THE CATHOLIC UNIVERSITY OF KOREA
EUNPYEONG ST. MARY'S HOSPITAL

호흡기내과 의사를 위한
Respiratory Review of 2024 : Sleep

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Eunpyeong St. Mary's Hospital, College of Medicine, The Catholic University of Korea

Contents

- Diagnosis
- Moving beyond AHI
- Emerging treatment
- OSA & CV outcome
- ASV for SDB in HF
- Etc.

Contents

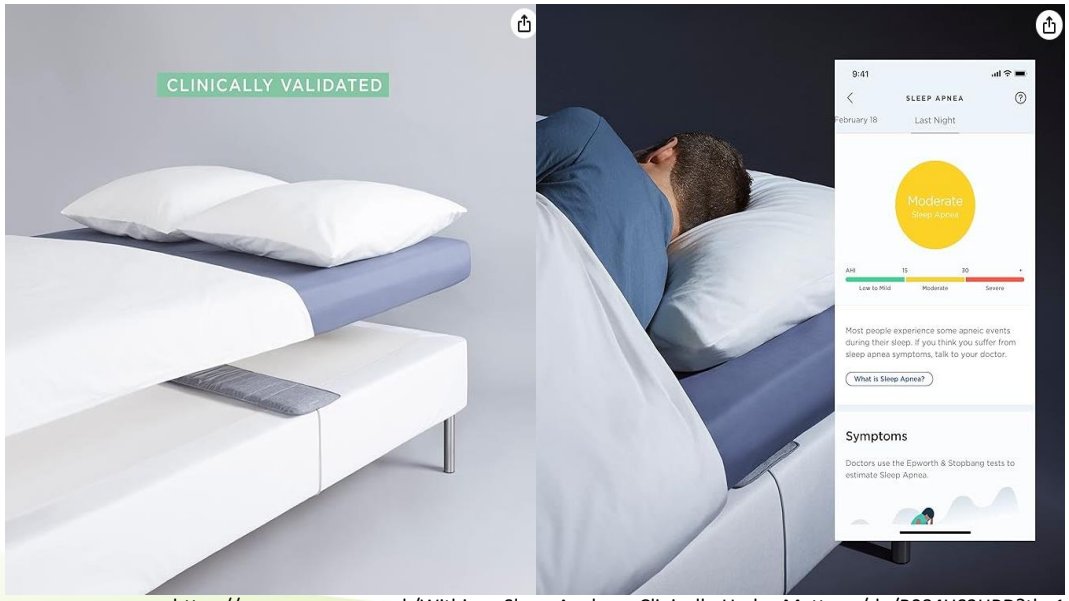
ORIGINAL ARTICLE

Multinight Prevalence, Variability, and Diagnostic Misclassification of Obstructive Sleep Apnea

Bastien Lechat[1], Ganesh Naik[1], Amy Reynolds[1], Atqiya Aishah[1,2], Hannah Scott[1], Kelly A. Loffler[1], Andrew Vakulin[1], Pierre Escourrou[3], R. Doug McEvoy[1], Robert J. Adams[1], Peter G. Catcheside[1], and Danny J. Eckert[1]

[1]Adelaide Institute for Sleep Health and Flinders Health and Medical Research Institute Sleep Health, College of Medicine and Public Health, Flinders University, Adelaide, Australia; [2]School of Medical Sciences, University of New South Wales, Sydney New South Wales, Australia; and [3]Centre Interdisciplinaire du Sommeil, Paris, France

- OSA severity : vary markedly from night to night
- Validated, under-mattress sleep analyzer
- N=67,278, 151 countries
- Average of approximately 170 nights/participant

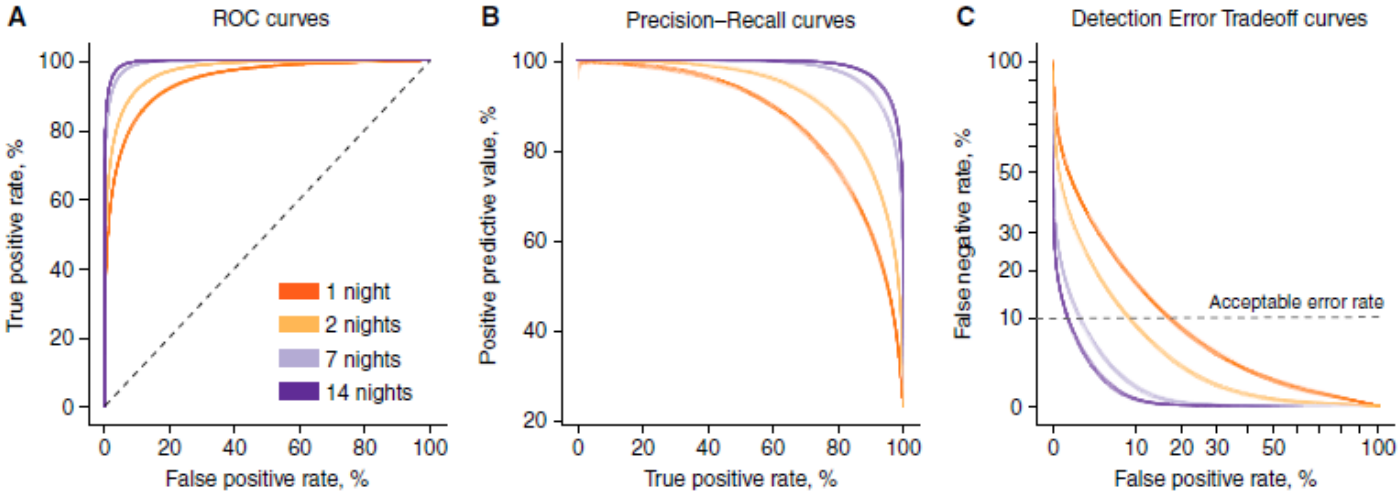


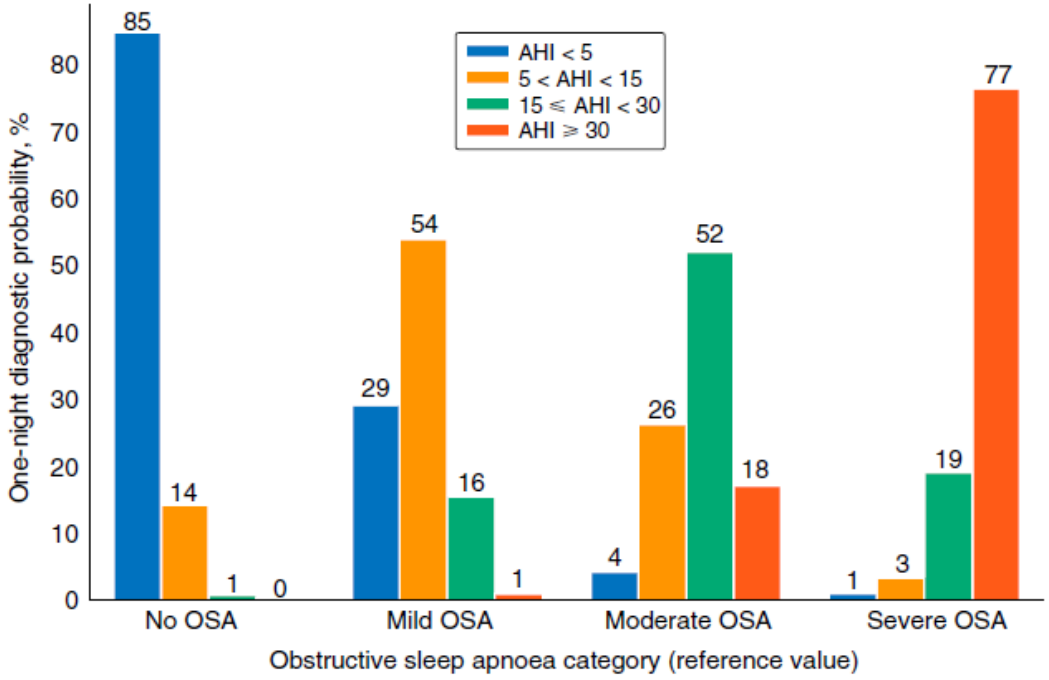
https://www.amazon.co.uk/Withings-Sleep-Analyzer-Clinically-Under-Mattress/dp/B084HS3HRD?th=1

- **Pneumatic & sound sensors**
detect body movements, RR, HR, snoring, and episodes of breathing cessation.

- **Clinical validation**
good agreement with PSG-derived AHI with high predictive performance (88% sensitivity & 88% specificity) to classify mod to severe OSA

Am J Respir Crit Care Med. 2022 Mar 1;205(5):563-569.





- Misdiagnosis based on a single night : about 20% ~ 50%
- Misdiagnosis error rates decreased with increased monitoring nights
- Remained stable after 14 nights of monitoring

Am J Respir Crit Care Med. 2022 Mar 1;205(5):563-569.

J Clin Sleep Med. 2024 Feb 28. doi: 10.5664/jcsm.11070. Online ahead of print.

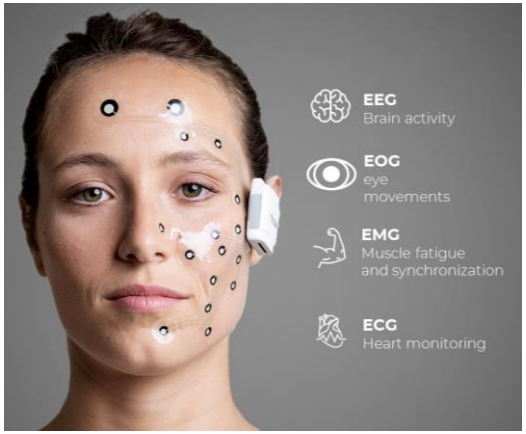
Long-term night-to-night variability of sleep-disordered breathing using a radar-based home sleep apnea test: a prospective cohort study

Samuel Tschopp [1,2], Urs Borner [1], Marco Caversaccio [1], Kurt Tschopp [2]

- Contactless radar-based HSAT with automated scoring (Sleepiz One) over 10 nights
- Feasible & well tolerated, lower costs, multiple-night testing to increase accuracy
- Validation & reducing the failure rate are necessary

Jan. 25, 2022, FDA clearance
(Wesper Lab system)

Feb. 9, 2024
FDA De Novo authorization



Feb. 20, 2024 (X-trodes)
FDA 510(k) clearance

Am J Respir Crit Care Med. 2024 Mar 12. doi: 10.1164/rccm.202304-0767OC. Online ahead of print.

Predicting Obstructive Sleep Apnea Based on Computed Tomography Scan Using Deep Learning Models

Jeong-Whun Kim [1], Kyungsu Lee [2], Hyun Jik Kim [3], Hae Chan Park [4], Jae Youn Hwang [5], Seok-Won Park [6], Hyoun-Joong Kong [7], Jin Youp Kim [8]

- 798 participants, PSG + PNS CT, age/sex/BMI
- Deep learning model
  - Accuracy : about 85% (4 class classification), 90% (2 class classification)

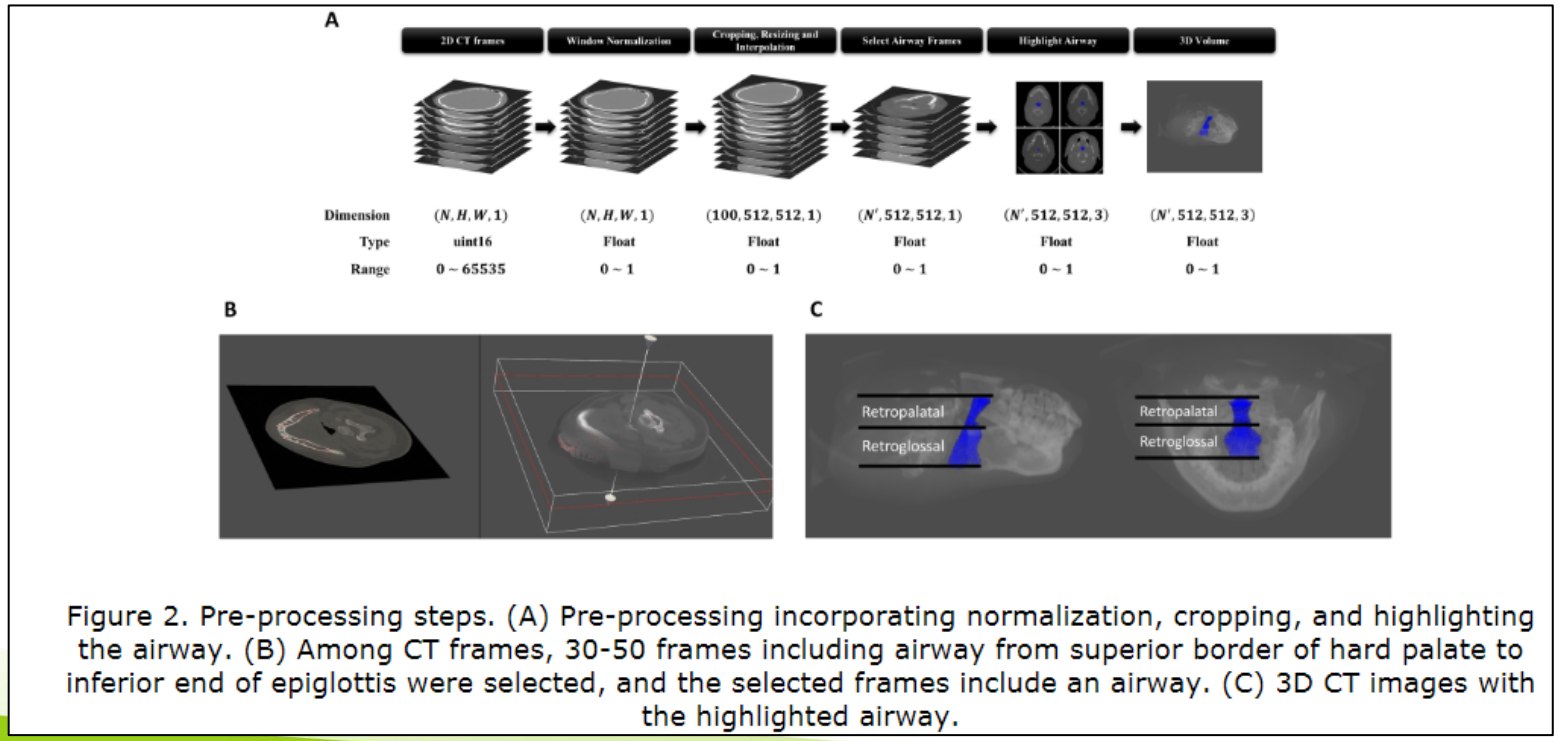


Figure 2. Pre-processing steps. (A) Pre-processing incorporating normalization, cropping, and highlighting the airway. (B) Among CT frames, 30-50 frames including airway from superior border of hard palate to inferior end of epiglottis were selected, and the selected frames include an airway. (C) 3D CT images with the highlighted airway.

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- Emerging treatment
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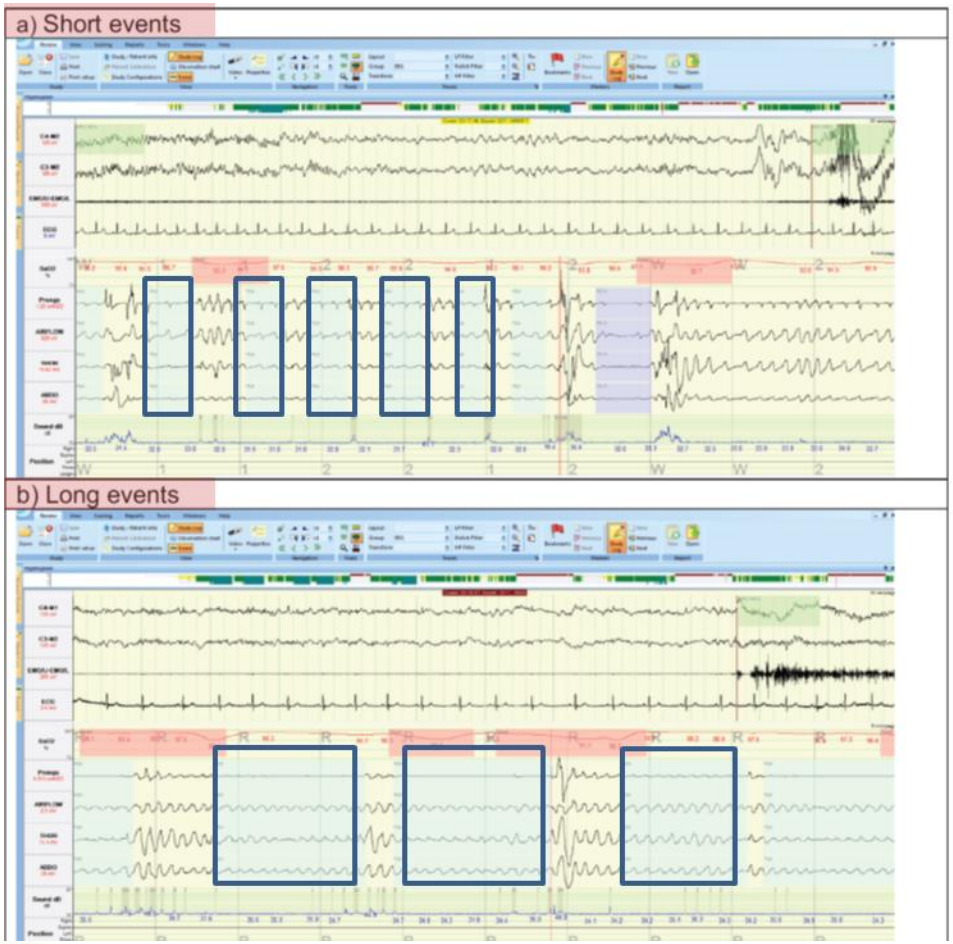
- Etc.

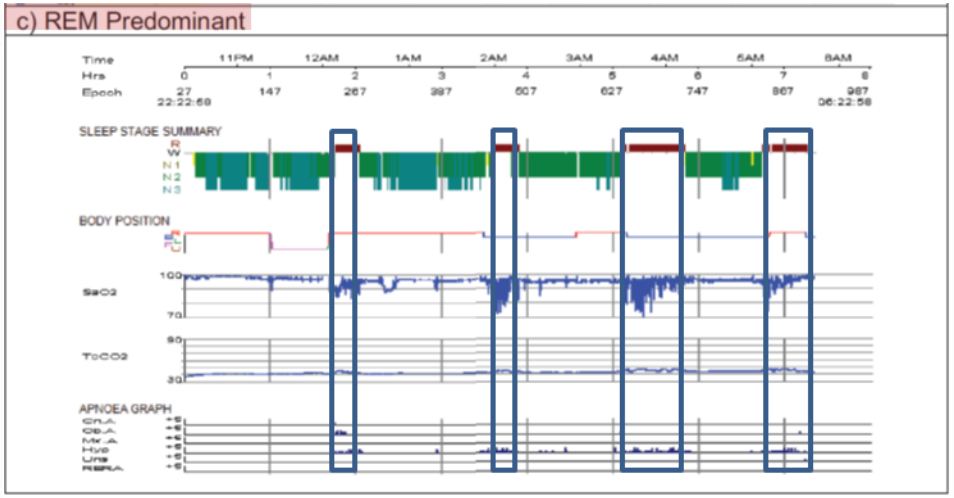
Special Article

Metrics of sleep apnea severity: beyond the apnea-hypopnea index

Atul Malhotra[1,*], Indu Ayappa[2], Najib Ayas[3], Nancy Collop[4], Douglas Kirsch[5,•], Nigel Mcardle[6], Reena Mehra[7], Allan I. Pack[8,•], Naresh Punjabi[9], David P. White[10] and Daniel J. Gottlieb[11,•]—for SRS Task Force

Sleep Research Society





Different patterns of obstructive respiratory events for people with AHI (range 20–30)

(a) <u>Short events</u> (AHI = 21.3, Average hypopnea duration 20 sec, max duration 55 sec)

(b) <u>Long events</u> (AHI = 25.6, Average hypopnea duration 31 sec, max duration 92 sec),

(c) <u>REM predominant</u> (AHI= 21.5, REM AHI = 67.5, NREM AHI = 5.5)

Sleep. 2021 Jul 9;44(7):zsab030.

SPECIAL ARTICLE

Metrics of sleep apnea severity: beyond the apnea-hypopnea index

Atul Malhotra[1,*], Indu Ayappa[2], Najib Ayas[3], Nancy Collop[4], Douglas Kirsch[5,•], Nigel Mcardle[6], Reena Mehra[7], Allan I. Pack[8,•], Naresh Punjabi[9], David P. White[10] and Daniel J. Gottlieb[11,•]—for SRS Task Force

Sleep Research Society®

- **Limitations of AHI**
  - Inconsistent methodology
  - Fails to capture the physiological abnormalities accurately
  - Fails to predict clinical consequences of OSA or response to OSA Tx.

- **Alternative metrics**
  - Hypoxic burden
  - Arousal intensity
  - Odds ratio product (ORP)
  - Cardiopulmonary coupling (CPC)
  - Apnea-hypopnea event duration

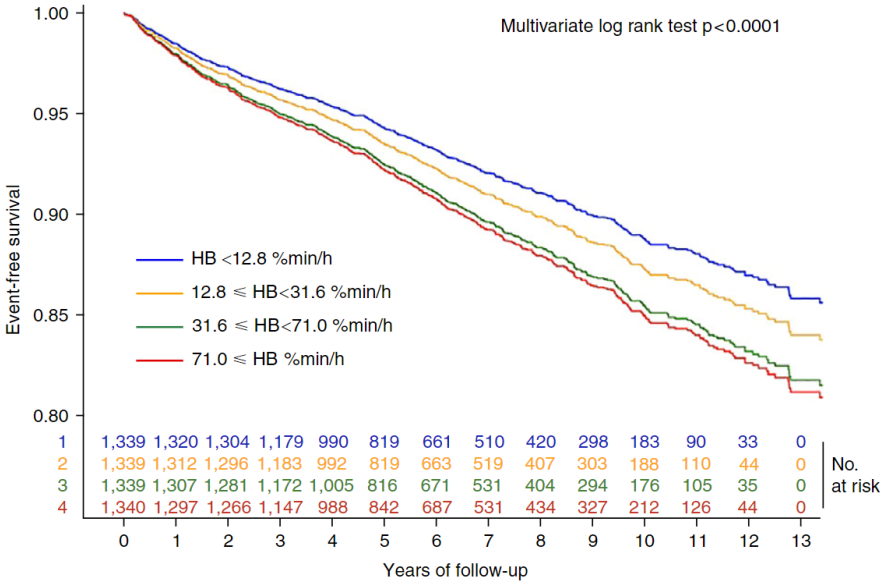
Sleep. 2021 Jul 9;44(7):zsab030.

ORIGINAL ARTICLE

Sleep Apnea–Specific Hypoxic Burden, Symptom Subtypes, and Risk of Cardiovascular Events and All-Cause Mortality

Wojciech Trzepizur[1,2], Margaux Blanchard[3,4], Timothée Ganem[1], Frédéric Balusson[5], Mathieu Feuilloy[3,4], Jean-Marc Girault[3,4], Nicole Meslier[1,2], Emmanuel Oger[5], Audrey Paris[6], Thierry Pigeanne[7], Jean-Louis Racineux[8], AbdelKebir Sabil[9], Chloé Gervès-Pinquié[8], and Frédéric Gagnadoux[1,2]; on behalf of the ERMES study group

- Sx. subtypes & OSA–specific HB
- Elevated OSA-specific HB : higher risk of a CV event & all-cause mortality
- Sx. subtypes : not associated with MACE after adjustment for confounders



Am J Respir Crit Care Med. 2022 Jan 1;205(1):108-117.

Pulse Wave Amplitude Drops Index: A Biomarker of Cardiovascular Risk in Obstructive Sleep Apnea

Geoffroy Solelhac[1*], Manuel Sánchez-de-la-Torre[4,6,7*], Margaux Blanchard[8,9*], Mathieu Berger[1], Camila Hirotsu[1], Théo Imler[1], Alicia Sánchez-de-la-Torre[4,6,7], Jose Haba-Rubio[1], Nicola Andrea Marchi[1], Virginie Bayon[1], Sébastien Bailly[10], François Goupil[11], Adrien Waeber[1], Grégory Heiniger[1], Thierry Pigeanne[12], Esther Gracia-Lavedan[5], Andrea Zapater[4,6], Jorge Abad[13], Estrella Ordax[14], María José Masdeu[13], Valentin Cabriada-Nuño[16], Carlos Egea[7,17], Sandra Van Den Broecke[1,18], Peter Vollenweider[2], Pedro Marques-Vidal[2], Julien Vaucher[2], Giulio Bernardi[19], Monica Betta[19], Francesca Siclari[1,20,21], Ferran Barbé[7,5‡], Frédéric Gagnadoux[22,23‡], and Raphael Heinzer[1,3‡]

- Which patients with OSA are at increased cardiovascular risk?
- **Pulse wave amplitude drops (PWADs)**
  - Reflecting sympathetic activations & vasoreactivity
  - Biomarker of cardiovascular risk in OSA

* **PWAD index** : No. of PWADs (>30%) per hour during sleep

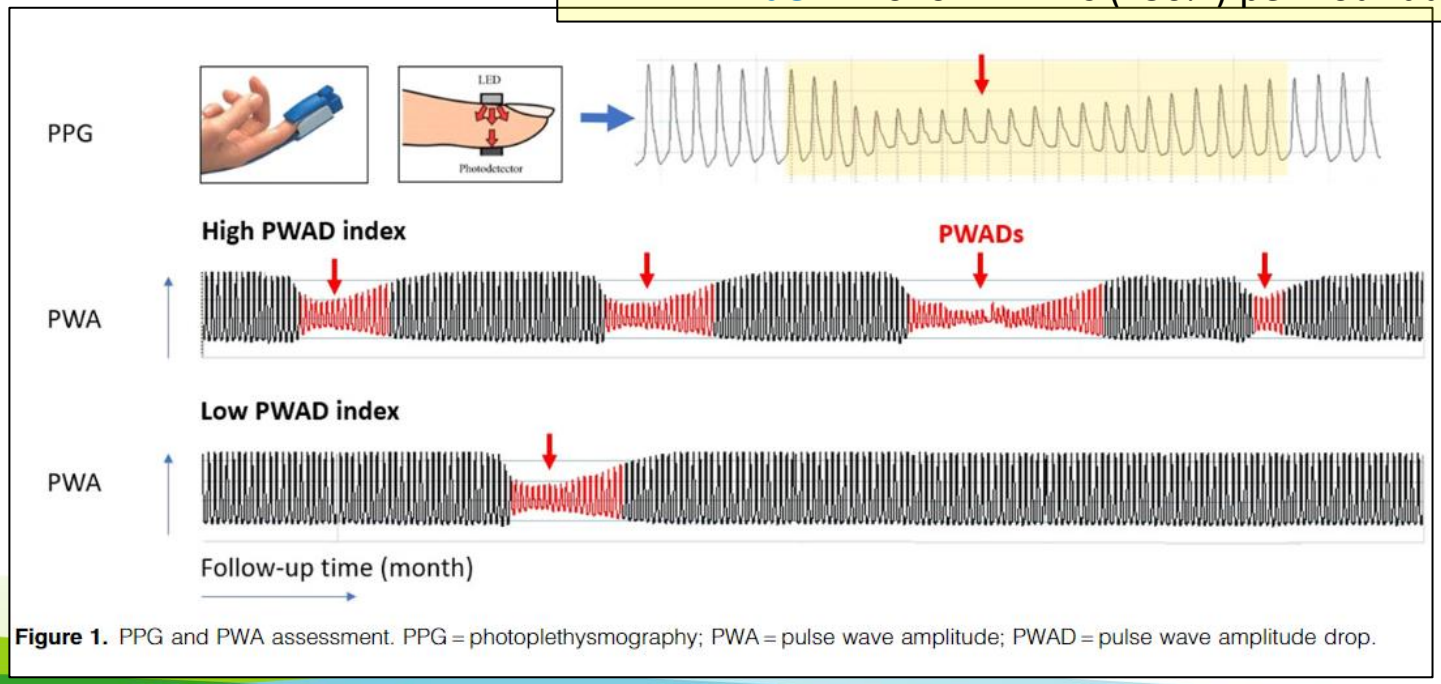
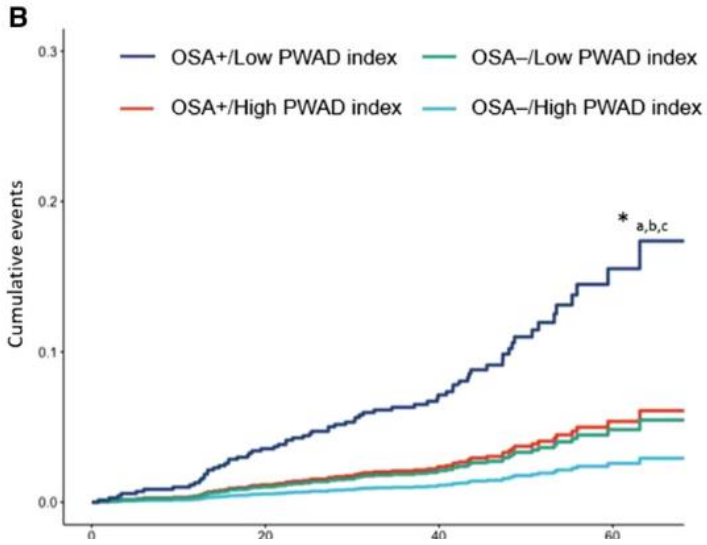


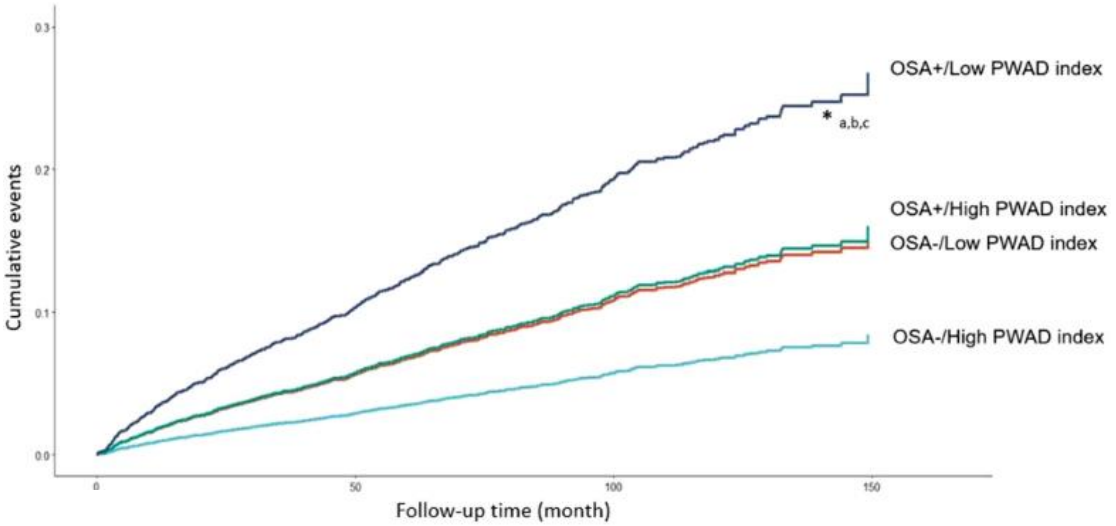
Figure 1. PPG and PWA assessment. PPG = photoplethysmography; PWA = pulse wave amplitude; PWAD = pulse wave amplitude drop.

Am J Respir Crit Care Med. 2023 Jun 15;207(12):1620-1632.

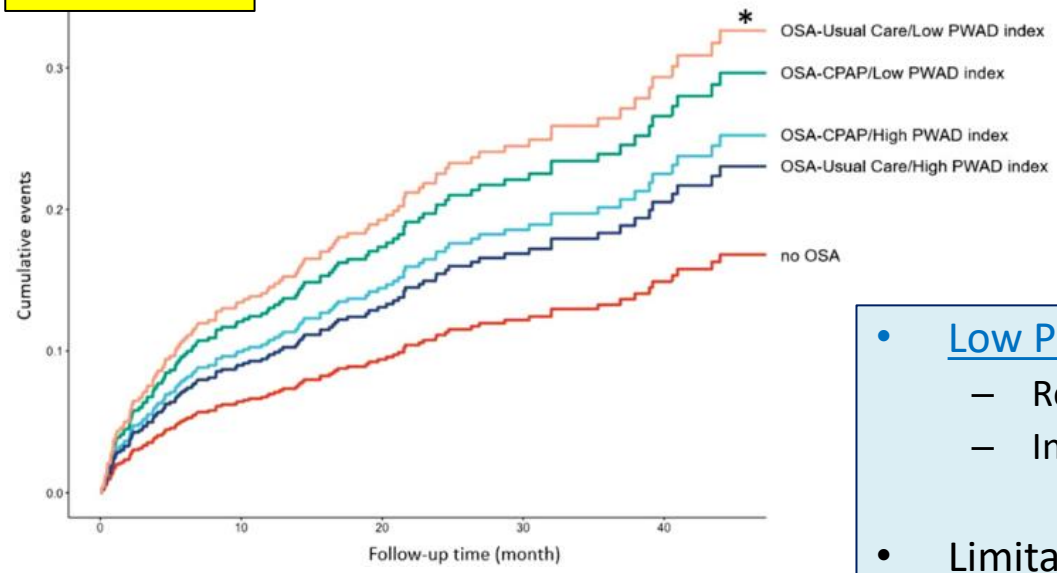
HypnoLaus study



Pays de la Loire Sleep Cohort



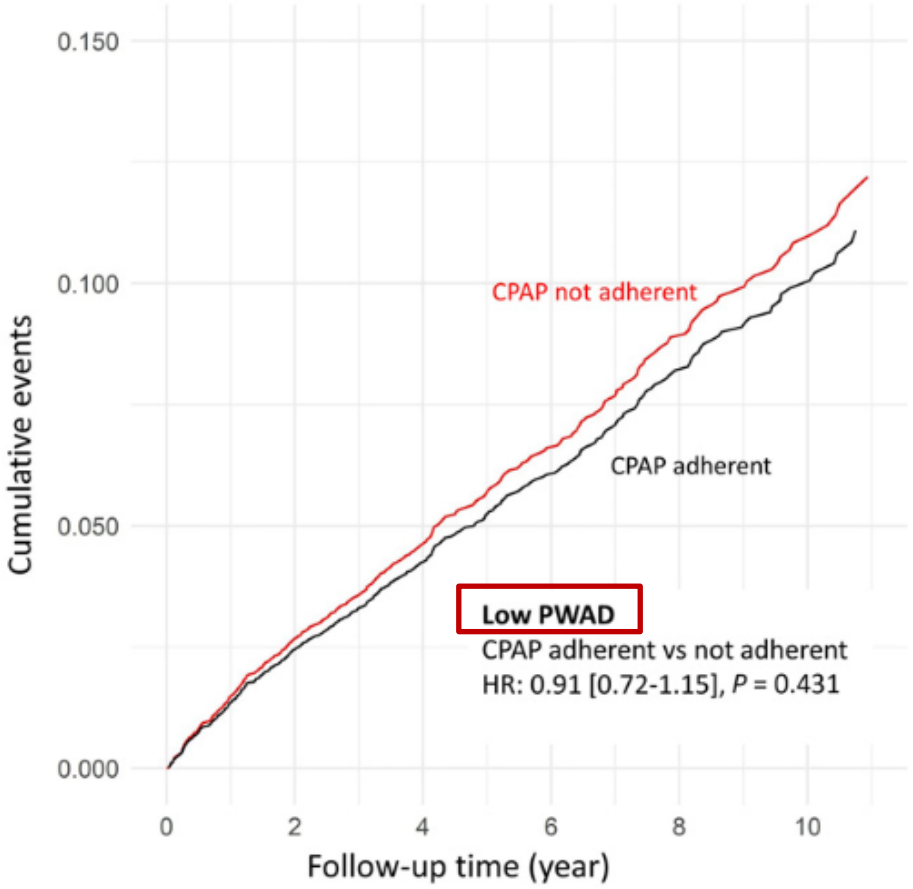
ISAACC study

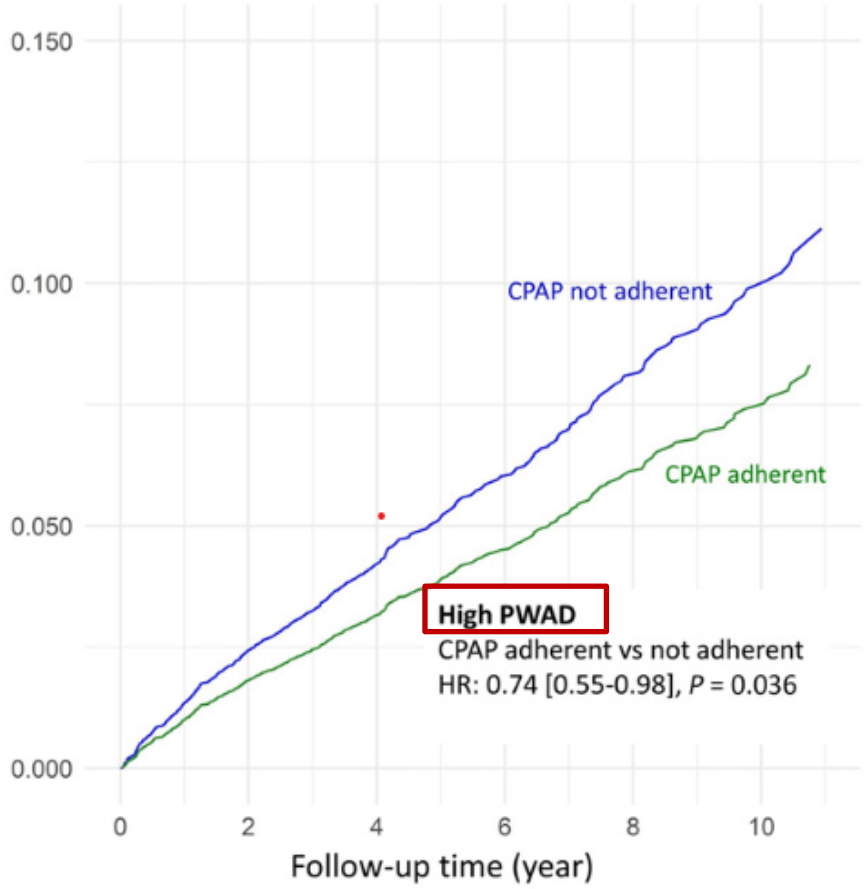


- Low PWAD index in pts with OSA
  - Reflecting poor autonomic & vascular reactivity
  - Independently associated with a higher CV risk
- Limitation : preexisting CVD, A.fib etc.

Am J Respir Crit Care Med. 2023 Jun 15;207(12):1620-1632.

Pays de la Loire Sleep Cohort





Am J Respir Crit Care Med. 2023 Jun 15;207(12):1620-1632.

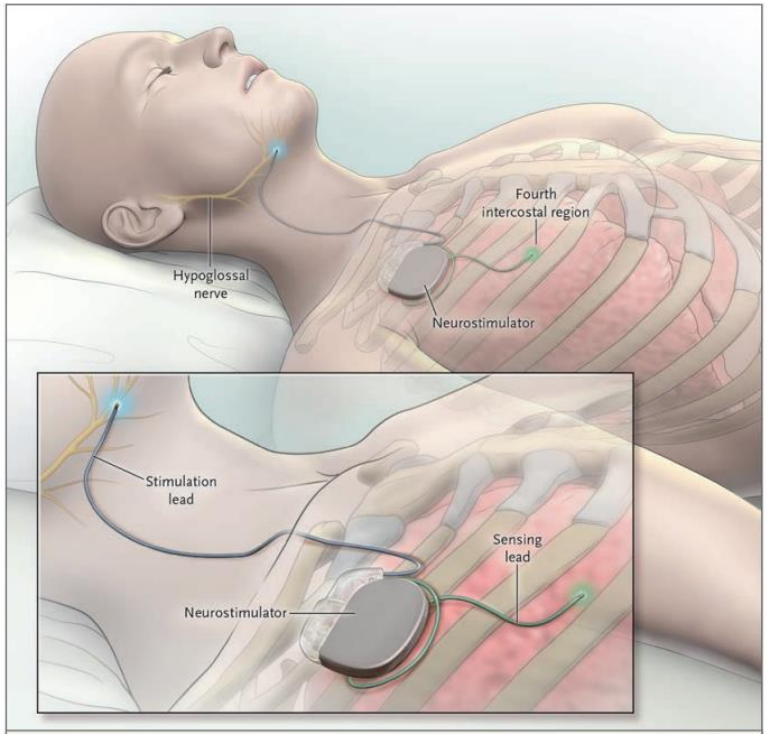
Contents

EUROPEAN RESPIRATORY REVIEW
ERS OFFICIAL DOCUMENTS
W. RANDERATH ET AL.

European Respiratory Society guideline on non-CPAP therapies for obstructive sleep apnoea

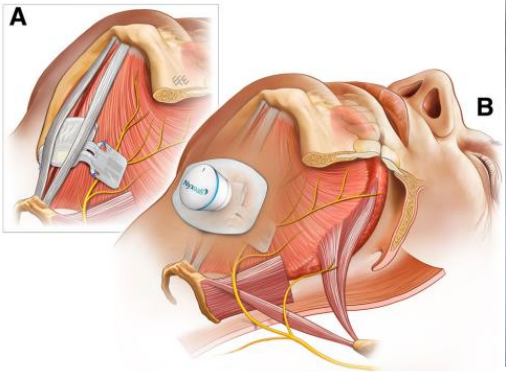
- Gastric bypass surgery
- Custom-made dual-block mandibular advancement devices
- Hypoglossal nerve stimulation (HNS)
- Myofunctional therapy
- Maxillo-mandibular osteotomy
- Carbonic anhydrase inhibitors
- Positional therapy

Randerath W et. al., Eur Respir Rev. 2021 Nov 30;30(162):210200.



N Engl J Med. 2014 Jan 9;370(2):139-49.

https://www.inspiresleep.com/en-us/



Laryngoscope Investig Otolaryngol. 2019 Nov 22;4(6):703-707.

https://www.geniosleep.com/en/

Treatment	Description	Advantages	Disadvantages and adverse effects
Hypoglossal nerve stimulation	Surgically implanted electrode stimulates the hypoglossal nerve to enhance tongue protrusion and stabilize the upper airway during inspiration	Highly effective and well tolerated in select patients (body mass index <32 and absence of concentric collapse of the retropalatal airway on drug-induced sleep endoscopy)	Expensive compared with alternative therapies; potential complications include temporary tongue weakness and tongue soreness and discomfort from stimulation

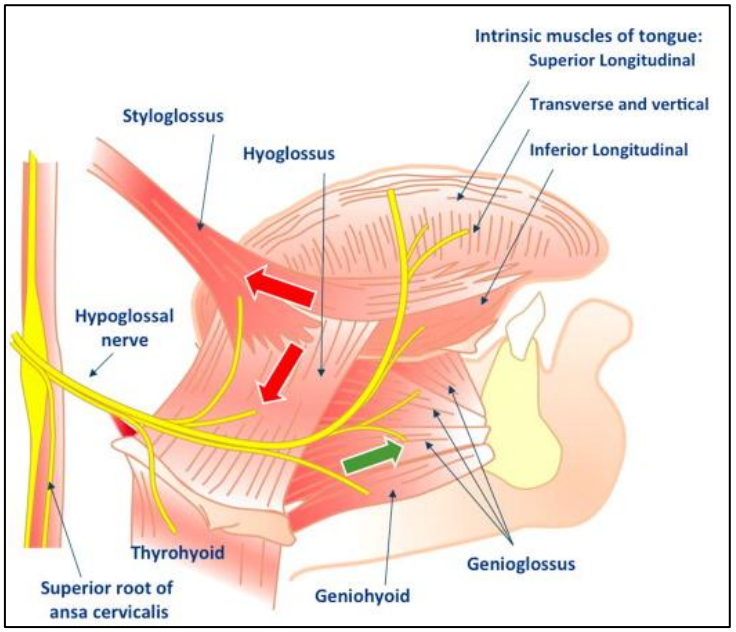
Gottlieb DJ et. al., JAMA. 2020 Apr 14;323(14):1389-1400.

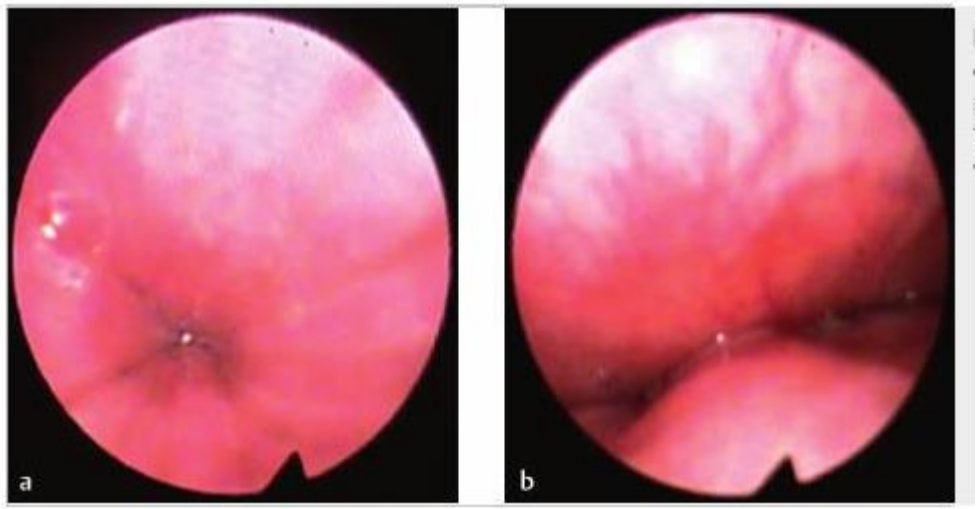
ORIGINAL RESEARCH

Upper Airway Stimulation versus Untreated Comparators in Positive Airway Pressure Treatment–Refractory Obstructive Sleep Apnea

Reena Mehra[1*], Armin Steffen[2*], Clemens Heiser[3], Benedikt Hofauer[3], Kirk Withrow[4], Karl Doghramji[5], Maurits Boon[5], Colin Huntley[5], Ryan J. Soose[6], Suzanne Stevens[7], Chris Larsen[7], Joachim T. Maurer[8], Tina Waters[1], Harneet K. Walia[1], Alan H. Kominsky[1], Doug Trask[1], Richard J. Schwab[9], Erica R. Thaler[9], and Patrick J. Strollo[6]; on behalf of the ADHERE Registry Study

- Medical insurance with OSA & PAP intolerance meeting UAS implantation criteria
  - Pre-op AHI : 15-65/h
  - < 25% central & mixed apneas
  - CPAP intolerance
  - Absence of complete concentric collapse at the soft palate during drug-induced sleep endoscopy



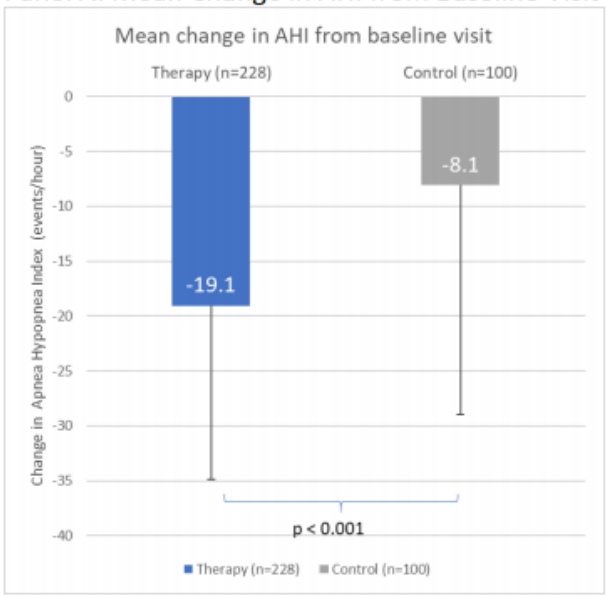


Vries, Nico de et al.: 2021Drug-Induced Sleep Endoscopy

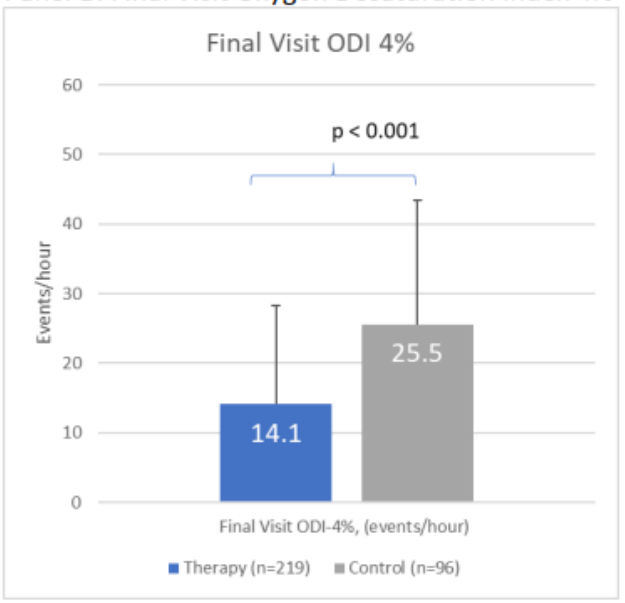
(a) Complete concentric collapse at palate : **Not** a good candidate
(b) Complete AP collapse at palate : **Good** candidate

Ann Am Thorac Soc. 2020 Dec;17(12):1610-1619.

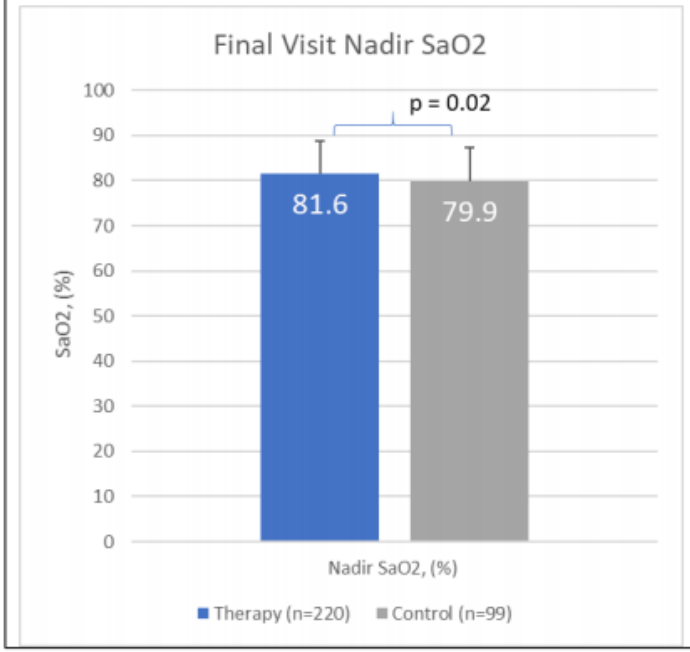
Panel A: Mean Change in AHI from Baseline Visit



Panel B: Final Visit Oxygen Desaturation Index 4%

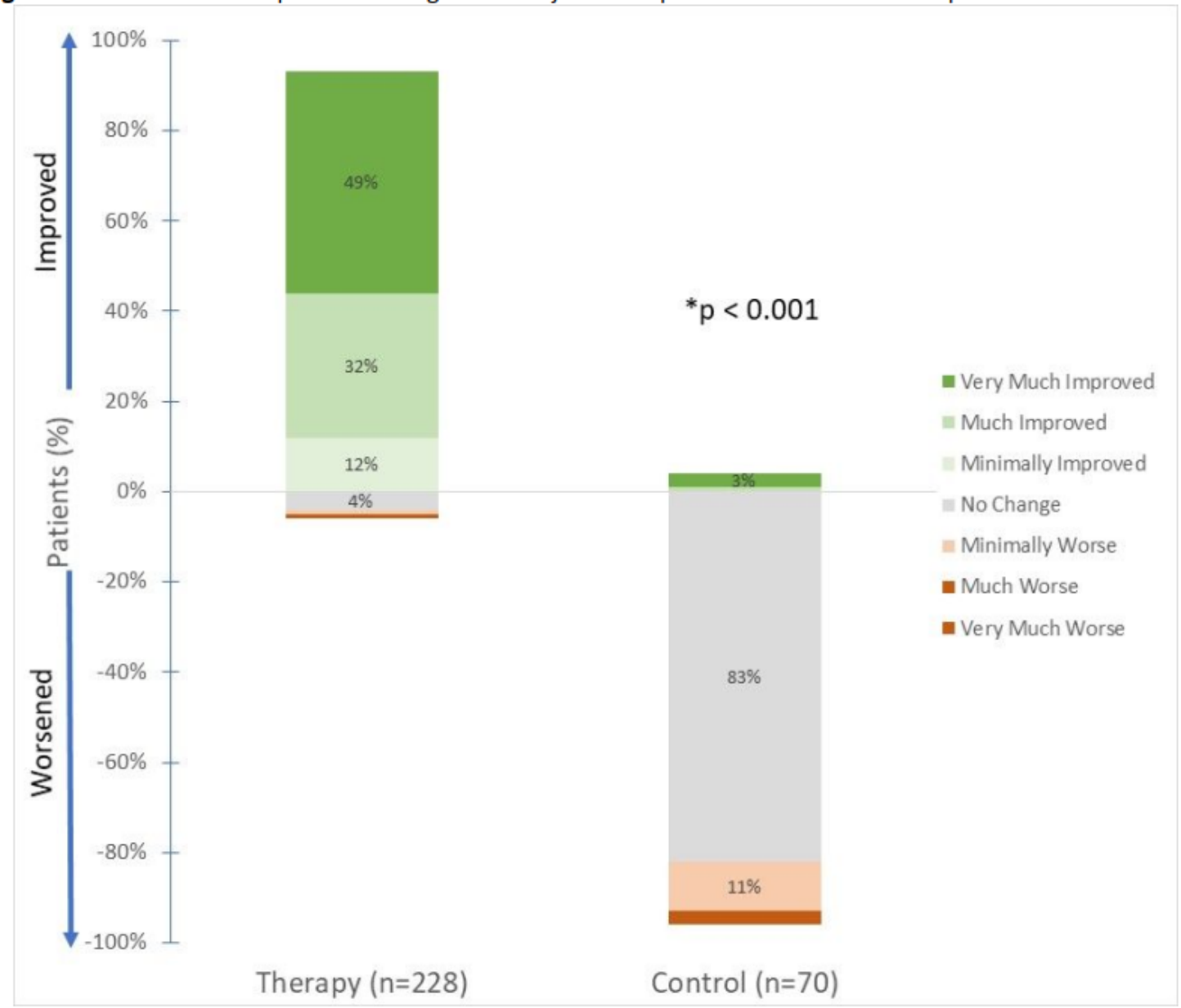


Panel C: Final Visit Nadir SaO2



Ann Am Thorac Soc. 2020 Dec;17(12):1610-1619.

Figure 3. Clinical Global Impression – Degree of Subjective Improvement between Groups



Ann Am Thorac Soc. 2020 Dec;17(12):1610-1619.

SLEEP BREATHING PHYSIOLOGY AND DISORDERS • REVIEW

Hypoglossal nerve stimulation long-term clinical outcomes: a systematic review and meta-analysis

Andrea Costantino[1] · Vittorio Rinaldi[1] · Antonio Moffa[2] · Vitaliana Luccarelli[1] · Federica Bressi[3] · Michele Cassano[2] · Manuele Casale[1] · Peter Baptista[4]

- Hypoglossal nerve stimulation (HNS) clinical outcomes in mod-severe OSA
- 12 studies (no RCT), 350 patients
  - Median age 54.3, BMI 29.8
- Results : surgical success rate (50% reduction in AHI & overall AHI < 20)
  - 12months : 72.4% (Inspire), 76.9% (ImThera), 55% (Apnex)
  - 60months : 75% (Inspire)
- Limitations
  - STAR trial was the only prospective cohort with a follow-up >1 year
  - Majority of patients were treated in highly specialized centers

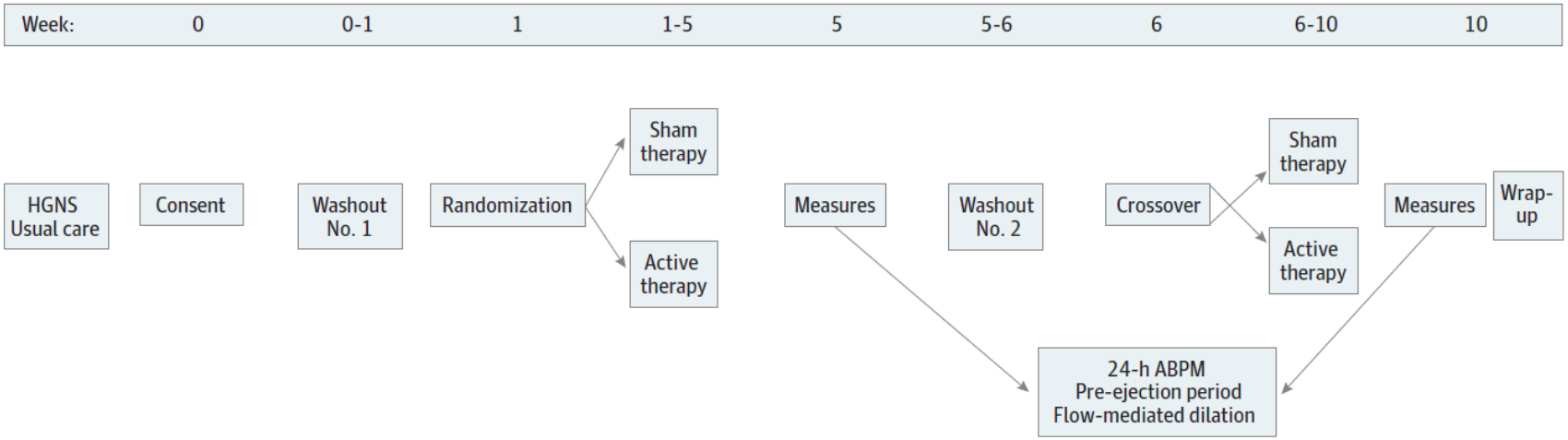
Sleep Breath. 2020 Jun;24(2):399-411.

JAMA Otolaryngology–Head & Neck Surgery | Original Investigation

Hypoglossal Nerve Stimulation and Cardiovascular Outcomes for Patients With Obstructive Sleep Apnea

A Randomized Clinical Trial

Raj C. Dedhia, MD, MSCR; Donald L. Bliwise, PhD; Arshed A. Quyyumi, MD; Erica R. Thaler, MD; Maurits S. Boon, MD; Colin T. Huntley, MD; Everett G. Seay, RPSGT; Akshay Tangutur, MS; Patrick J. Strollo, MD; Nil Gurel, PhD; Brendan T. Keenan, MS



- N=60, severe OSA at baseline (mean AHI : 33.1)
- Mean 24-hour SBP & other CV measures were not significantly different between sham and active HGNS therapy

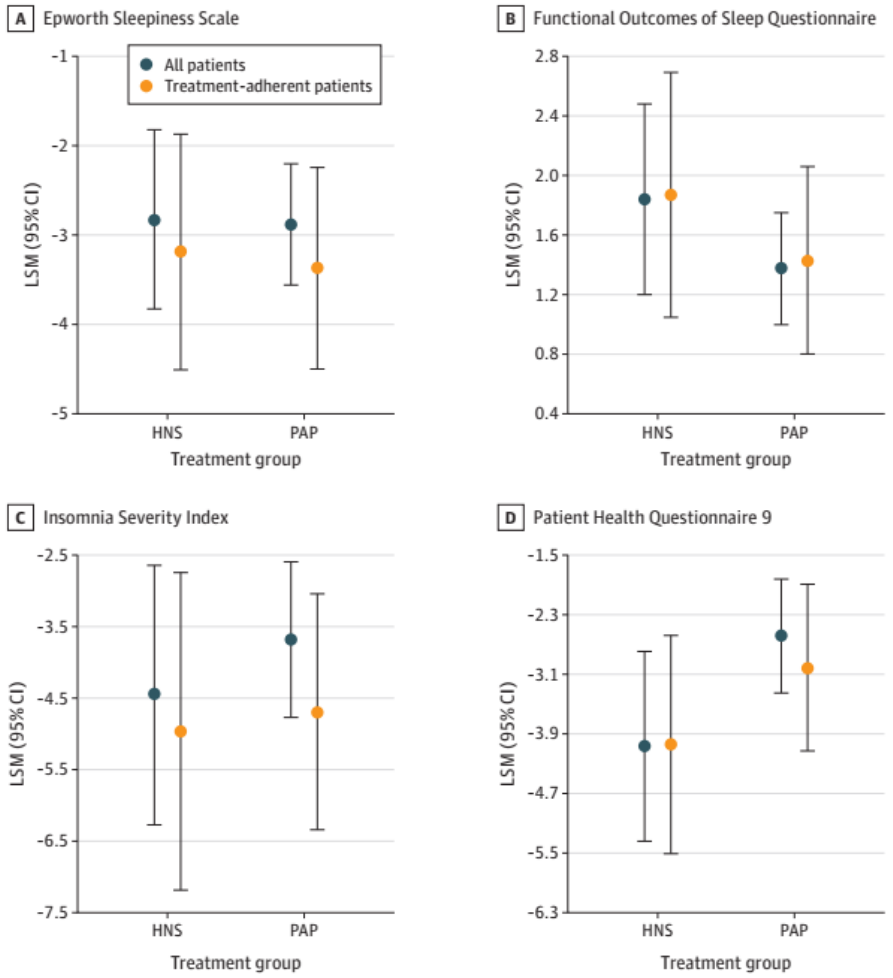
JAMA Otolaryngol Head Neck Surg. 2024 Jan 1;150(1):39-48.

JAMA Otolaryngology–Head & Neck Surgery | Original Investigation

Association of Hypoglossal Nerve Stimulation With Improvements in Long-term, Patient-Reported Outcomes and Comparison With Positive Airway Pressure for Patients With Obstructive Sleep Apnea

Maeve Pascoe, BS; Lu Wang, MS; Joan Aylor, BA; Reena Mehra, MD, MS; Alan Kominsky, MD; Nancy Foldvary-Schaefer, DO, MS; Vaishal Shah, MD; Tina Waters, MD; Harneet K. Walia, MD

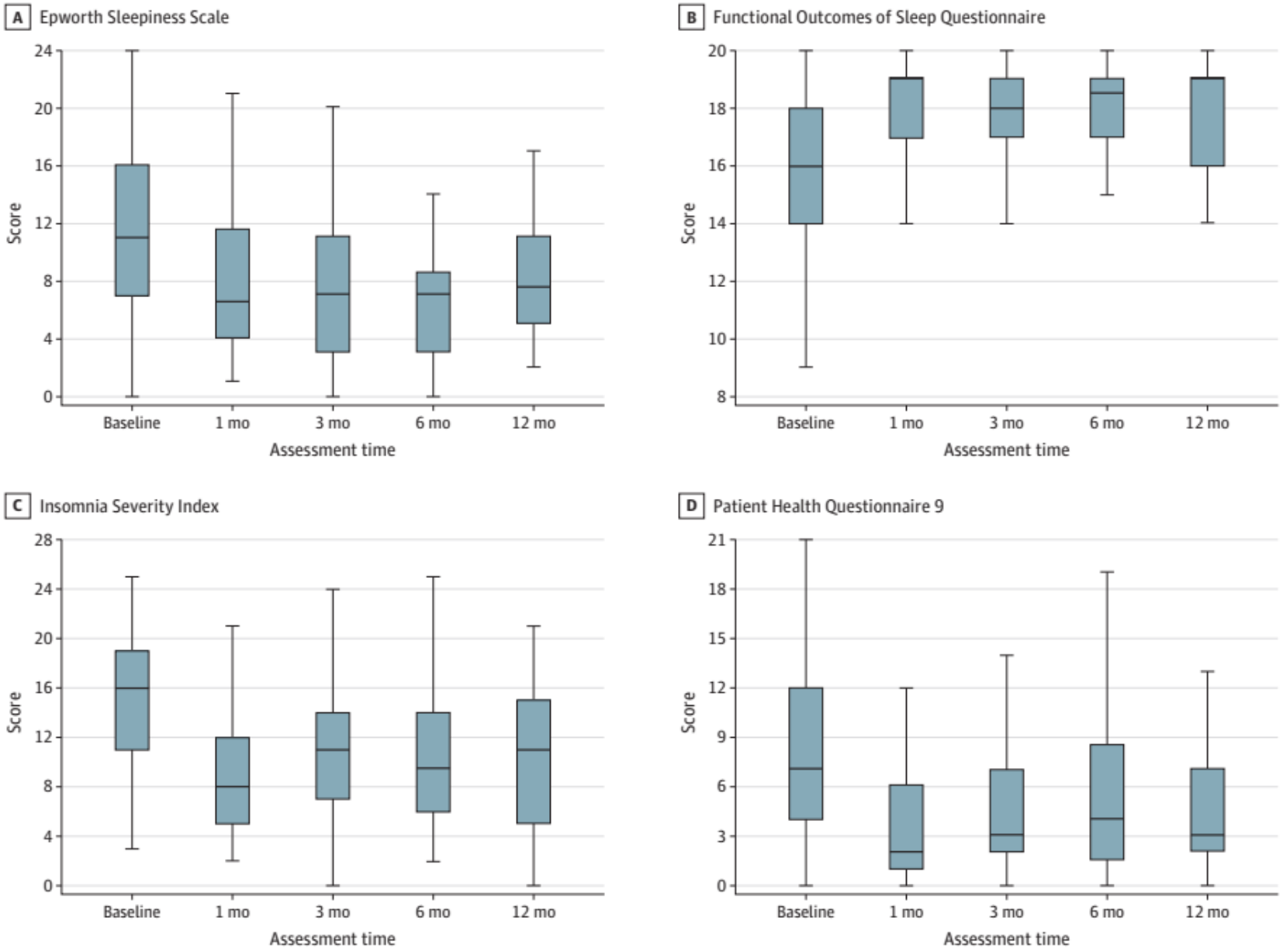
Figure 1. Changes in Patient-Related Outcomes From Baseline to 3-Month Follow-up in Hypoglossal Nerve Stimulation (HNS) and Positive Airway Pressure (PAP) Groups



- Retrospective cohort study
- Patients treated at the Cleveland Clinic for OSA

JAMA Otolaryngol Head Neck Surg. 2022 Jan 1;148(1):61-69.

Figure 2. Longitudinal Changes in Patient-Related Outcomes (PROs) With Hypoglossal Nerve Stimulation Use



JAMA Otolaryngol Head Neck Surg. 2022 Jan 1;148(1):61-69.

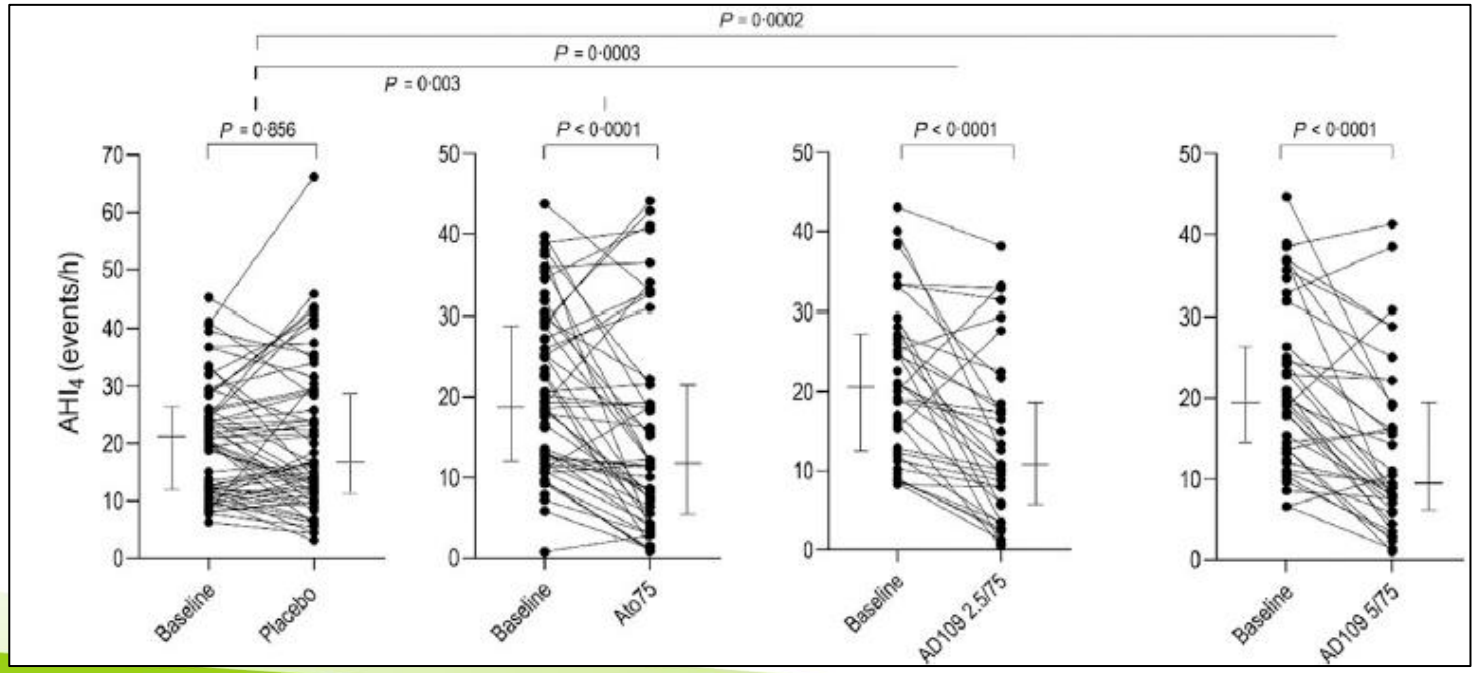
ORIGINAL ARTICLE

The Combination of Aroxybutynin and Atomoxetine in the Treatment of Obstructive Sleep Apnea (MARIPOSA)

A Randomized Controlled Trial

Paula K. Schweitzer[1], Luigi Taranto-Montemurro[2], Joseph M. Ojile[3], Stephen G. Thein[4], Christopher L. Drake[5], Russell Rosenberg[6], Bruce Corser[7], Brian Abaluck[8], R. Bart Sangal[9,10], and James Maynard[11]

- Antimuscarinic agent (aroxybutynin) & norepinephrine reuptake inhibitor (atomoxetine)
- Phase II randomized, double-blind, placebo controlled, parallel-group, 4-wk trial comparing AD109 2.5/75 mg, AD109 5/75 mg, atomoxetine 75 mg alone, and placebo
- Side effects : dry mouth, insomnia, urinary hesitation/flow decrease

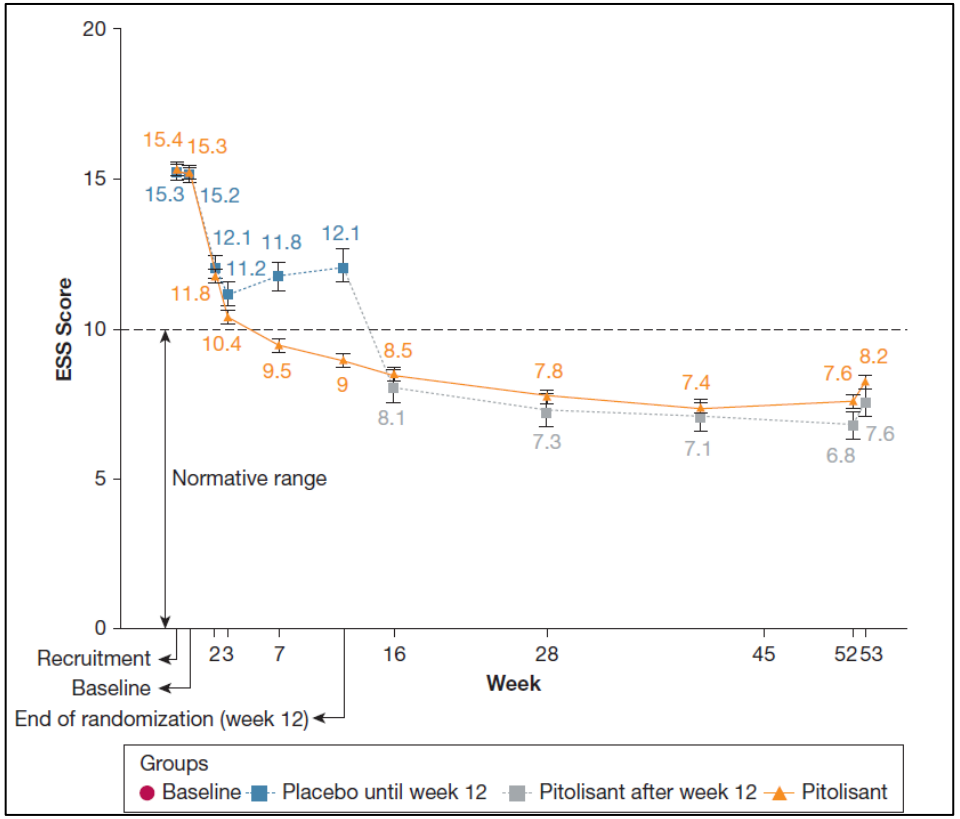


Am J Respir Crit Care Med. 2023 Dec 15;208(12):1316-1327.

Long-Term Efficacy and Safety of Pitolisant for Residual Sleepiness Due to OSA

Jean-Louis Pépin, MD; Valérie Attali, MD; Christian Caussé, MD; Johan Verbraecken, MD; Jan Hedner, MD; Isabelle Lecomte, MD; Renaud Tamisier, MD; Patrick Lévy, MD; Philippe Lehert, PhD; and Yves Dauvilliers, MD

- Pitolisant (Wakix)
  - Effective in reducing daytime sleepiness in 12wk RCTs
  - Patients with moderate to severe OSA and EDS, adherent to CPAP (HAROSA 1) or refusing or not tolerating CPAP (HAROSA 2)
- 512 adults included in the two RCTs, 376 completed the 1-yr FU
- Effective in reducing daytime sleepiness over 1 yr with or without CPAP Tx
  - Mean difference in ESS score from baseline to 1 yr : 8.0 (95% CI, 8.3 to 7.5).
- Good safety profile



Chest. 2024 Mar;165(3):692-703.

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- Moving beyond AHI
- Emerging treatment
- **OSA & CV outcome**
- ASV for SDB in HF
- Etc.

Table 1. Trial Designs, Patient Characteristics, and Definitions Used in Meta-Analyses[a]

	SAVE Study (McEvoy et al,[6] 2016)	ISAACC Study (Sánchez-de-la-Torre et al,[7] 2020)	RICCADSA Study (Peker et al,[8] 2016)
Patients	2687 (CPAP = 1346; usual care = 1341)	1255 (CPAP = 629; usual care = 626)	244 (CPAP = 122; no CPAP = 122)
Condition or disease	Coronary artery disease and/or cerebrovascular disease Nonsleepy OSA (Epworth Sleepiness Scale[b] score <15)	Acute coronary syndrome Nonsleepy OSA (Epworth Sleepiness Scale[b] score <11)	Coronary artery disease Nonsleepy OSA (Epworth Sleepiness Scale[b] score <10)
Setting	89 Centers in 7 countries (Australia, Brazil, China, India, New Zealand, Spain, and United States)	15 Hospitals across Spain	Two sites in Skaraborg County, West Sweden
Recruiting period	2008-2013	2011-2018	2005-2010
Design	International, multicenter, randomized, parallel-group, open-label trial with blinded end point assessment	Multicenter, open-label, parallel, prospective, randomized clinical trial	Single-center (2 sites), prospective, open, randomized, parallel, interventional, superiority trial
OSA diagnosis	Home sleep-study screening device Oxygen desaturation index[c] ≥12 events/h	Hospital respiratory polygraphy Apnea-hypopnea index[d] ≥15 events/h	Home respiratory polygraphy Apnea-hypopnea index[d] ≥15 events/h
Study groups	CPAP group (CPAP plus usual care) Usual care group (usual care alone)	CPAP group (CPAP plus usual care) Usual care group (usual care alone)	CPAP group No CPAP group
Intervention	Device: fixed CPAP Other: usual care (standard care of cardiovascular risk factors)	Device: fixed CPAP Other: usual care (hygienic-dietary measures, standard care of cardiovascular risk factors, and sleep hygiene counseling)	Device: AutoCPAP Other: usual care (standard care of cardiovascular risk factors)
Primary outcome	A composite of the cardiovascular end points of cardiovascular death, nonfatal acute myocardial infarction, nonfatal stroke, hospital admission for heart failure, and new hospitalization for unstable angina or transient ischemic attack	Rate of cardiovascular events: cardiovascular death, nonfatal acute myocardial infarction, nonfatal stroke, hospital admission for heart failure, and new hospitalization for unstable angina or transient ischemic attack	The combined rate of cardiovascular mortality, stroke, myocardial infraction, and the need for new revascularization

JAMA. 2023 Oct 3;330(13):1255-1265.

Major exclusions	12 608 Excluded 3944 Did not meet inclusion criteria 2716 Did not give consent 529 Excluded because of poor adherence 326 Lived too far from the clinical center 324 Used device <3 hours/night 68 Cheyne-Stokes respiration 39 Problems attending clinic 3359 Other reasons	5172 Excluded 4410 Did not meet inclusion criteria 762 Did not give consent 283 Excluded with >50% of central apneas or the presence of Cheyne-Stokes respiration	629 Excluded 597 Not interested in the study 101 Borderline OSA 32 Known OSA 29 Declined further investigations 21 Predominant central sleep apnea/ Cheyne-Stokes respiration
Follow-up, mean (IQR), mo	37.8 (25.9-55.2)	31.3 (13.7-55.0)	52.1 (35.6-70.8)
Baseline characteristics			
Age, mean (SD), y	61.2 (7.8)	60.3 (10.2)	66 (8.4)
Sex, No. (%)			
Men	2174 (81)	1058 (84)	205 (84)
Women	513 (19)	197 (16)	39 (16)
BMI, median (IQR)	28.1 (25.7-30.9)	29.0 (26.4-31.9)	28.4 (26.1-30.2)
Hypertension, %	78	56	64
Apnea-hypopnea index, median (IQR), events/h[d]	25.0 (16.0-40.0)	31.3 (21.0-46.0)	24.4 (18.4-35.9)
Epworth Sleepiness Scale score, median (IQR)[b]	7.0 (5.0-10.0)	5.0 (3.0-7.0)	6.0 (4.0-7.0)
CPAP use, median (IQR), hours/d	3.3 (1.3-5.1)	2.2 (0.03-5.1)	2.4 (0.2-4.8)

JAMA. 2023 Oct 3;330(13):1255-1265.

Heterogeneous Effects of CPAP in Non-Sleepy OSA on CVD Outcomes: Post-hoc Machine Learning Analysis of the ISAACC Trial (ECSACT Study)

Oren Cohen[1*], Manuel Sánchez-de-la-Torre[2*], Zainab Al-Taie[3], Samira Khan[1], Vaishnavi Kundel[1], Jason C. Kovacic[4,5], Esther Gracia-Lavedan[6], Jordi De Batlle[6], Girish Nadkarni[7], Ferran Barbé[6#], Mayte Suárez-Fariñas[3#], Neomi A. Shah[1#]

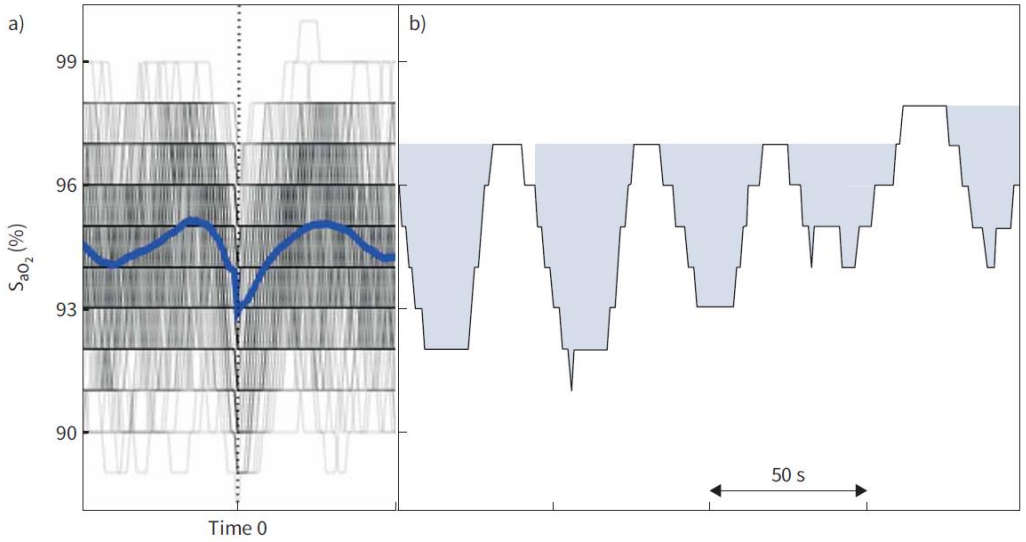
- 1,224 non-sleepy OSA participants
- Of fifty-five features entered into our model only two appeared in the final model (i.e., average OSA event duration and hypercholesterolemia)
- Longer OSA event duration and hypercholesterolemia : nearly 2.5-times more CVD events with CPAP compared to UC
  - Longer event duration (>19.5 seconds), HR 2.24, p=0.011
- Shorter OSA event duration had roughly half the rate of CVD events if randomized to CPAP
  - Below the model-derived average event duration threshold (19.5s), HR 0.46, p=0.002

Cohen O et. al., Ann Am Thorac Soc. 2024 Feb 15.

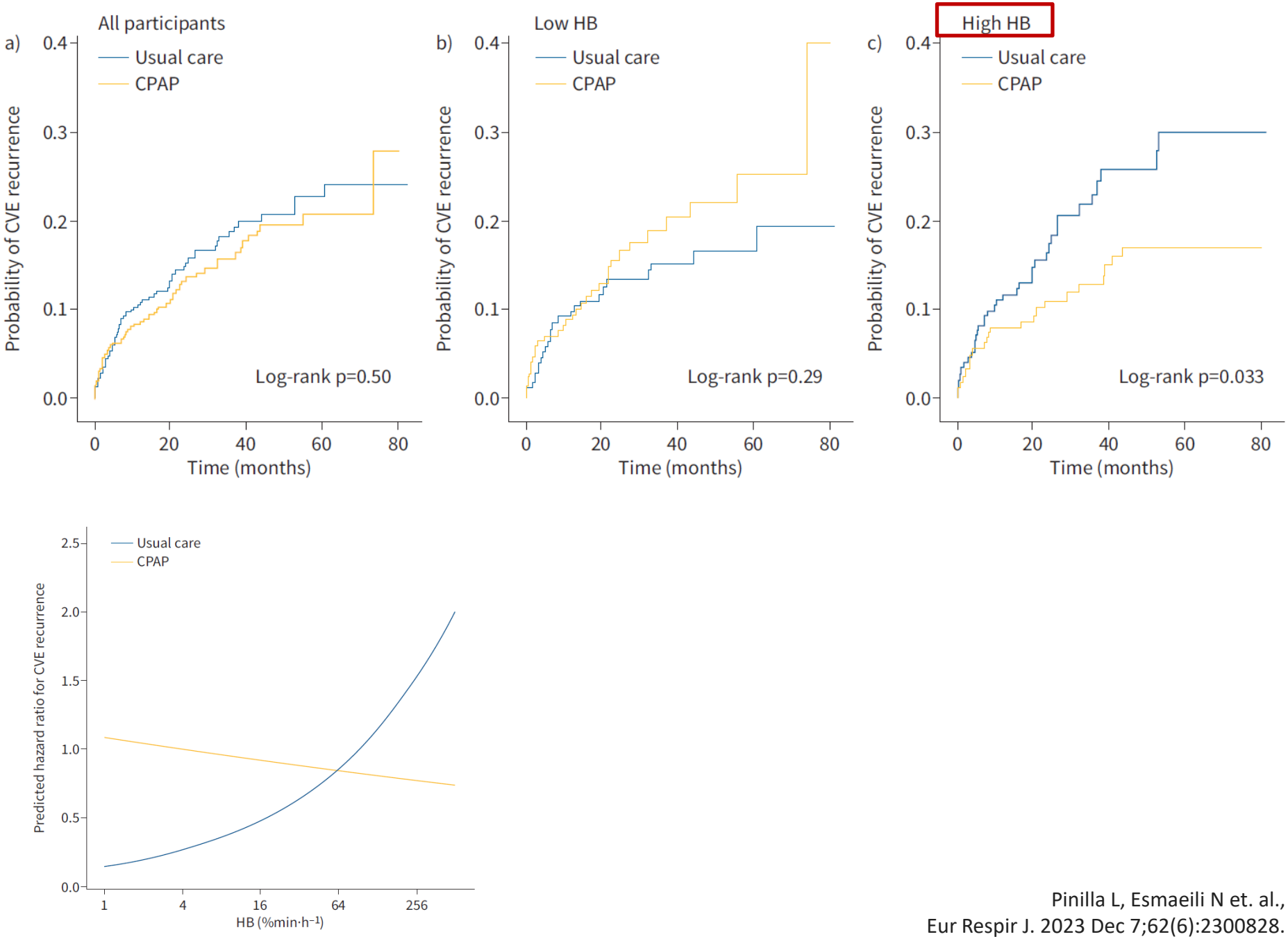
EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
L. PINILLA ET AL.

Hypoxic burden to guide CPAP treatment allocation in patients with obstructive sleep apnoea: a *post hoc* study of the ISAACC trial

- Hypoxic burden (HB) : emerged as a strong predictor of CV risk in OSA
- Post hoc analysis of the ISAACC trial
  - Non-sleepy pts with ACS diagnosed with OSA (AHI≥15) by respiratory polygraphy
- CPAP or usual care and followed for a minimum of 1 yr



Pinilla L, Esmaeili N et. al.,
Eur Respir J. 2023 Dec 7;62(6):2300828.



Pinilla L, Esmaeili N et. al.,
Eur Respir J. 2023 Dec 7;62(6):2300828.

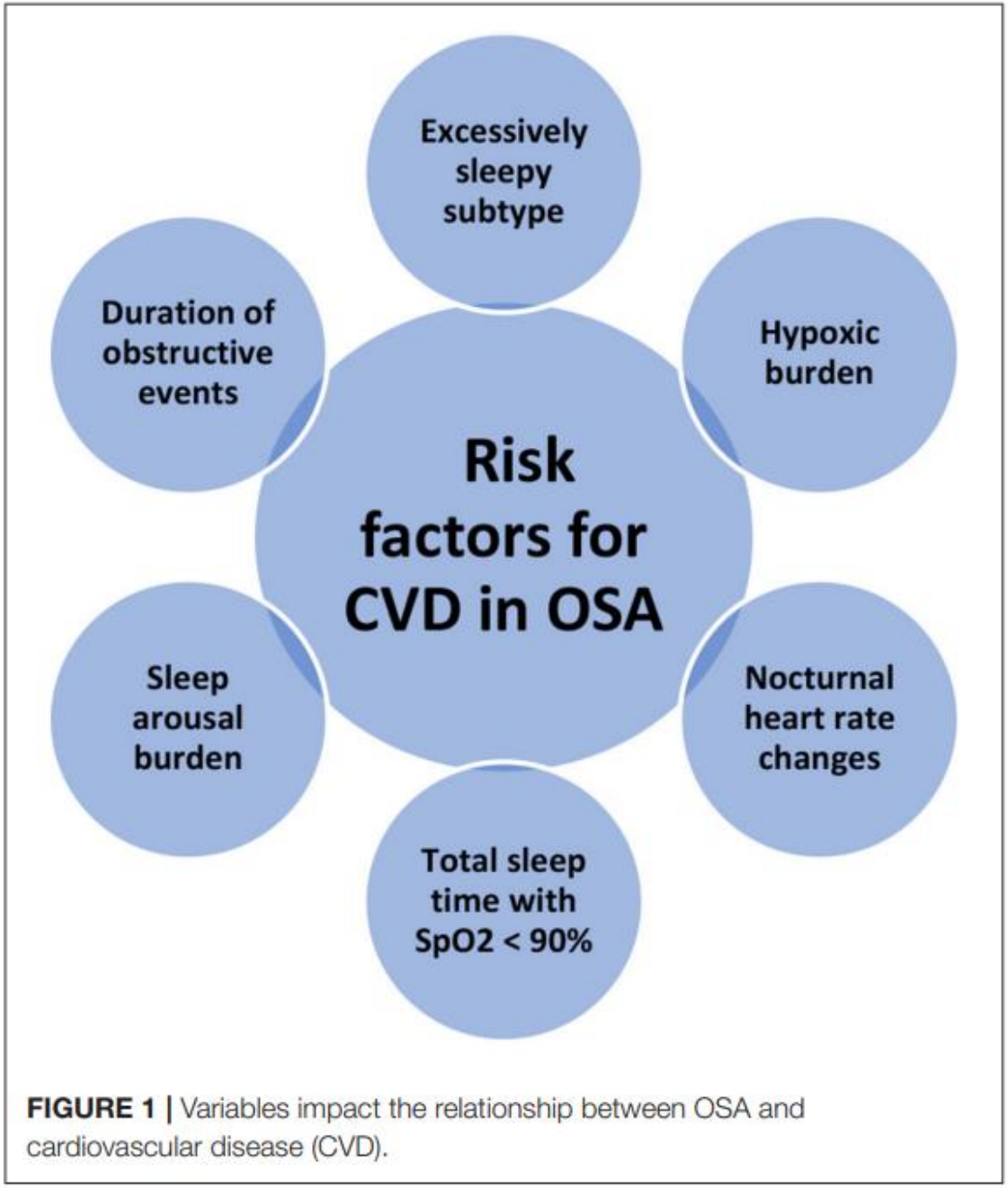
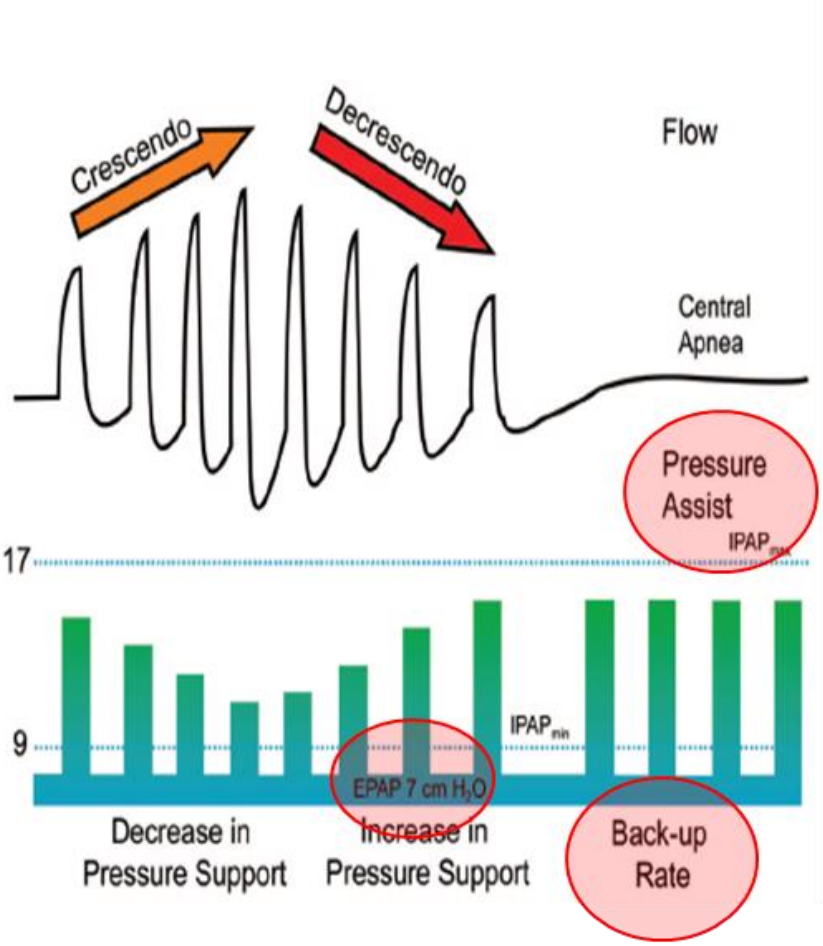


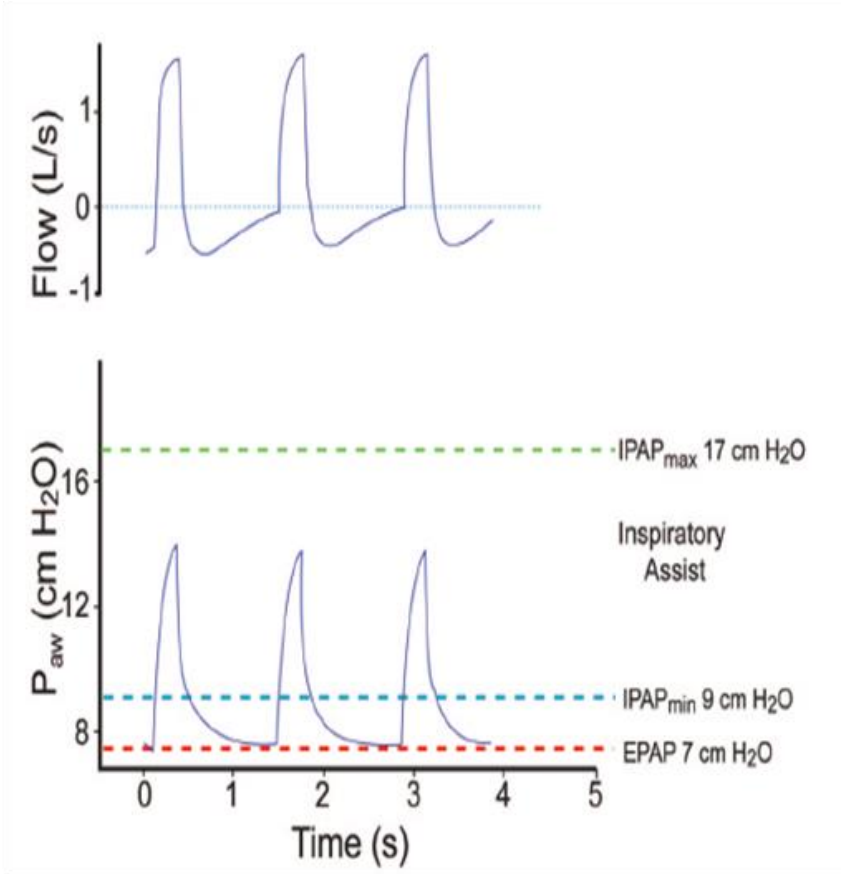
FIGURE 1 | Variables impact the relationship between OSA and cardiovascular disease (CVD).

Front Neurol. 2022 Mar 15;13:801167.

Contents

Adaptive servo-ventilation (ASV)





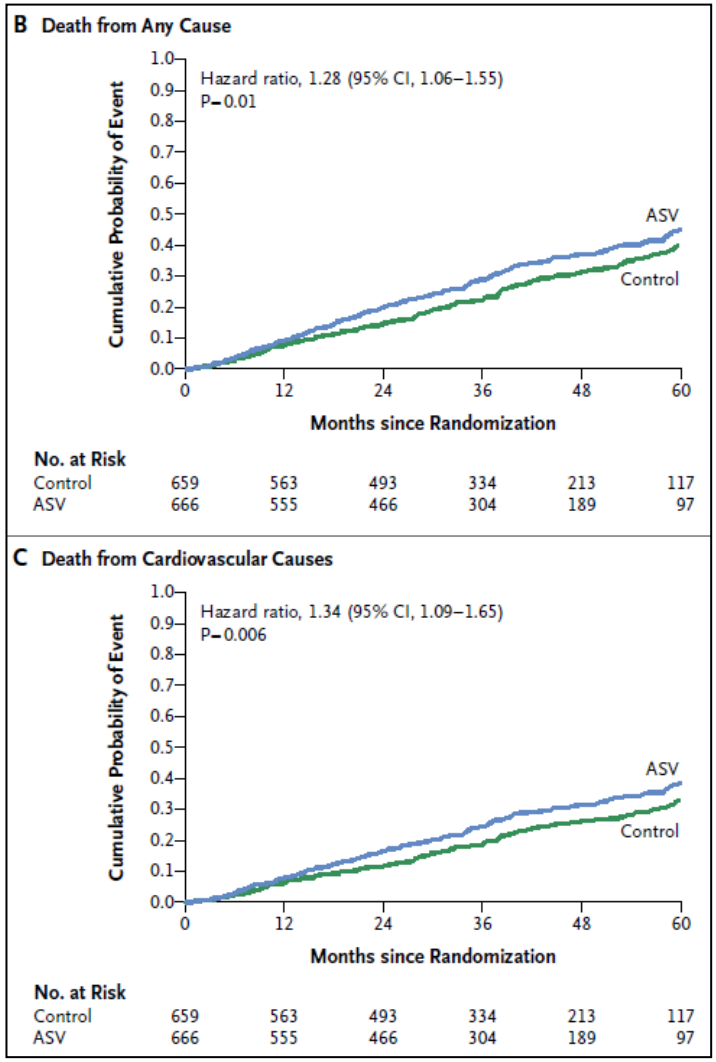
Variable EPAP maintains upper airway patency
Variable IPAP with back-up rate delivers pressure support

Respir Care. 2010 Sep;55(9):1216-29.

ASV for CSA in HFrEF

- **SERVE-HF trial**
  - International, multicenter, randomized study
  - 1325 pts
  - LVEF≤45%, AHI≥ 15/hr
  - No beneficial effect in QoL
  - ↑all-cause & CV mortality

  - CSA may be a compensatory mechanism in pts with HF?
  - PAP may impair cardiac function in at least some patients with HF?



N Engl J Med. 2015 Sep 17;373(12):1095-105.

Adaptive servo-ventilation for sleep-disordered breathing in patients with heart failure with reduced ejection fraction (ADVENT-HF): a multicentre, multinational, parallel-group, open-label, phase 3 randomised controlled trial

T Douglas Bradley, Alexander G Logan, Geraldo Lorenzi Filho, R John Kimoff, Joaquin Durán Cantolla, Michael Arzt, Stefania Redolfi, Gianfranco Parati, Takatoshi Kasai, Mark E Dunlap, Diego Delgado, Shoichiro Yatsu, Adriana Bertolami, Rodrigo Pedrosa, George Tomlinson, Jose M Marin Trigo, Claudio Tantucci, John S Floras, on behalf of the ADVENT-HF Investigators

ADVENT-HF

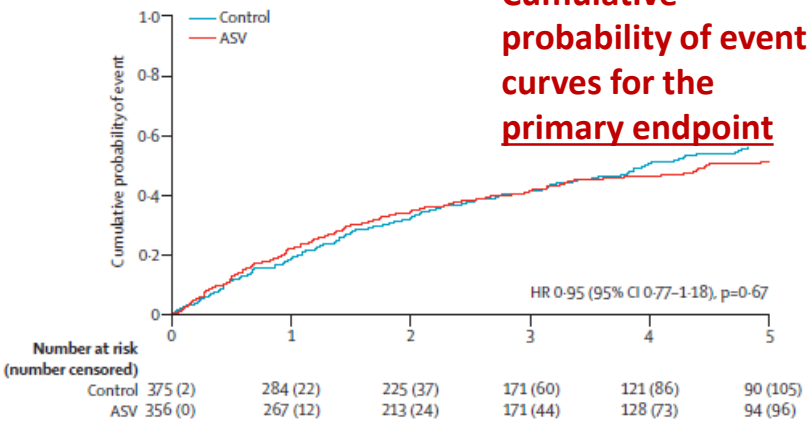
- Enroll : Sep 2010 ~ Mar 2021
  - Premature termination : SERVE-HF, COVID-19, Philips recall (not reached sample size)
- 731 pts (375 control/356 ASV)
  - CSA 198 (106 control/92 ASV)
- Patients
  - LVEF ≤ 45% (on optimal HF therapy)
  - AHI ≥ 15 (both CSA and non-sleepy OSA)
- ASV (Philips Respironics)
- Primary endpoint : all-cause mortality + 1st admission to hospital for a CV reason + new onset A.fib or flutter + delivery of an appropriate cardioverter-defibrillator shock
- Secondary endpoint : all-cause mortality

Lancet Respir Med. 2024 Feb;12(2):153-166.

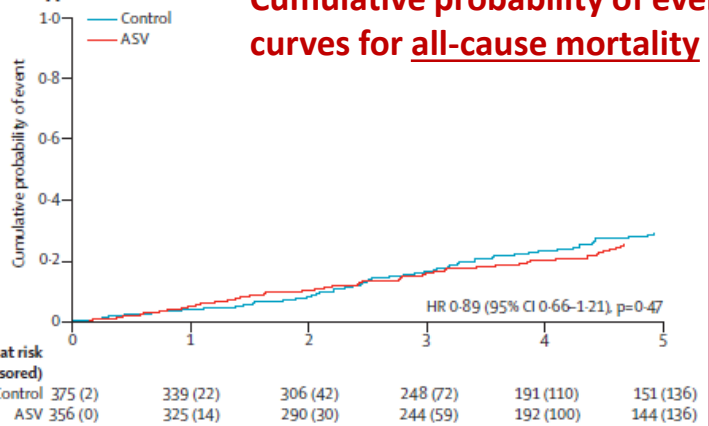
Cumulative probability of event curves for the primary endpoint

Cumulative probability of event curves for all-cause mortality

All

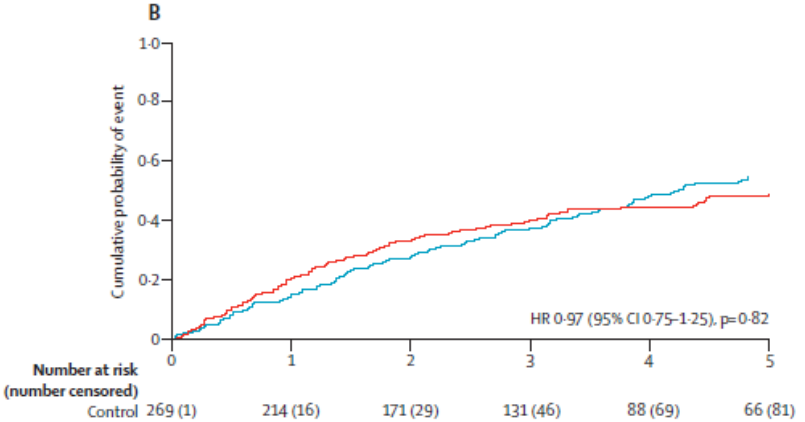


Number at risk (number censored)						
Control	375 (2)	284 (22)	225 (37)	171 (60)	121 (86)	90 (105)
ASV	356 (0)	267 (12)	213 (24)	171 (44)	128 (73)	94 (96)

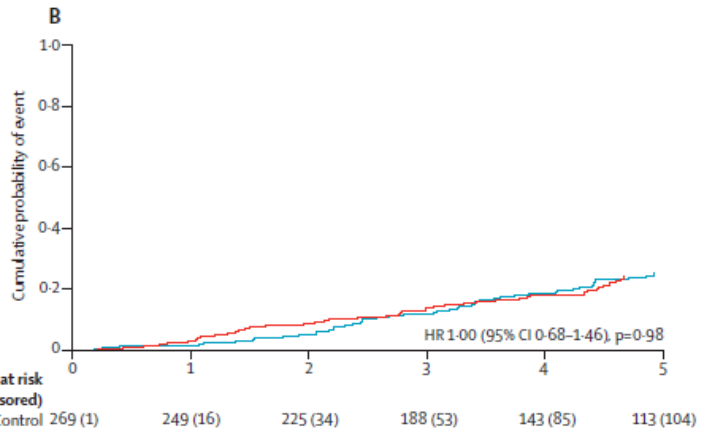


Number at risk (number censored)						
Control	375 (2)	339 (22)	306 (42)	248 (72)	191 (110)	151 (136)
ASV	356 (0)	325 (14)	290 (30)	244 (59)	192 (100)	144 (136)

OSA

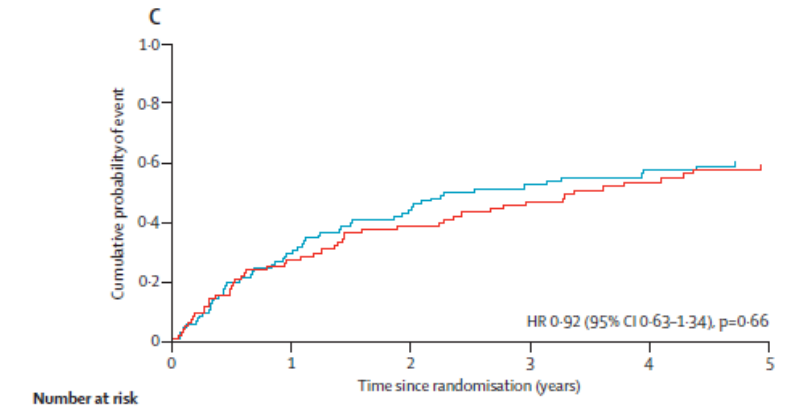


Number at risk (number censored)						
Control	269 (1)	214 (16)	171 (29)	131 (46)	88 (69)	66 (81)
ASV	264 (0)	202 (10)	158 (22)	126 (39)	95 (61)	68 (81)

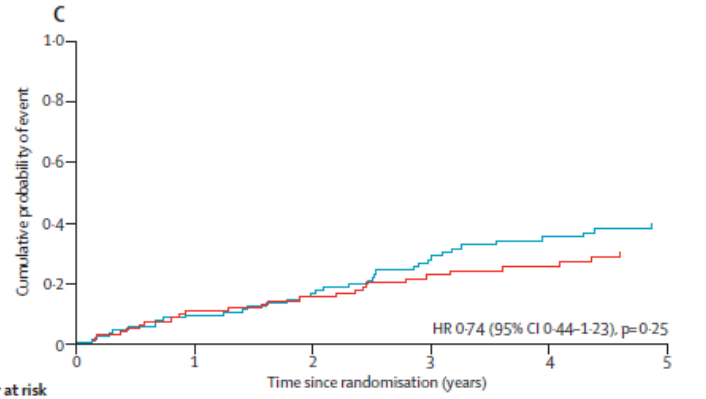


Number at risk (number censored)						
Control	269 (1)	249 (16)	225 (34)	188 (53)	143 (85)	113 (104)
ASV	264 (0)	246 (11)	216 (26)	182 (49)	142 (80)	100 (113)

CSA



Number at risk (number censored)						
Control	106 (1)	70 (6)	54 (8)	40 (14)	33 (17)	24 (24)
ASV	92 (0)	65 (2)	55 (2)	45 (5)	33 (12)	26 (15)



Number at risk (number censored)						
Control	106 (1)	90 (6)	81 (8)	60 (19)	48 (25)	38 (32)
ASV	92 (0)	79 (3)	74 (4)	62 (10)	50 (20)	44 (23)

	All participants			OSA subgroup			CSA subgroup		
	Control group (n=335)	ASV group (n=318)	p value	Control group (n=242)	ASV group (n=234)	p value	Control group (n=93)	ASV group (n=84)	p value
AHI, events per h of sleep	−1·3 (17·1)	−34·2 (20·3)	<0·0001	−1·6 (15·5)	−33·5 (20·9)	<0·0001	−0·3 (20·9)	−36·1 (18·7)	<0·0001
O_2 desaturation index, events per h of sleep	−0·8 (17·3)	−32·0 (21·3)	<0·0001	−0·6 (16·2)	−31·2 (22·2)	<0·0001	−1·5 (19·9)	−34·3 (18·6)	<0·0001
Mean SaO_2, %	0·0 (1·6)	1·5 (2·9)	<0·0001	−0·1 (1·7)	1·6 (3·1)	<0·0001	0·1 (1·6)	1·0 (2·2)	0·0012
Minimum SaO_2, %	0·0 (7·2)	9·8 (11·6)	<0·0001	−0·1 (7·1)	10·5 (12·0)	<0·0001	0·2 (7·5)	7·8 (10·1)	<0·0001
Total sleep time, min	2·4 (71·6)	2·3 (76·1)	0·36	0·4 (70·4)	−5·7 (74·1)	0·87	7·6 (74·9)	24·6 (77·4)	0·13
Sleep efficiency, %	−0·7 (15·4)	1·9 (15·5)	0·074	0·7 (15·3)	0·6 (15·1)	0·42	0·8 (15·8)	5·4 (16·2)	0·046
N1 sleep, min	0·3 (28·9)	−17·5 (32·8)	<0·0001	0·8 (28·5)	−17·1 (32·8)	<0·0001	−0·8 (29·9)	−18·5 (33·0)	<0·0001
N2 sleep, min	−0·8 (57·8)	0·3 (64·8)	0·23	−2·5 (56·2)	−4·3 (61·9)	0·70	3·7 (61·7)	13·2 (71·1)	0·12
N3 sleep, min	0·8 (27·4)	10·5 (30·4)	<0·0001	1·1 (28·6)	9·9 (29·6)	0·0013	0·0 (24·0)	12·2 (32·6)	0·0011
REM sleep, min	0·3 (26·7)	8·9 (29·6)	<0·0001	0·1 (25·3)	7·2 (31·0)	0·0005	1·0 (30·1)	13·5 (25·2)	0·0035
Total arousal index, events per h of sleep	−1·3 (17·7)	−18·0 (22·2)	<0·0001	−1·8 (17·5)	−17·6 (22·6)	<0·0001	0·2 (18·3)	−19·3 (21·2)	<0·0001
Respiratory arousal index, events per h of sleep	−1·4 (16·2)	−23·9 (19·0)	<0·0001	−2·0 (14·7)	−23·7 (19·1)	<0·0001	0·0 (19·7)	−24·4 (18·5)	<0·0001

Data are mean (SD). AHI=apnoea-hypopnoea index. ASV=adaptive servo-ventilation. CSA=central sleep apnoea. OSA=obstructive sleep apnoea. REM=rapid eye movement. SaO_2=arterial oxyhaemoglobin saturation.

Table 2: **Changes in polysomnographic variables from baseline at 1 month**

Improved objective measures of sleep quality, as well as health-related quality of life and Sx.

Lancet Respir Med. 2024 Feb;12(2):153-166.

Contents

- Diagnosis
- Moving beyond AHI
- Emerging treatment
- OSA & CV outcome
- ASV for SDB in HF
- Etc.

OSA & cognitive function

EUROPEAN RESPIRATORY JOURNAL
ORIGINAL RESEARCH ARTICLE
N.A. MARCHI ET AL.

Obstructive sleep apnoea and 5-year cognitive decline in the elderly

Nicola Andrea Marchi[1,2,3,4], Geoffroy Solelhac[1], Mathieu Berger[1], José Haba-Rubio[1], Nadia Gosselin[3,4], Peter Vollenweider[5], Pedro Marques-Vidal[5], Julius Popp[6,7], Armin von Gunten[6], Martin Preisig[8], Bogdan Draganski[2,9,10] and Raphael Heinzer[1,10]

Eur Respir J. 2023 Apr 27;61(4):2201621.

ORIGINAL RESEARCH

The Effect of Obstructive Sleep Apnea on Sleep-dependent Emotional Memory Consolidation

Tony J. Cunningham[1,2], Divya Kishore[3], Meng Guo[3,4], Moroké Igue[3], Atul Malhotra[4], Robert Stickgold[1], and Ina Djonlagic[3,4]

Ann Am Thorac Soc. 2023 Feb;20(2):296-306.

JAMA Network | Open

Original Investigation | Neurology

Sleep Architecture, Obstructive Sleep Apnea, and Cognitive Function in Adults

Matthew P. Pase, PhD; Stephanie Harrison, PhD; Jeffrey R. Misialek, MPH; Christopher E. Kline, PhD; Marina Cavuoto, PhD; Andree-Ann Baril, PhD; Stephanie Yiallourou, PhD; Alycia Bisson, PhD; Dibya Himali, MS; Yue Leng, PhD; Qiong Yang, PhD; Sudha Seshadri, MD; Alexa Beiser, PhD; Rebecca F. Gottesman, MD, PhD; Susan Redline, MD, MPH; Oscar Lopez, MD; Pamela L. Lutsey, PhD; Kristine Yaffe, MD; Katie L. Stone, PhD; Shaun M. Purcell, PhD; Jayandra J. Himali, PhD

JAMA Netw Open. 2023 Jul 3;6(7):e2325152.

RESEARCH Open Access

Breathing cessation events that compose the apnea–hypopnea index are distinctively associated with the adverse outcomes in Alzheimer's disease

Adriano D. S. Targa[1,2*], Iván D. Benítez[1,2], Anna Moncusí-Moix[1,2], Farida Dakterzada[3], Olga Minguez[1,2], Rafaela Vaca[1,2], Mireia Dalmases[1,2], Manuel Sanchez-de-la-Torre[2,4], Ferran Barbé[1,2] and Gerard Piñol-Ripoll[3*]

Alzheimers Res Ther. 2023 Jul 14;15(1):123.

Contents lists available at ScienceDirect

Sleep Medicine

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

ELSEVIER

Are there any differences at gray matter sites between severe obstructive sleep apnea patients and healthy controls?

O.T. Selcuk[a], D. Aydenizoz[a,*], F. Genc[b], M.B. Ozkan[c], N. Turkoglu Selcuk[d], B. Cekic[c], E. A. Cetinkaya[a], R. Taga Senirli[a], H. Eyigor[a]

Sleep Med. 2024 Feb 17;116:27-31.

Contents lists available at ScienceDirect

Sleep Medicine Reviews

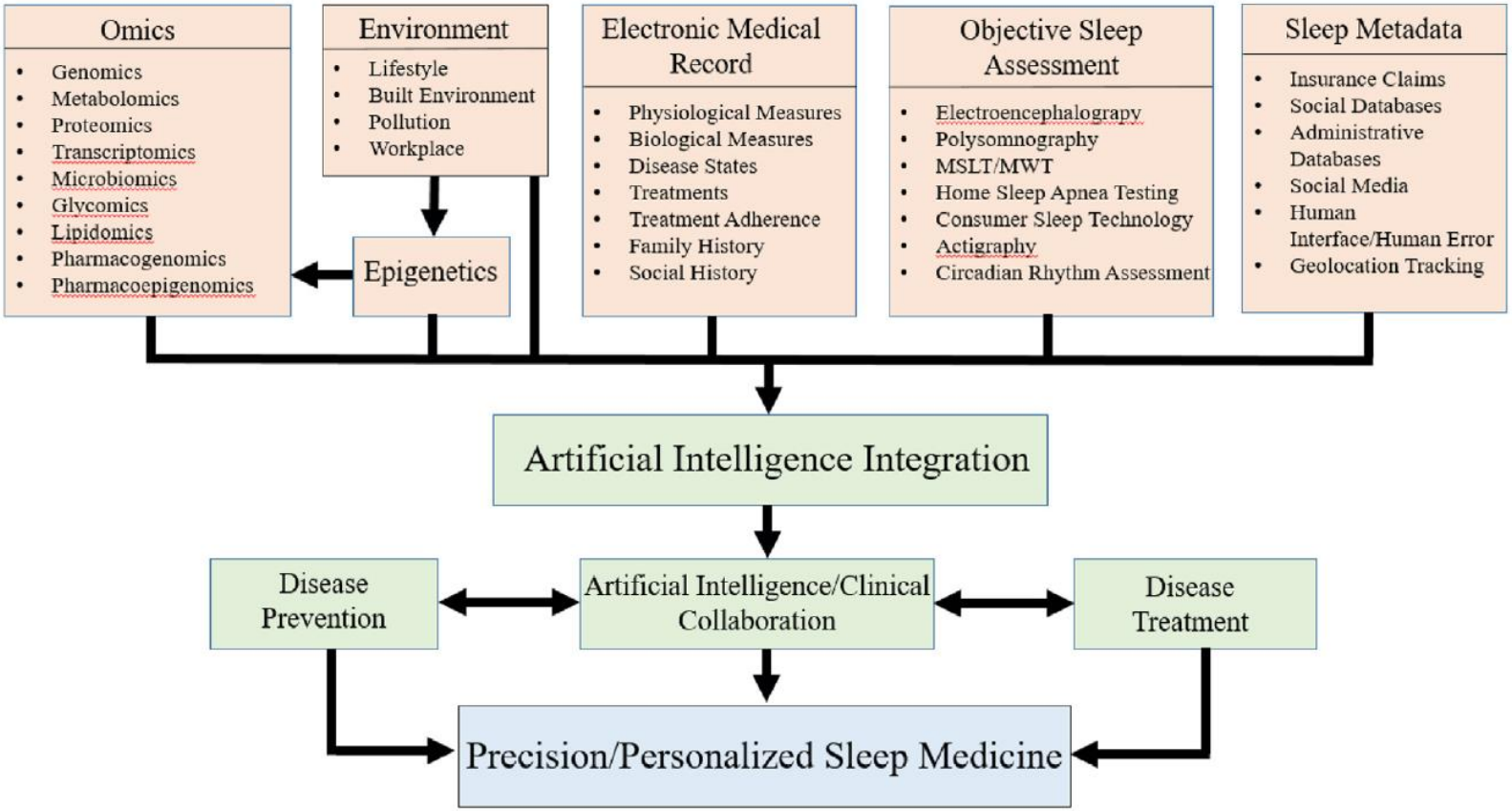
journal homepage: www.elsevier.com/locate/smrv

CLINICAL REVIEW

Artificial intelligence and sleep: Advancing sleep medicine☆

Nathaniel F. Watson [a, b, *], Christopher R. Fernandez [c]

[a] Department of Neurology, University of Washington (UW) School of Medicine, USA
[b] UW Medicine Sleep Center, USA
[c] EnsoData, USA



Sleep Med Rev. 2021 Oct;59:101512.

Contents lists available at ScienceDirect

Sleep Medicine Reviews

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

CLINICAL REVIEW

Artificial intelligence and sleep: Advancing sleep medicine☆

Nathaniel F. Watson [a, b, *], Christopher R. Fernandez [c]

[a] Department of Neurology, University of Washington (UW) School of Medicine, USA
[b] UW Medicine Sleep Center, USA
[c] EnsoData, USA

- 1. AI can score sleep studies in a quick and accurate manner.
- 2. AI will allow screening of sleep disorder risk based on currently available clinical and objective test data from EMR.
- 3. AI has the potential to transform & simplify the diagnosis of sleep disorders, increase access to diagnostic services for patients, and make the process more cost-effective.
- 4. AI will be the key to personalized medicine in the future by integrating “omic” and clinical data to better understand the specifics of an individual’s sleep pathology.
- 5. AI facilitates endotyping of sleep disorders expediting effective treatment.

Sleep Med Rev. 2021 Oct;59:101512.

Summary

- **Diagnosis**
  - Variability, misclassification of OSA, new sleep tech devices
- **Moving beyond AHI**
  - Hypoxic burden, Pulse wave amplitude drops (PWADs)
- **Emerging treatment**
  - Hypoglossal nerve stimulation (HGNS), Drugs (Aroxybutynin + Atomoxetine, Pitolisant)
- **OSA & CV outcome**
  - Previous studies : SAVE, ISAACC, RICCADSA
  - Post-hoc study of the ISAACC trial : hypoxic burden, Machine learning analysis
- **ASV for CSA in HFrEF**
  - ADVENT-HF
- **Etc.**
  - OSA & cognitive function, Artificial intelligence