for the SURMOUNT-OSA Investigators*

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Antibody blockade of activin type II receptors preserves skeletal muscle mass and enhances fat loss during GLP-1 receptor agonism

Elizabeth Nunn[1,2], Natasha Jaiswal[1,2], Matthew Gavin[1,2], Kahealani Uehara[1,2], Megan Stefkovich[1,2], Karima Drareni[1,3], Ryan Calhoun[1,3], Michelle Lee[1,2], Corey D. Holman[1,2], Joseph A. Baur[1,2], Patrick Seale[1,3], Paul M. Titchenell[1,2,*]

ABSTRACT

Objective: Glucagon-like peptide 1 (GLP-1) receptor agonists reduce food intake, producing remarkable weight loss in overweight and obese individuals. While much of this weight loss is fat mass, there is also a loss of lean mass, similar to other approaches that induce calorie deficit. Targeting signaling pathways that regulate skeletal muscle hypertrophy is a promising avenue to preserve lean mass and modulate body composition. Myostatin and Activin A are TGFβ-like ligands that signal via the activin type II receptors (ActRII) to antagonize muscle growth. Preclinical and clinical studies demonstrate that ActRII blockade induces skeletal muscle hypertrophy and reduces fat mass. In this manuscript, we test the hypothesis that combined ActRII blockade and GLP-1 receptor agonism will preserve muscle mass, leading to improvements in skeletomuscular and metabolic function and enhanced fat loss.

Methods: In this study, we explore the therapeutic potential of bimagrumab, a monoclonal antibody against ActRII, to modify body composition alone and during weight loss induced by GLP-1 receptor agonist semaglutide in diet-induced obese mice. Mechanistically, we define the specific role of the anabolic kinase Akt in mediating the hypertrophic muscle effects of ActRII inhibition *in vivo*.

Results: Treatment of obese mice with bimagrumab induced a ∼10 % increase in lean mass while simultaneously decreasing fat mass. Daily treatment of obese mice with semaglutide potently decreased body weight; this included a significant decrease in both muscle and fat mass. Combination treatment with bimagrumab and semaglutide led to superior fat mass loss while simultaneously preserving lean mass despite reduced food intake. Treatment with both drugs was associated with improved metabolic outcomes, and increased lean mass was associated with improved exercise performance. Deletion of both Akt isoforms in skeletal muscle modestly reduced, but did not prevent, muscle hypertrophy driven by ActRII inhibition.

Conclusions: Collectively, these data demonstrate that blockade of ActRII signaling improves body composition and metabolic parameters during calorie deficit driven by GLP-1 receptor agonism and demonstrate the existence of Akt-independent pathways supporting muscle hypertrophy in the absence of ActRII signaling.

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Which Diets Improve Health?

- Ornish
- Mediterranean
- Mind
- Whole Food Plant Based
- Dash

Rostami et al. BMC Psychiatry (2019) 19:234
https://doi.org/10.1186/s12888-019-2220-6

BMC Psychiatry

RESEARCH ARTICLE Open Access

The relationship between adherence to a Dietary Approach to Stop Hypertension (DASH) dietary pattern and insomnia

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Abstract

Background: Adherence to a DASH- style diet has been reported to be associated with several health-related outcomes. A limited number of reports suggest that diet is an important behavioral determinant of insomnia. The current study aimed to explore the relationship between adherence to a DASH diet and the prevalence of insomnia in adolescent girls.

Methods: A total of 488 adolescent girls aged 12–18 years old were recruited from different regions of Khorasan Razavi in northeastern of Iran, using a random cluster sampling method. DASH scores were determined according to the method of Fung et al. A validated Iranian version of the Insomnia Severity Index questionnaire was used to assess sleep insomnia. To assess the association between the DASH dietary pattern and insomnia, we applied logistic regression analysis in crude and adjusted models.

Results: As may be expected, participants in the upper quintile of the DASH diet had significantly higher intakes of fruits, vegetables, low fat dairy products, fish and nuts and lower consumption of refined grains, red and processed meat, sugar-sweetened beverages and sweets. We found that a high adherence to a DASH-style diet was associated with a lower odds of insomnia (OR: 0.51; 95% CI 0.26–1.00) compared with those with lowest adherence. Similar results were found after adjustment for potential confounders.

Conclusions: There is an inverse association between adherence to DASH dietary patterns and insomnia. Further prospective studies are required to demonstrate these findings.

nutrients

Review

Mediterranean Diet on Sleep: A Health Alliance

Egeria Scoditti [1,*], Maria Rosaria Tumolo [2] and Sergio Garbarino [3]

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Abstract: The Mediterranean diet is a plant-based, antioxidant-rich, unsaturated fat dietary pattern that has been consistently associated with lower rates of noncommunicable diseases and total mortality, so that it is considered one of the healthiest dietary patterns. Clinical trials and mechanistic studies have demonstrated that the Mediterranean diet and its peculiar foods and nutrients exert beneficial effects against inflammation, oxidative stress, dysmetabolism, vascular dysfunction, adiposity, senescence, cognitive decline, neurodegeneration, and tumorigenesis, thus preventing age-associated chronic diseases and improving wellbeing and health. Nocturnal sleep is an essential physiological function, whose alteration is associated with health outcomes and chronic diseases. Scientific evidence suggests that diet and sleep are related in a bidirectional relationship, and the understanding of this association is important given their role in disease prevention. In this review, we surveyed the literature concerning the current state of evidence from epidemiological studies on the impact of the Mediterranean diet on nighttime sleep quantity and quality. The available studies indicate that greater adherence to the Mediterranean diet is associated with adequate sleep duration and with several indicators of better sleep quality. Potential mechanisms mediating the effect of the Mediterranean diet and its foods and nutrients on sleep are described, and gap-in-knowledge and new research agenda to corroborate findings are discussed.

Citation: Scoditti, E.; Tumolo, M.R.;

Original Investigation | Pulmonary Medicine

Effect of an Interdisciplinary Weight Loss and Lifestyle Intervention on Obstructive Sleep Apnea Severity
The INTERAPNEA Randomized Clinical Trial

Almudena Carneiro-Barrera, PhD; Francisco J. Amaro-Gahete, PhD; Alejandro Guillén-Riquelme, PhD; Lucas Jurado-Fasoli, MSc; Germán Sáez-Roca, MD; Carlos Martín-Carrasco, MD; Gualberto Buela-Casal, PhD; Jonatan R. Ruiz, PhD

CONCLUSIONS AND RELEVANCE In this study, an interdisciplinary weight loss and lifestyle intervention involving Spanish men with moderate to severe OSA and had overweight or obesity and were receiving CPAP therapy resulted in clinically meaningful and sustainable improvements in OSA severity and comorbidities as well as health-related quality of life. This approach may therefore be considered as a central strategy to address the substantial impact of this increasingly common sleep-disordered breathing condition.

TRIAL REGISTRATION ClinicalTrials.gov Identifier: NCT03851653

JAMA Network Open. 2022;5(4):e228212. doi:10.1001/jamanetworkopen.2022.8212

A Note on Sleep Insufficiency

Immediate Gratification

Takeaways

- Obstructive sleep apnea is a “systemic disease”
- CPAP reduces sleepiness and snoring
- CPAP is effective but can have adverse effects
- Lifestyle changes are paramount

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Journals of Gerontology: Medical Sciences
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doi:10.1093/gerona/glab051
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Research Article

Optimism and Longevity Beyond Age 85

Jeremy M. Jacobs, MBBS,[1,2,*] **Yoram Maaravi, MD,**[1,2] **and Jochanan Stessman, MD**[1,2]

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Received: October 30, 2020; Editorial Decision Date: February 11, 2021

Decision Editor: Anne B. Newman, MD, MPH, FGSA

Abstract

Background: Optimism is associated with health benefits and improved survival among adults older than 65 years. Whether or not optimism beyond age 85 continues to confer survival benefits is poorly documented. We examine the hypothesis that being optimistic at ages 85 and 90 is associated with improved survival.

Method: The Jerusalem Longitudinal Study (1990–2020) assessed comorbidity, depression, cognition, social and functional status, and 5-year mortality among a representative community sample, born during 1920–1921, at age 85 (n = 1096) and age 90 (n = 533). Overall optimism (Op-Total) was measured using a validated 7-item score from the Scale of Subjective Wellbeing for Older Persons. The 4 questions concerning positive future expectations (Op-Future) and 3 questions concerning positive experiences (Op-Happy) were also analyzed separately. We determined unadjusted mortality hazards ratios and also adjusted for gender, financial difficulty, marital status, educational status, activities of daily living dependence, physical activity, diabetes mellitus, hypertension, ischemic heart disease, cognitive impairment, and depression.

Results: Between ages 85–90 and 90–95 years, 33.2% (364/1096) and 44.3% (236/533) people died, respectively. All mean optimism scores declined from age 85 to 90, with males significantly more optimistic than females throughout. All measures of optimism (Op-Total, Op-Future, and Op-Happy) at ages 85 and 90 were significantly associated with improved 5-year survival from age 85 to 90 and 90 to 95, respectively, in both unadjusted and adjusted models. Findings remained unchanged after separately excluding depressed subjects, cognitively impaired subjects, and subjects dying within 6 months from baseline.

Conclusions: These finding support the hypothesis that being optimistic continues to confer a survival benefit irrespective of advancing age.

Keywords: Life orientation, Life skills, Positive expectations, Psychological well-being, Resilience

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Having a Happy Spouse Is Associated With Lowered Risk of Mortality

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Abstract

Studies have shown that individuals' choice of a life partner predicts their life outcomes, from their relationship satisfaction to their career success. The present study examined whether the reach of one's spouse extends even further, to the ultimate life outcome: mortality. A dyadic survival analysis using a representative sample of elderly couples (N = 4,374) followed for up to 8 years showed that a 1-standard-deviation-higher level of spousal life satisfaction was associated with a 13% lower mortality risk. This effect was robust to controlling for couples' socioeconomic situation (e.g., household income), both partners' sociodemographic characteristics, and baseline health. Exploratory mediation analyses pointed toward partner and actor physical activity as sequential mediators. These findings suggest that life satisfaction has not only intrapersonal but also interpersonal associations with longevity and contribute to the fields of epidemiology, positive psychology, and relationship research.

How To Reduce CPAP With Better Results

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