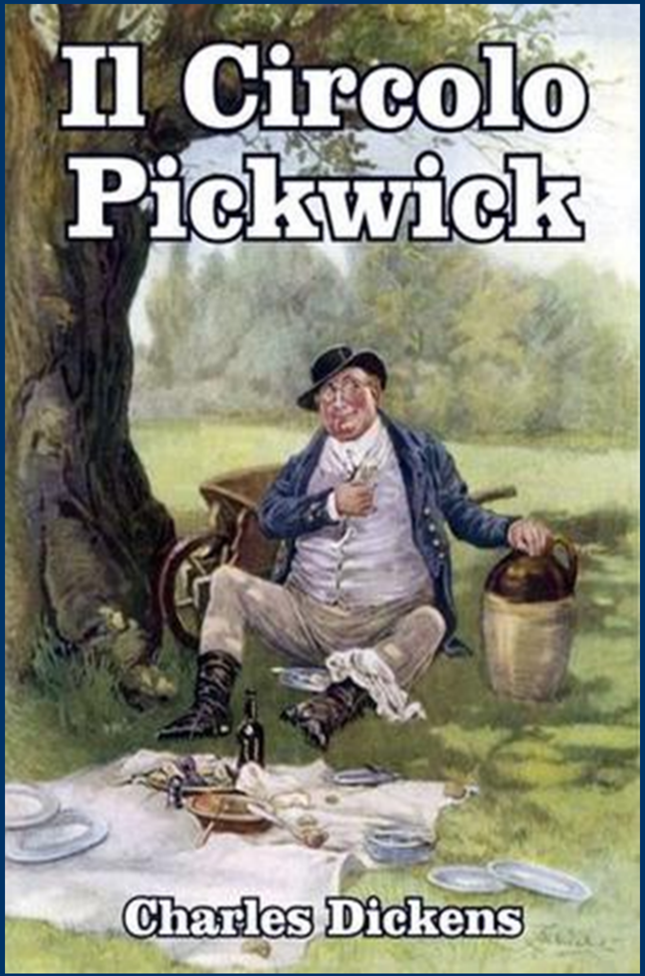
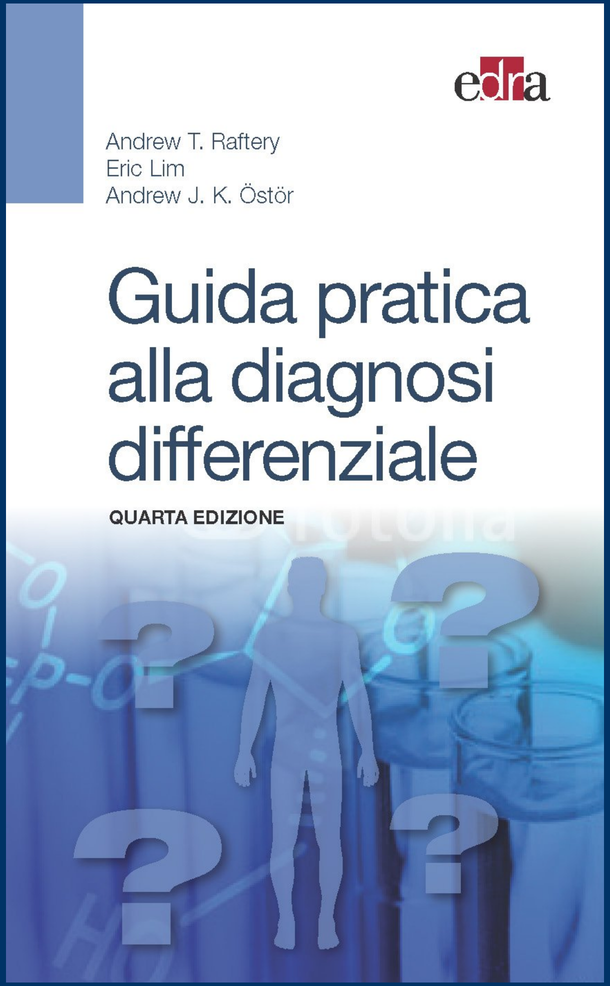

# SINCOPE O « COLPO DI SONNO» NEL PAZIENTE CON APNEE NOTTURNE

Prof. Carolina Lombardi
Sleep Disorders Center
Dept Cardiology, St. Luca Hospital,
Istituto Auxologico Italiano,
Milano Bicocca University
Milan, Italy



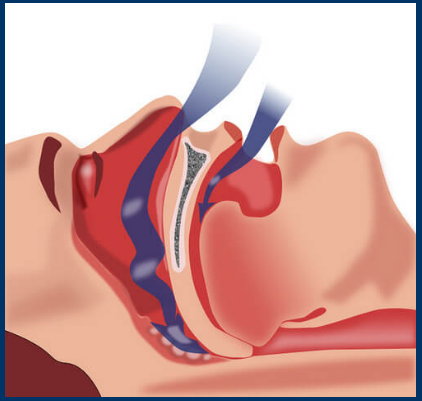

Maledetto ragazzo, s'è addormentato di nuovo!— esclamò il vecchio signore. – Va per una commissione e dorme, serve a tavola e dorme.–
…Il ragazzo grasso si scosse, aprì gli occhi, ingoiò il pezzo di pasticcio che teneva in bocca nel punto che s'era addormito, e lentamente eseguì gli ordini del padrone…..“

"Tutti erano eccitati, meno il ragazzo grasso, il quale se la dormiva saporitamente come se il tuonar del cannone fosse stata la sua ninna nanna" (Capitolo IV)



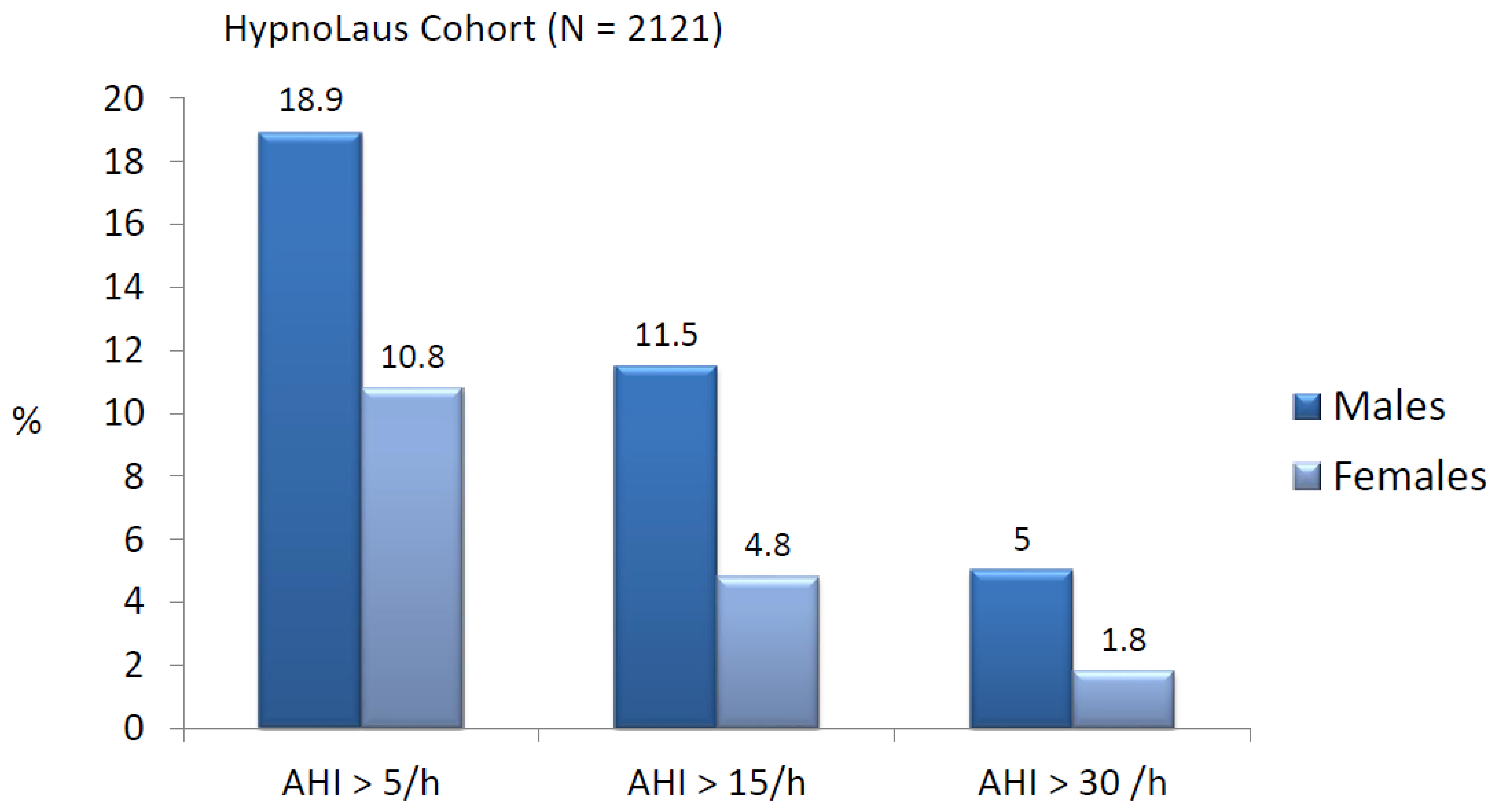

Episodio di «PDC»

- Colpo di sonno?
- Alterazione modulazione autonomica?
- Aritmia?
- Evento cerebro/cardiovascolare?
- Epilessia?



# Prevalence of sleep apnea syndrome

## (sleep disordered breathing + Epworth >10)



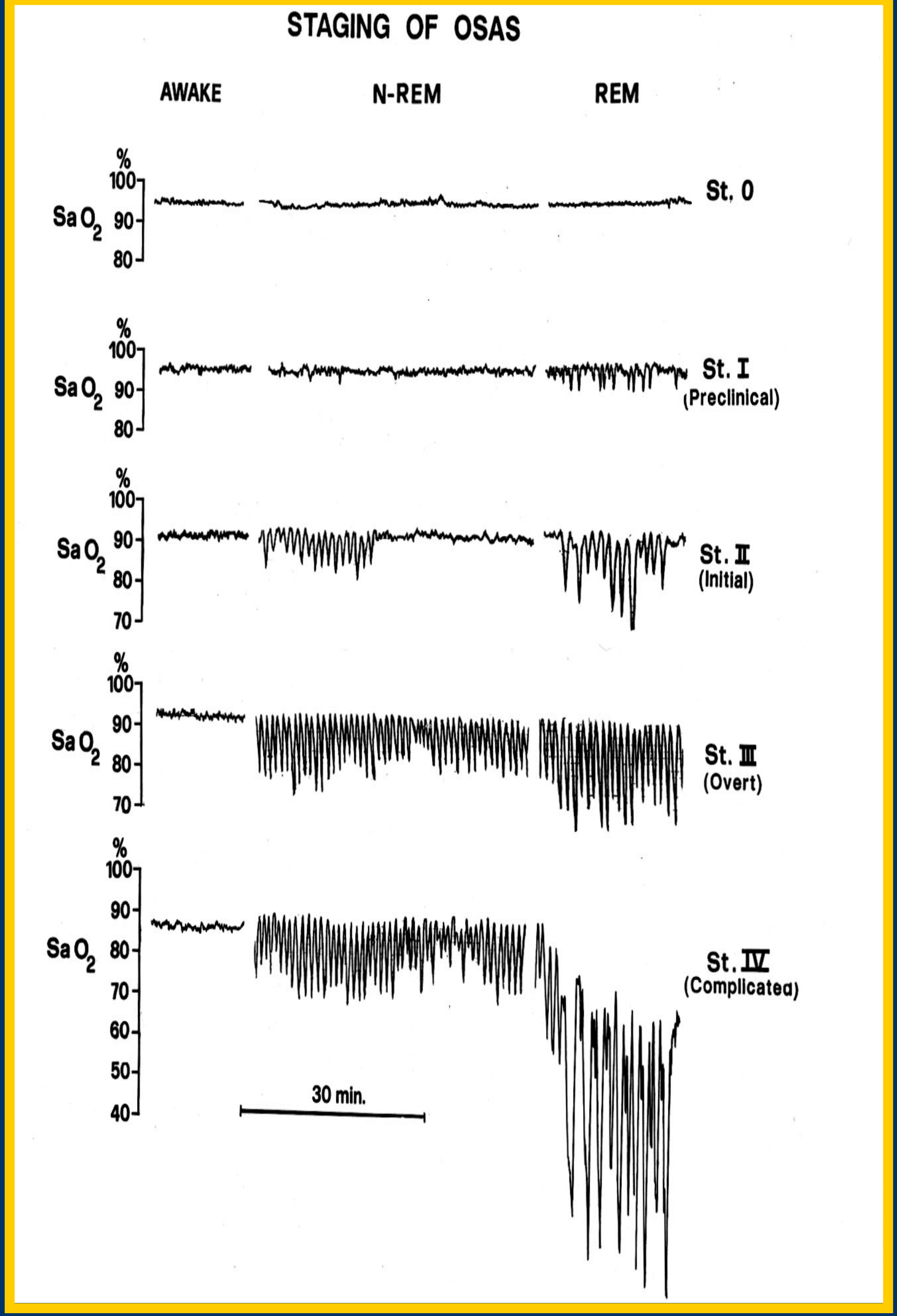


COMPLICATIONS





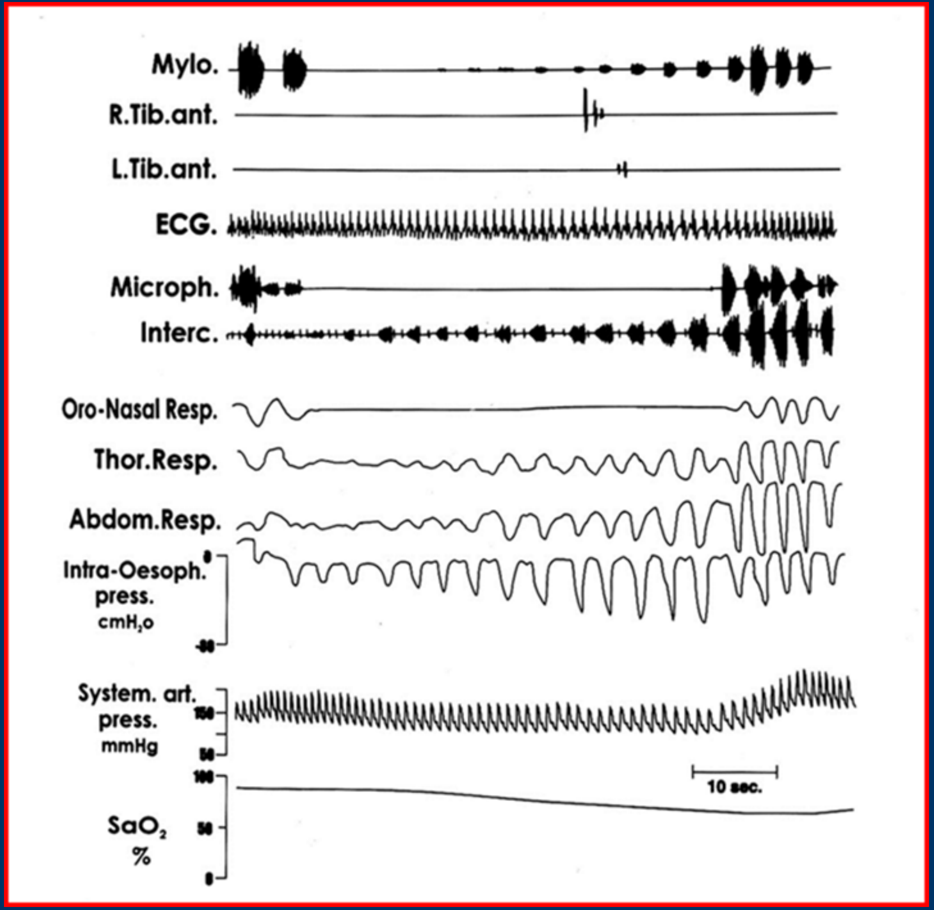
MINISTERO DELL'INTERNO


STAGING OF OSAS
AWAKE
N-REM
REM
% 100 90 80
Sa $O_2$
St. 0
St. I
(Preclinical)
St. II
(Initial)
St. III
(Overt)
St. IV
(Complicated)
70 60 50 40
30 min.

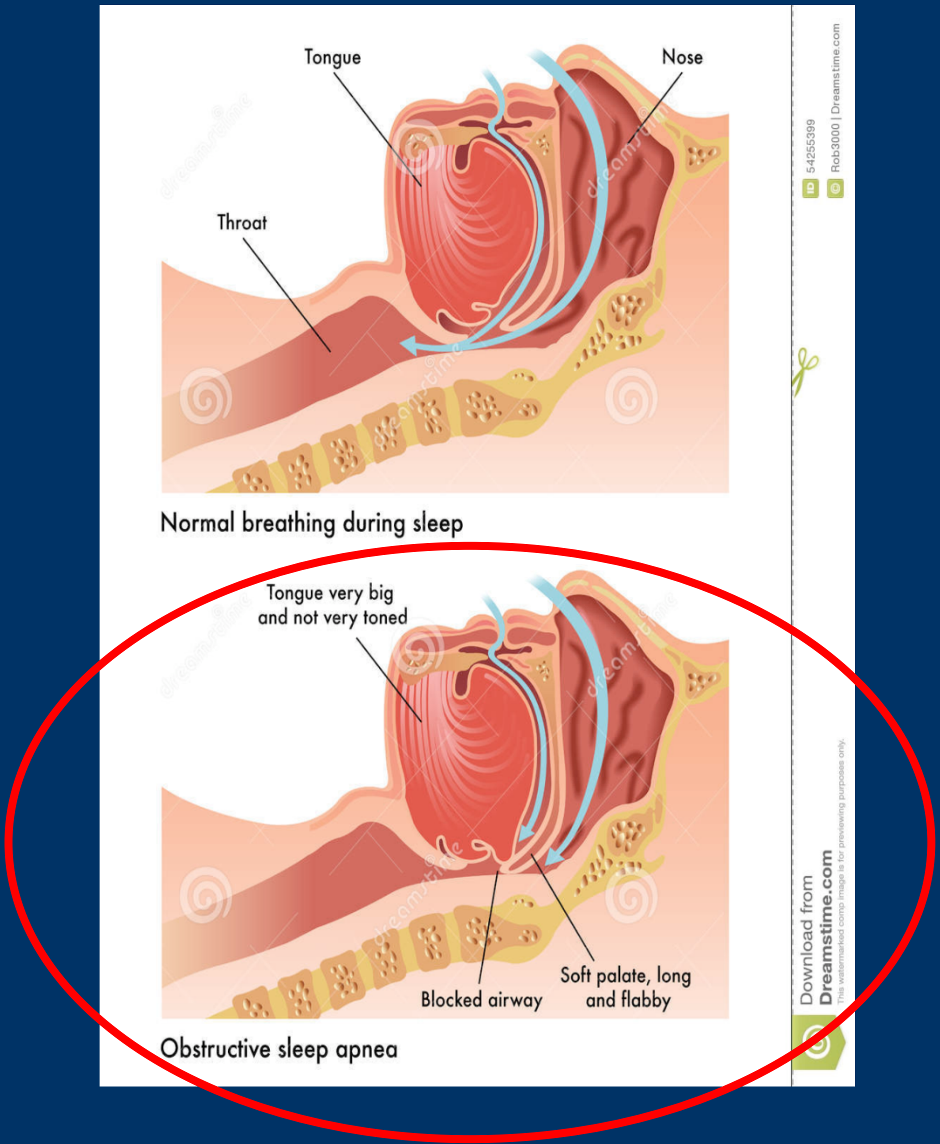
≠ Somnolence

# Sleep — A New Cardiovascular Frontier

*Virend K. Somers, M.D., Ph.D.*

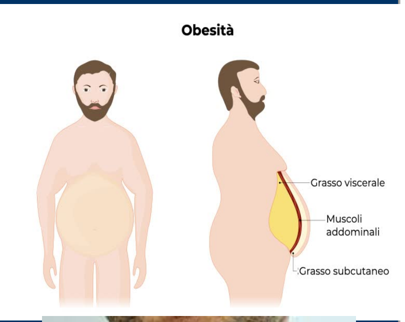


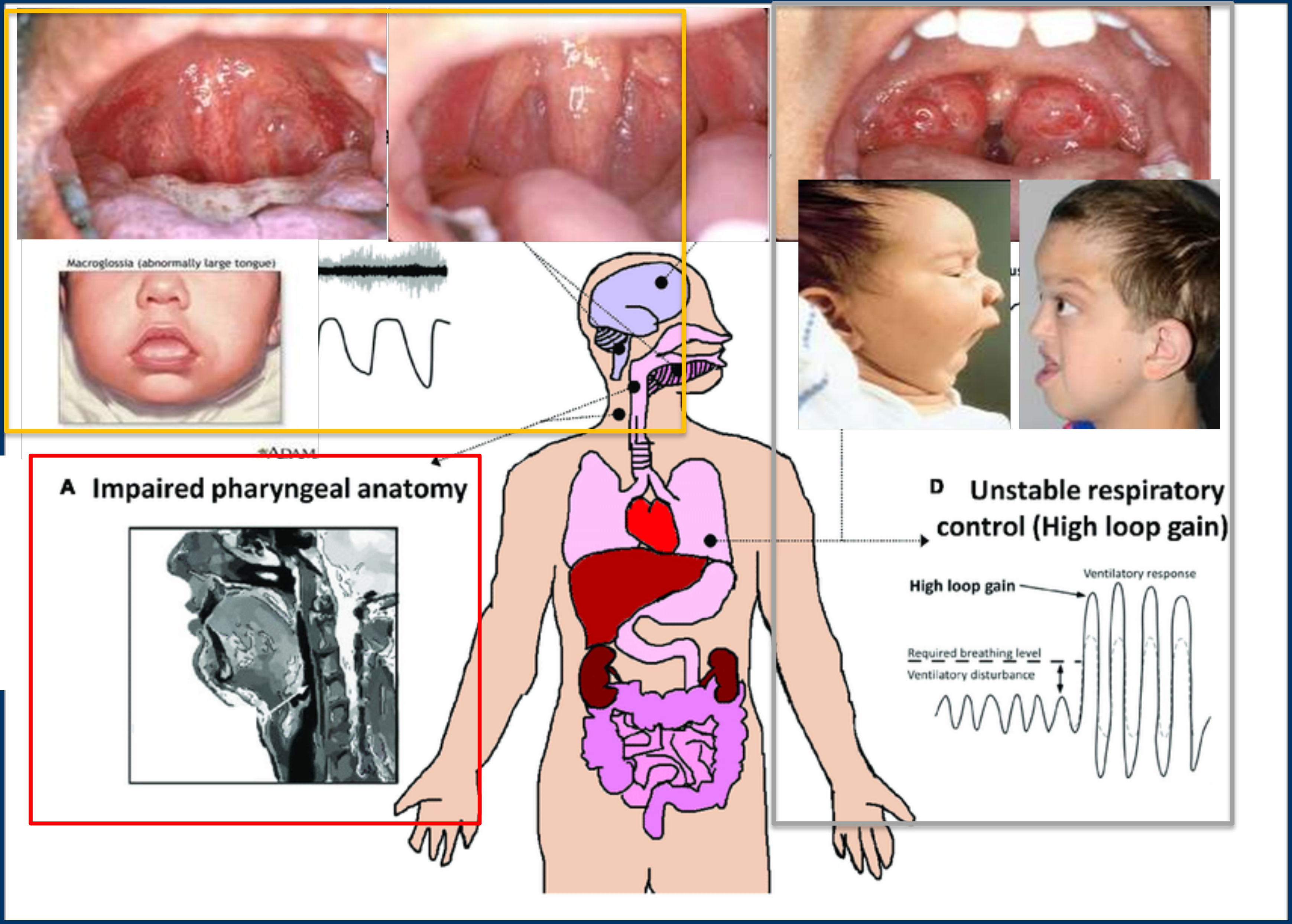
Mylo.
R.Tib.ant.
L.Tib.ant.
ECG.
Microph.
Interc.
Oro-Nasal Resp.
Thor.Resp.
Abdom.Resp.
Intra-Oesoph. press. cmH2O
System. art. press. mmHg
SaO2 %
10 sec.

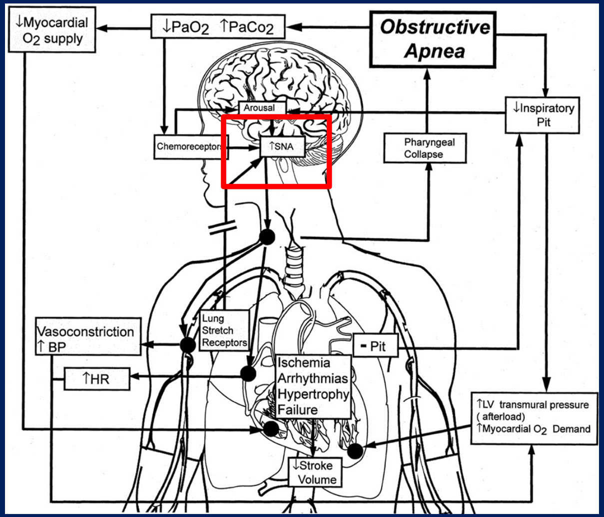



Tongue
Nose
Throat
Normal breathing during sleep
Tongue very big and not very toned
Blocked airway
Soft palate, long and flabby
Obstructive sleep apnea
Download from Dreamstime.com
54255399
Rob3000 | Dreamstime.com

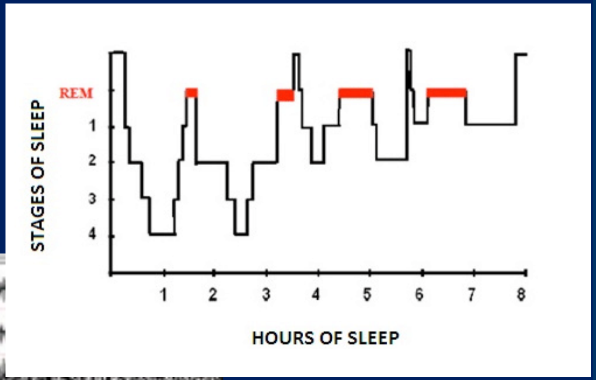
# Pathogenesis

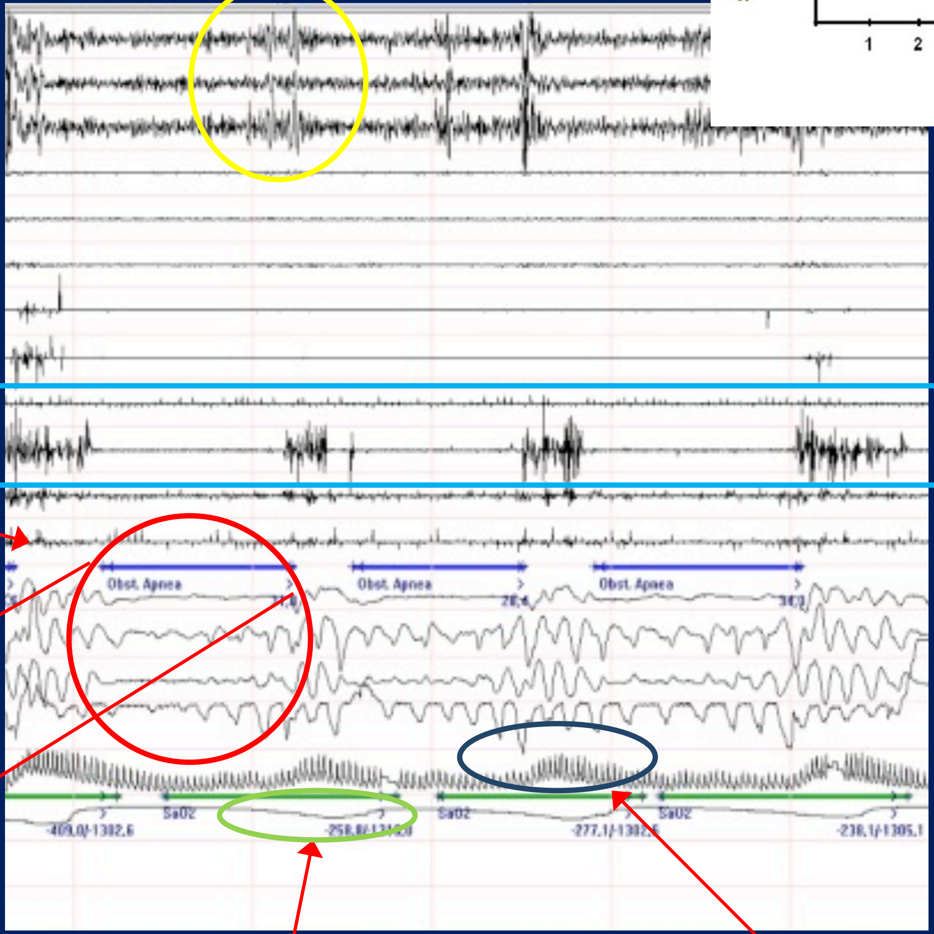




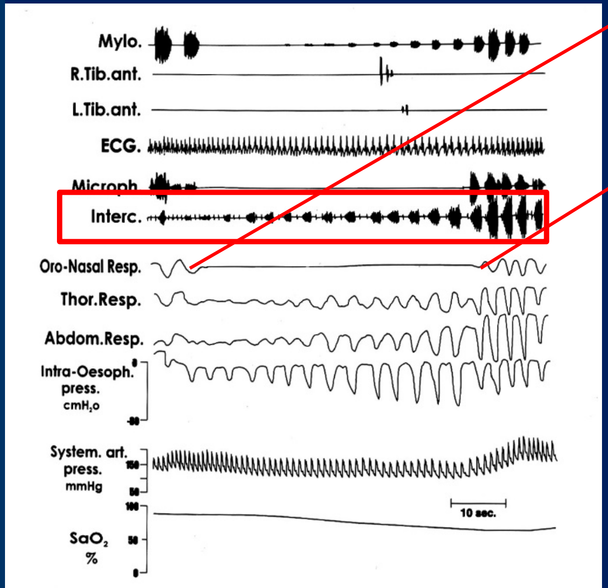

arousal




Obstructive apnea

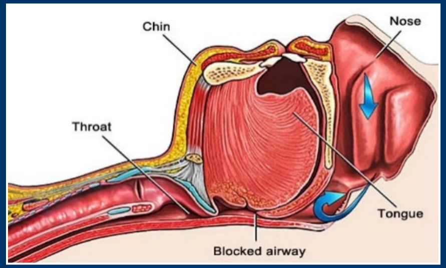
Periodic limb movements




O2 and CO2 changes

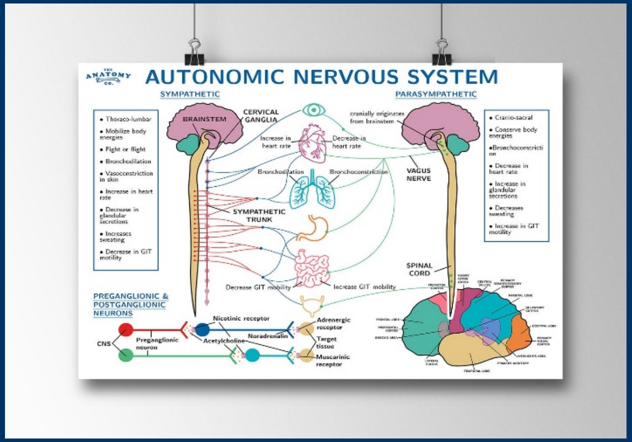
Blood pressure and heart rate changes

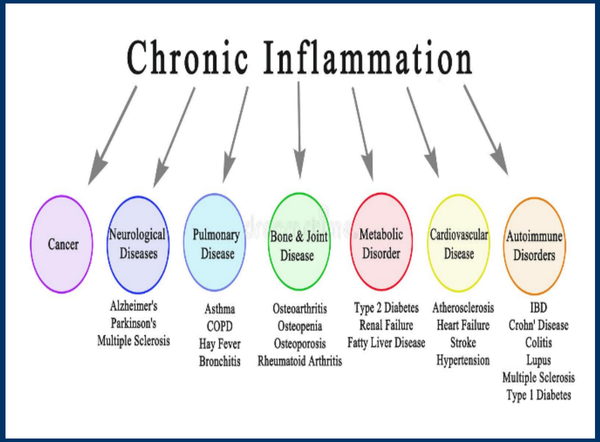
# CHRONIC ⇦ ⇨ ACUTE

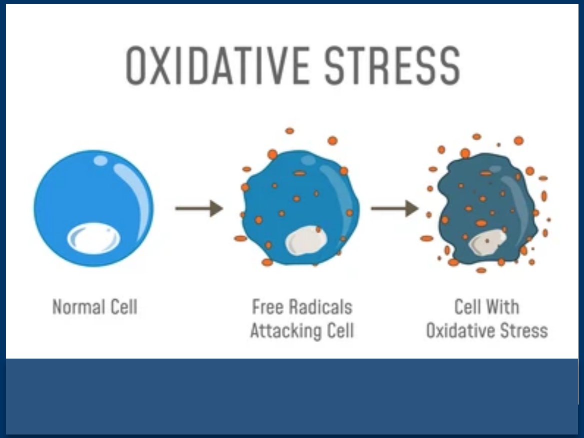



## MECHANICS OF BREATHING

## HYPOXIA



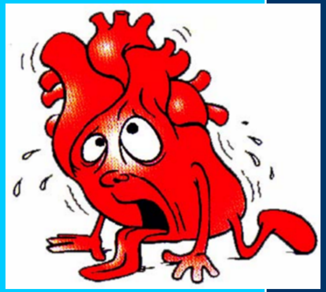



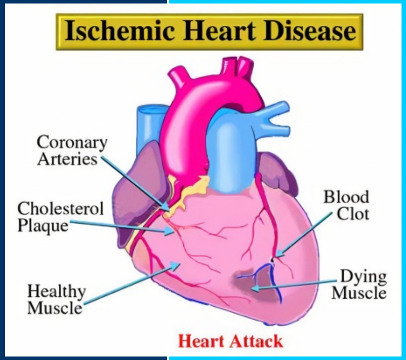





**OSA**

**Congestive Cardiac Failure**






**Acute Coronary Syndromes**

**Arrhythmias**

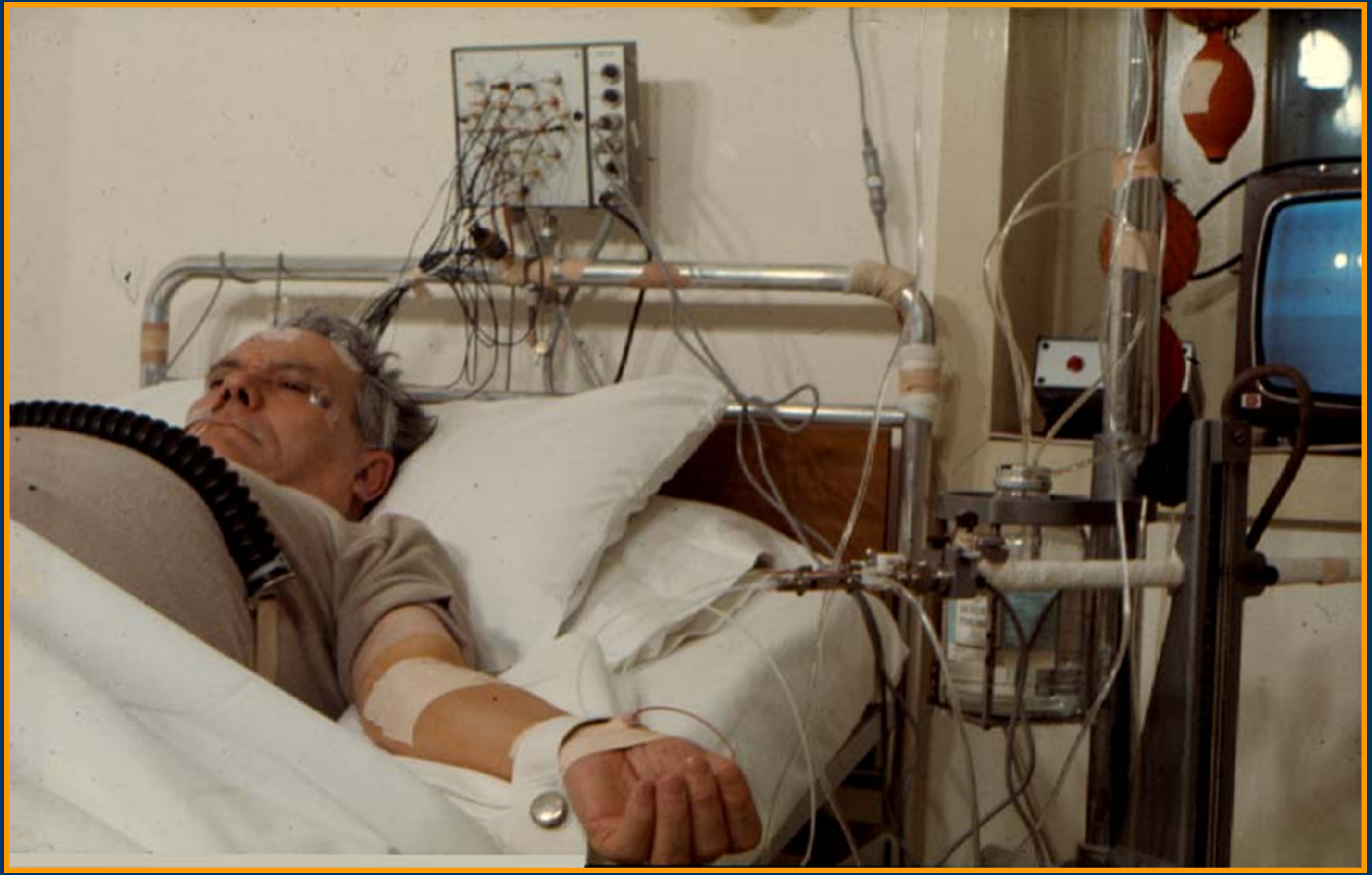
**Stroke**



Bull Physiopathol Respir (Nancy). 1972 Sep-Oct;8(5):1159-72.

# Continuous recording of the pulmonary and systemic arterial pressure during sleep in syndromes of hypersomnia with periodic breathing.

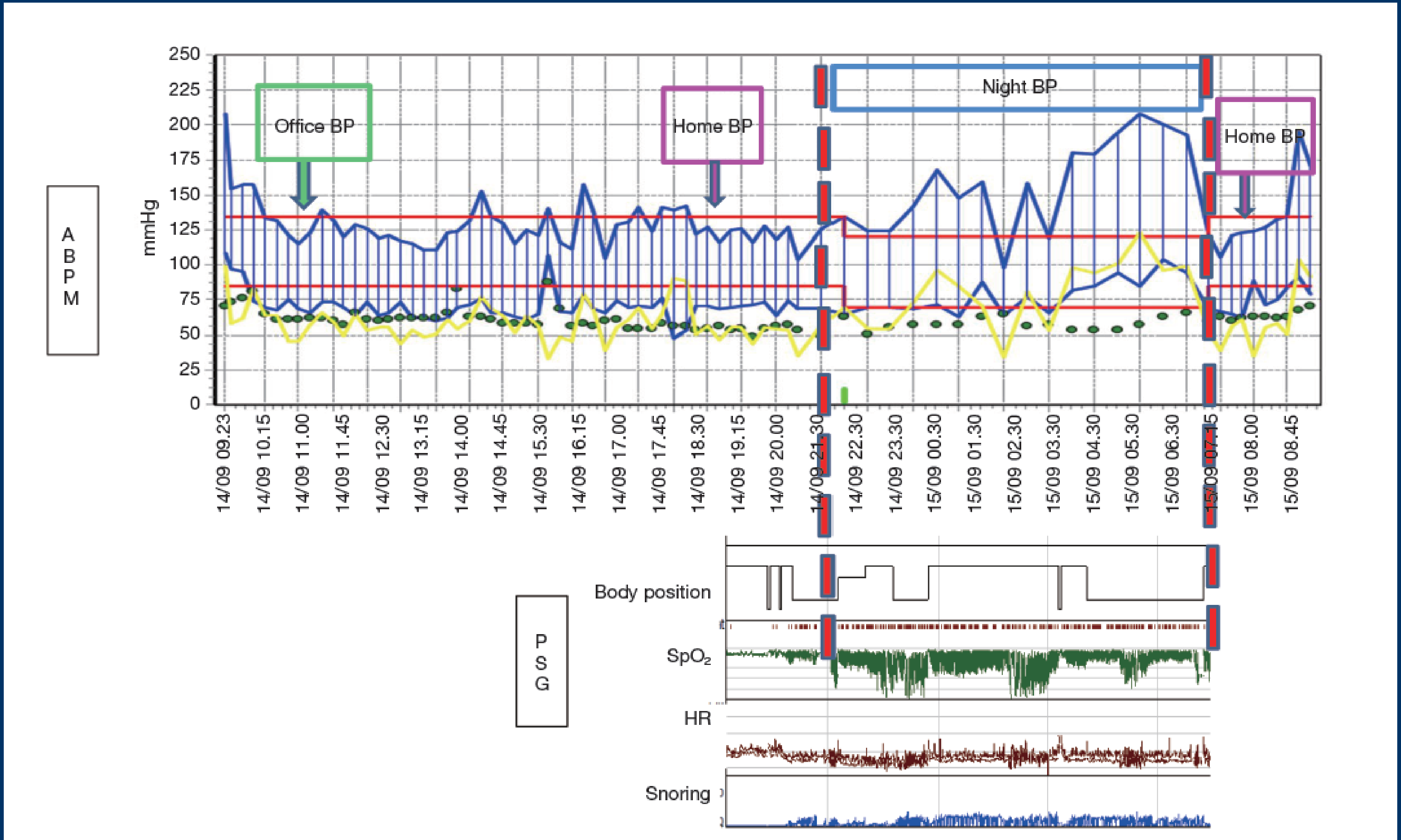
Coccagna G, Mantovani M, Brignani F, Parchi C, Lugaresi E.



Review Article

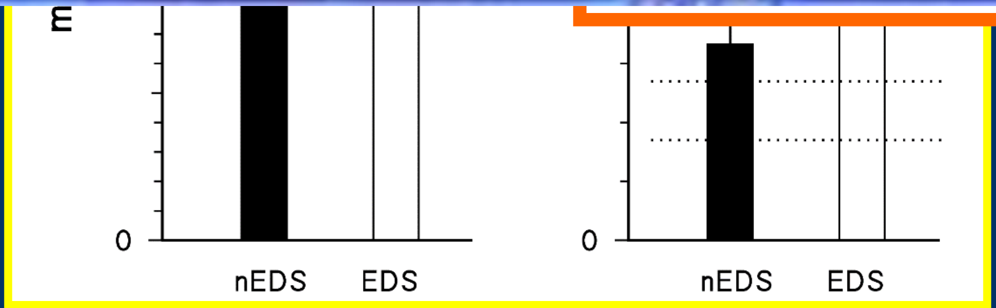
# Systemic hypertension in obstructive sleep apnea

Carolina Lombardi[1,2], Martino F. Pengo[1], Gianfranco Parati[1,2] J Thorac Dis 2018;10(Suppl 34):S4231-S4243



J. Sleep Res. (2008) 17, 263–270 Sleep disordered breathing
doi: 10.1111/j.1365-2869.2008.00659.x

# Daytime sleepiness and neural cardiac modulation in sleep-related breathing disorders




# Obstructive Sleep Apnea

## Obstructive Sleep Apnea With Objective Daytime Sleepiness Is Associated With Hypertension

Rong Ren,* Yun Li,* Jihui Zhang, Junying Zhou, Yuanfeng Sun, Lu Tan, Taomei Li,
Yun-Kwok Wing, Xiangdong Tang

**SO……..SLEEPINESS AND NOT ONLY SLEEP IS A NEW CARDIOVASCULAR FRONTIER!**

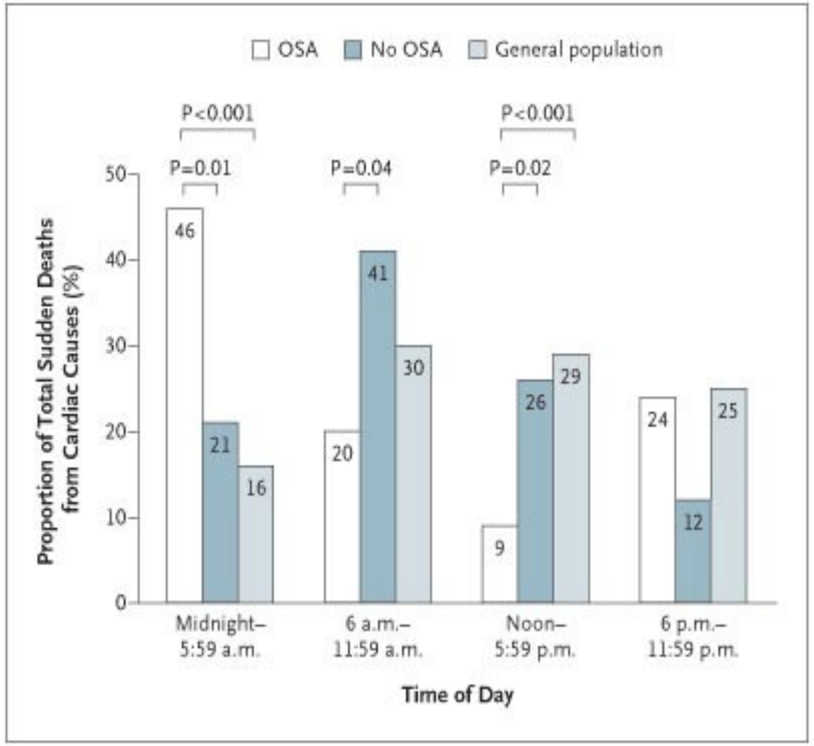
**Table 3. Adjusted ORs and 95% CIs for the Association of Hypertension With OSA and MSLT**

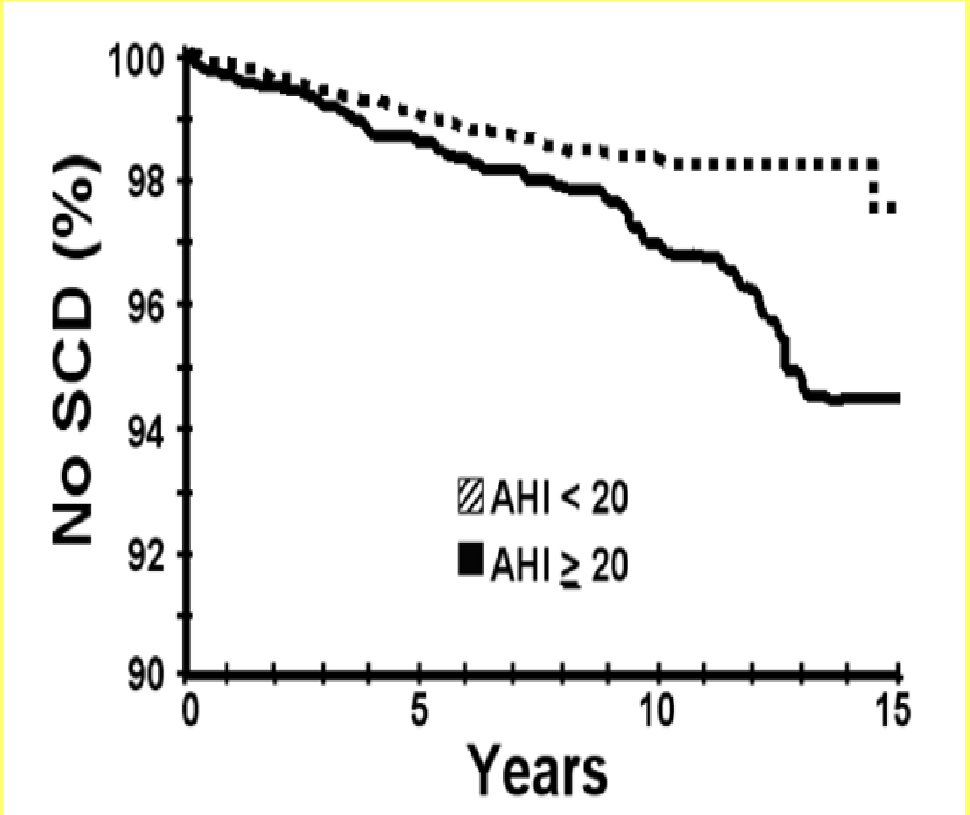
| Predictors | n | OR (95% CI) Model 1 | OR (95% CI) Model 2 | OR (95% CI) Model 3 |
|---|---|---|---|---|
| Primary snoring | | | | |
| MSLT >8 min | 353 | Reference | Reference | Reference |
| 5 min≤MSLT≤8 min | 85 | 1.03 (0.61–1.75) | 1.08 (0.64–1.84) | 1.13 (0.66–1.92) |
| MSLT <5 min | 46 | 0.88 (0.44–1.80) | 0.94 (0.46–1.89) | 1.00 (0.49–2.04) |
| OSA | | | | |
| MSLT >8 min | 736 | 1.83 (1.36–2.47) | 1.18 (0.59–2.34) | 1.28 (0.65–2.54) |
| 5 min≤MSLT≤8 min | 292 | 2.30 (1.61–3.28) | 1.76 (1.01–3.11) | 1.95 (1.10–3.46) |
| MSLT <5 min | 310 | 2.35 (1.62–3.32) | 1.85 (1.13–3.03) | 2.11 (1.22–3.31) |

*J Am Coll Cardiol*. 2013 August 13; 62(7): . doi:10.1016/j.jacc.2013.04.080.

# Obstructive Sleep Apnea and the Risk of Sudden Cardiac Death: A Longitudinal Study of 10,701 Adults

**Apoor S. Gami, M.D., M.Sc., F.A.C.C.**[1,2,5], **Eric J. Olson, M.D.**[3,4,5], **Win K. Shen, M.D., F.A.C.C.**[2,5], **R. Scott Wright, M.D., F.A.C.C.**[2,5], **Karla V. Ballman, Ph.D.**[6], **Dave O. Hodge, M.S.**[6], **Regina M. Herges, B.S.**[6], **Daniel E. Howard, M.D.**[5], and **Virend K. Somers, M.D., Ph.D., F.A.C.C.**[2,5]

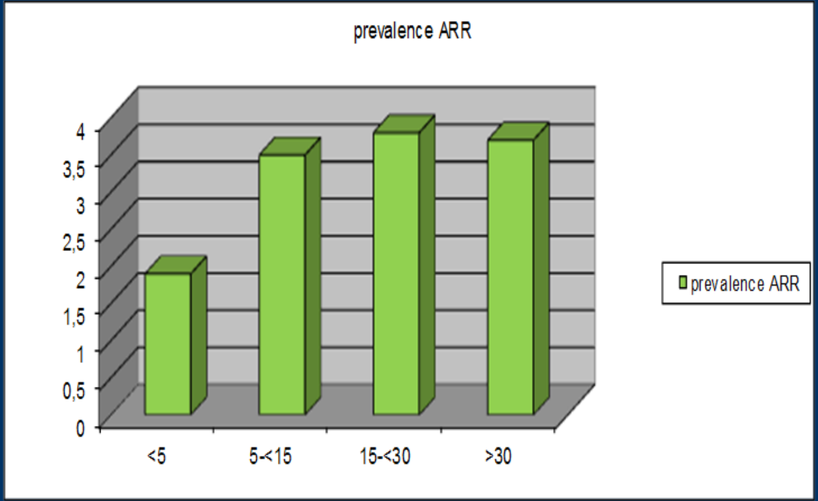


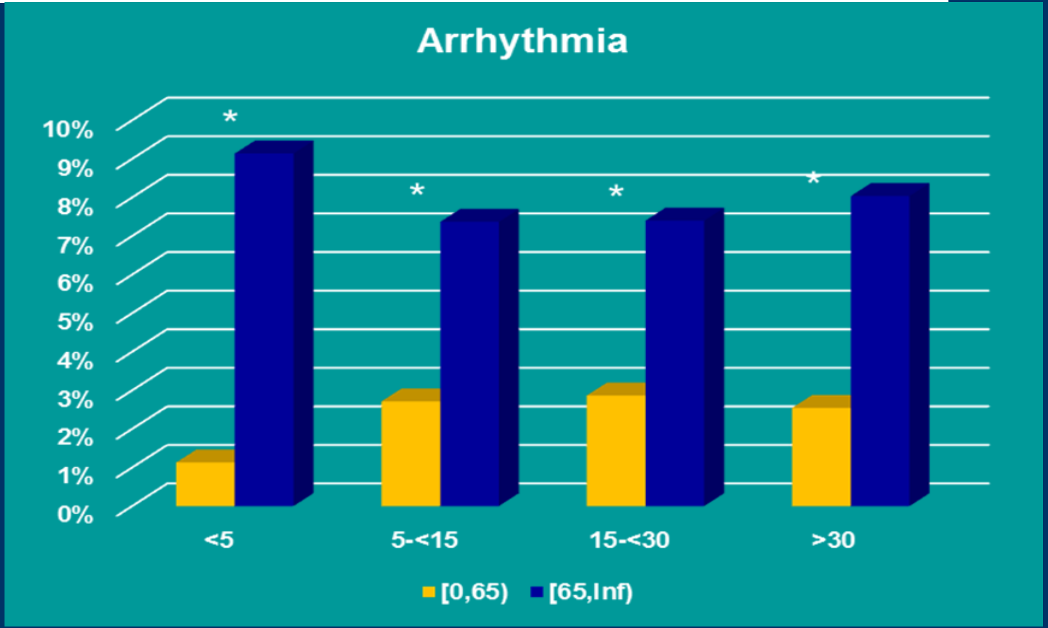



24th Congress of the European Sleep Research Society
Basel, Switzerland | 25–28 September 2018

# Arrhythmias and sleep related breathing disorders: data from the European Sleep Apnoea Database (ESADA)

**C. Lombardi *** , A. Faini , P. Castiglioni , T. Penzel , P. Steiropoulos, L. Grote, J. Hedner, O. Marrone, O.K. Basoglu , Paweł Śliwiński , Georgia Trakada , J. Verbraecken, Z. Dogas, Tarja Saaresranta , S. Schiza, O.Ludka, G.Parati[1].On behalf of ESADA collaborators



# Obstructive Sleep Apnea, Obesity, and the Risk of Incident Atrial Fibrillation

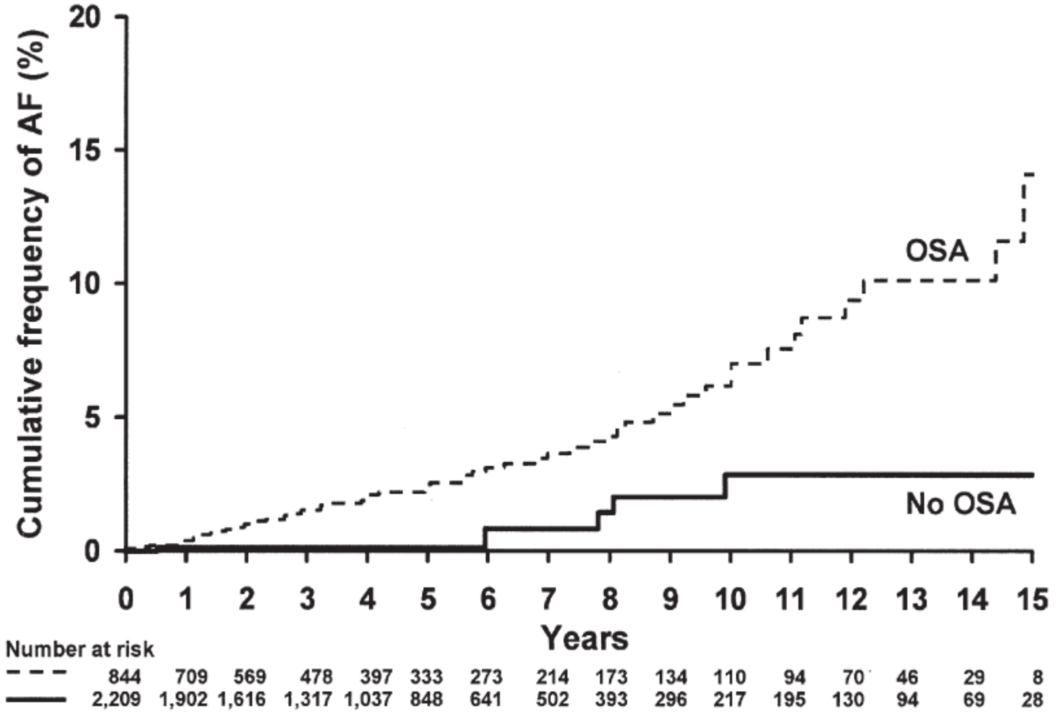



**Figure 1** Incidence of AF Based on Presence or Absence of OSA

Cumulative frequency curves for incident atrial fibrillation (AF) for subjects <65 years of age with and without obstructive sleep apnea (OSA) during an average 4.7 years of follow-up. p = 0.002.

Gami et al.. J Am Coll Cardiol 2007;49:565-571

# *OSA: a risk factor for recurrent AF*

There is a growing body of evidence consistently demonstrating that patients with OSA are much less likely to maintain sinus rhythm after treatment of AF with catheter ablation.

The risk of AF recurrence after ablation in a recent study was significantly higher in patients with versus without OSA (65.2% *vs.* 45.6%; P=0.001).

Sleep Breath (2015) 19:849–856
DOI 10.1007/s11325-014-1102-x

ORIGINAL ARTICLE

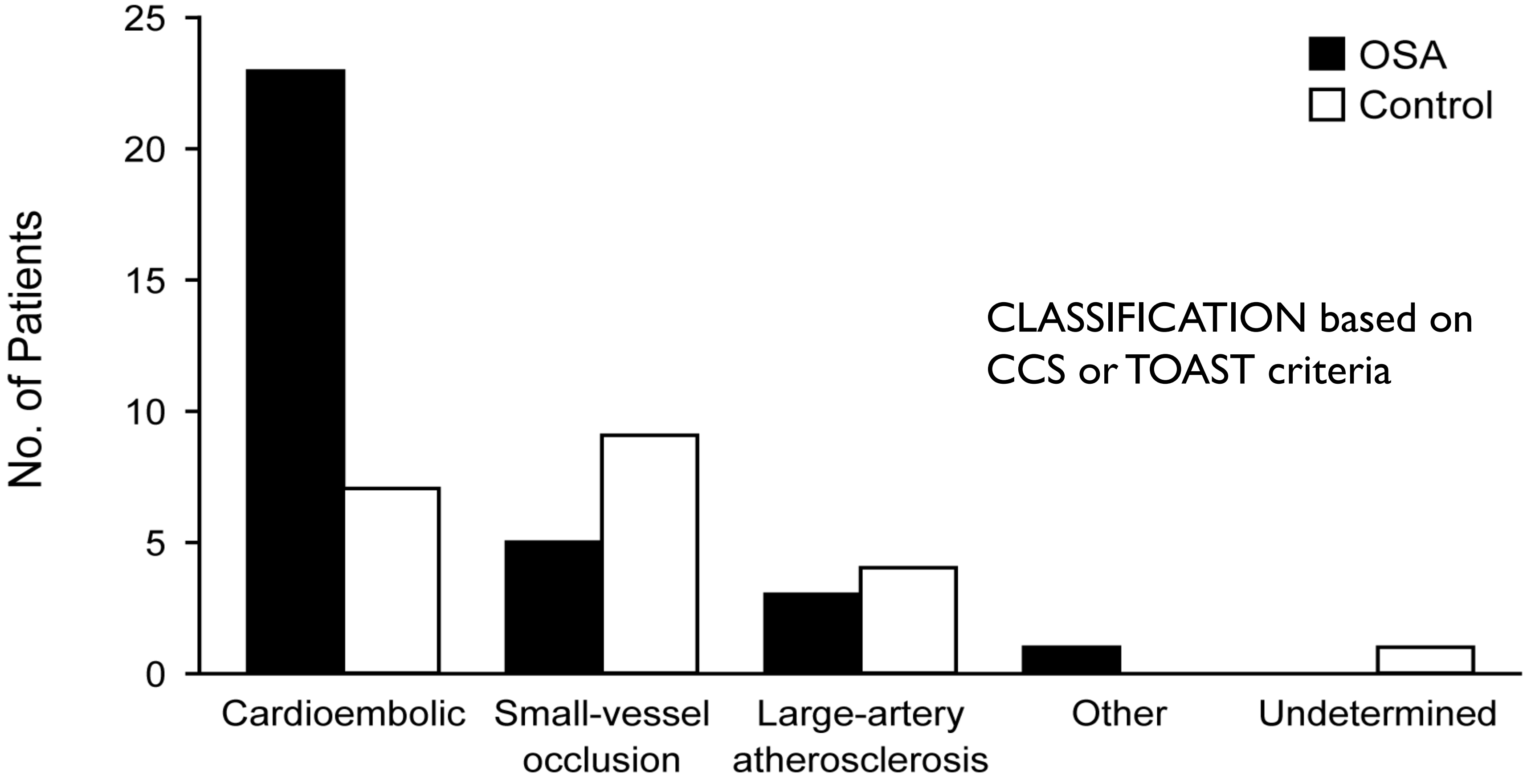
**Presence and severity of obstructive sleep apnea and remote outcomes of atrial fibrillation ablations — a long-term prospective, cross-sectional cohort study**

Filip M. Szymanski · Krzysztof J. Filipiak · Anna E. Platek · Anna Hrynkiewicz-Szymanska · Marcin Kotkowski · Edward Kozluk · Marek Kiliszek · Janusz Sierdzinski · Grzegorz Opolski

# Associations between Cardioembolic Stroke and Obstructive Sleep Apnea

Melissa C. Lipford, MD[1,2]; Kelly D. Flemming, MD[1]; Andrew D. Calvin, MD[3]; Jay Mandrekar, PhD[4]; Robert D. Brown Jr, MD[1]; Virend K. Somers, MD, PhD[3,5]; Sean M. Caples, DO[2,3]

*SLEEP* 2015;38(11):1699–1705



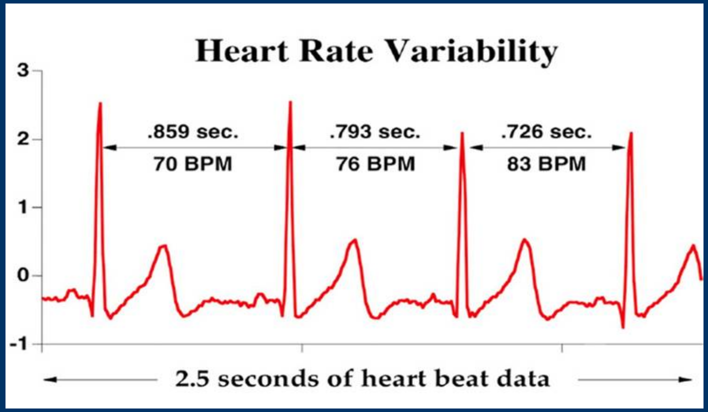

CLASSIFICATION based on CCS or TOAST criteria

**EDITORIAL**

## Obstructive Sleep Apnea as a Candidate Unifier in Atrial Fibrillation and Cryptogenic Stroke

Commentary on Lipford et al. Associations between cardioembolic stroke and obstructive sleep apnea. SLEEP 2015;38:1699–1705.

Reena Mehra, MD, MS; Nancy Foldvary-Schaefer, DO, MS




This analysis included data of 114 patients
Full Polysomnography (from Antwerp)

Patient data was selected based on the presence of 10-minute data segments pre- and post-dormitum.

Table 5 – *Metrics of Heart Rate Variability in pre- and post-dormitum period*

| AHI = | <10 N=32 | | | [10,30] N=45 | | | ≥30 N=37 | | |
|---|---|---|---|---|---|---|---|---|---|
| | PRE | POST | p-value | PRE | POST | p-value | PRE | POST | p-value |
| *Time Domain* | | | | | | | | | |
| HR (bpm) | 64 (9) | 63 (10) | 0.331 | 66 (8) | 65 (7) | 0.352 | 66 (11) | 66 (10) | 0.720 |
| pNN50 | 0.11 (0.14) | 0.15 (0.15) | 0.019 | 0.06 (0.07) | 0.10 (0.11) | 0.002 | 0.13 (0.17) | 0.14 (0.15) | 0.381 |
| pNN50+ | 0.05 (0.07) | 0.08 (0.08) | 0.007 | 0.03 (0.03) | 0.05 (0.05) | <0.001 | 0.06 (0.08) | 0.07 (0.07) | 0.298 |
| pNN50- | 0.06 (0.08) | 0.07 (0.07) | 0.032 | 0.03 (0.04) | 0.05 (0.05) | 0.003 | 0.07 (0.09) | 0.07 (0.08) | 0.486 |
| RMSSD (ms) | 31.0 (16.0) | 36.6 (18.6) | 0.012 | 24.7 (12.2) | 32.8 (16.8) | <0.001 | 31.4 (19.4) | 36.6 (22.3) | 0.153 |
| *Frequency Domain* | | | | | | | | | |
| VLF ($ms^2$) | 1238 (1163) | 4112 (3049) | <0.001 | 950 (870) | 3966 (3178) | <0.001 | 1166 (1180) | 4402 (3325) | <0.001 |
| LF ($ms^2$) | 489 (395) | 1118 (943) | <0.001 | 580 (692) | 1284 (1555) | <0.001 | 536 (449) | 1275 (1082) | <0.001 |
| HF ($ms^2$) | 275 (288) | 354 (372) | 0.036 | 212 (220) | 264 (245) | 0.046 | 319 (318) | 417 (419) | 0.177 |
| LF/HF | 2.93 (2.62) | 4.79 (3.73) | <0.001 | 3.90(4.25) | 5.47 (3.61) | 0.002 | 2.59 (2.08) | 5.34(5.5) | <0.001 |

a. Values are shown as mean; SD is shown between brackets.

b. AHI-index is divided into <10, [10,30] and >30 instead of quartiles, because the metric analysis was done by C. Lombardi and colleagues.

c. Green: vagal indices

d. Red: sympathetic-vagal indices

e. Blue: vagal and/or sympathetic tone indices

Journal of the American Heart Association

ORIGINAL RESEARCH

# Nocturnal Arrhythmias and Heart-Rate Swings in Patients With Obstructive Sleep Apnea Syndrome Treated With Beta Blockers

Carolina Lombardi, MD, PhD; Andrea Faini, Eng; Davide Mariani, MD; Federica Gironi, MD; Paolo Castiglioni, PhD*; Gianfranco Parati, MD, PhD*

J Am Heart Assoc. 2020; 9:e015926.
DOI: 10.1161/JAHA.120.015926

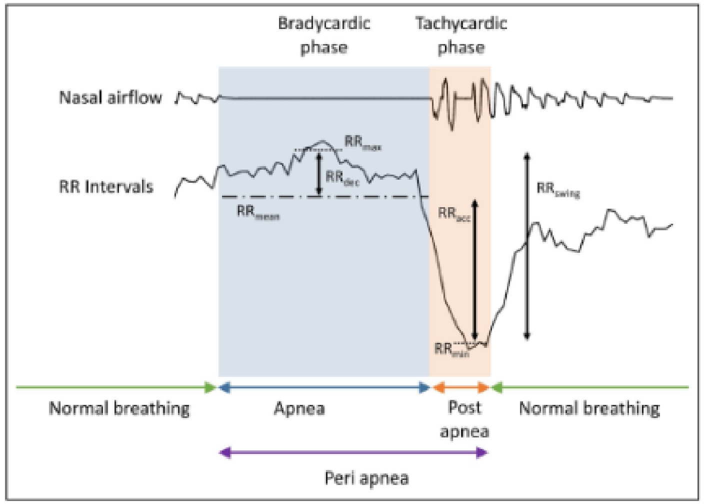



**Figure 2. HR accelerations and decelerations during a sleep apneic event.**
The figure shows the nasal airflow (upper) and the RR-interval series (lower) and the peri-apneic episode as composed of a bradycardic phase (blue area) followed by a tachycardic phase (orange area). $RR_{mean}$ is the mean of all RR intervals during the apneic phase (dot-dash line); $RR_{max}$ is the mean of the 3 longer RR intervals during the apneic phase (dotted line); $RR_{dec}$ is the difference between $RR_{max}$ and $RR_{mean}$ (double-headed arrow). $RR_{min}$ is the mean of the 3 shorter RR intervals during the postapneic phase (dot line); $RR_{acc}$ is the difference between the $RR_{mean}$ and $RR_{min}$ (double-headed arrow). $RR_{swing}$ is the difference between $RR_{max}$ and $RR_{min}$ (double-headed arrow). For further details, see the Methods section. HR indicates heart rate; and RR, RR interval.

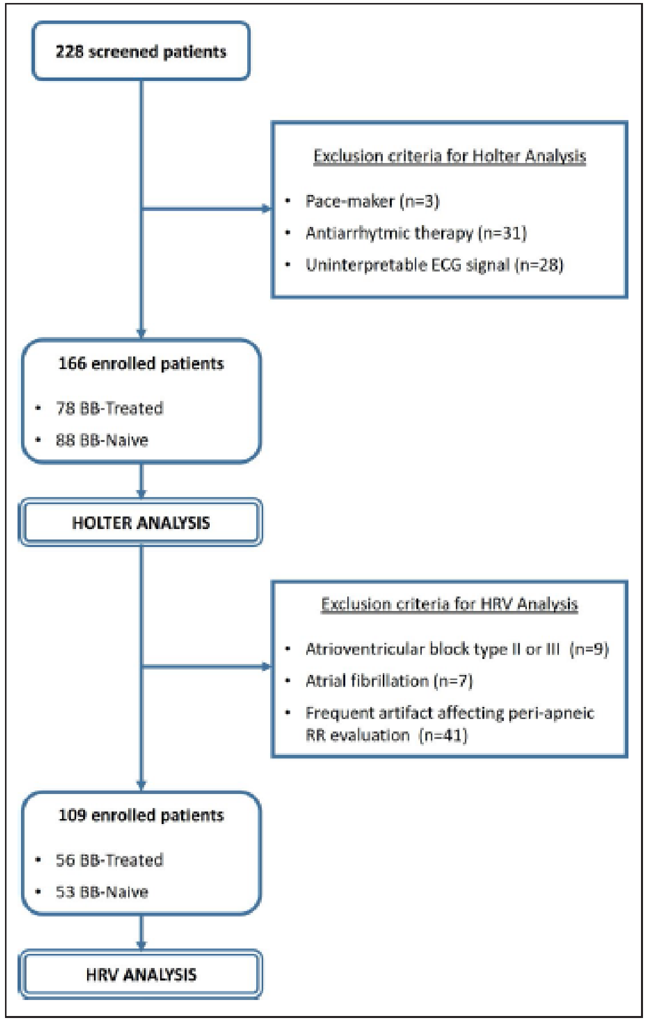



**Figure 1. Study flowchart.**
BB indicates beta blockers; HRV, heart rate variability; and RR RR interval.

**Table 1. General Characteristics of BB-Naïve and BB-Treated Groups**

| | BB-Naïve (N=88) | BB-Treated (N=78) | *P* Value |
|---|---|---|---|
| Anthropometric variables | | | |
| Male (%) | 64 (72.7 | | |
| Age, y | 61.0 (19. | | |
| Body mass index, kg/m$^2$ | 29.4 (6. | | |
| Comorbidities, n (%) | | | |
| Ischemic cardiomyopathy | 4 (4.5) | | |
| Heart failure | 0 (0) | | |
| Stroke/transient ischemic attack | 5 (5.7) | | |
| Chronic kidney disease | 2 (2.3) | | |
| Chronic obstructive pulmonary disease | 3 (3.4) | | |
| Diabetes mellitus | 3 (3.4) | | |
| Hypertension | 41 (46.6 | | |
| AF/PAF (patients) | 1 (1.1) | | |
| Polysomnographic indices | | | |
| Average sleep time, min | 439 (83 | | |
| Mean $SpO_2$ (%) | 93.4 (2.0 | | |
| Minimum $SpO_2$ (%) | 80.0 (10. | | |
| Oxygen desaturation index, events/h | 20.2 (24. | | |
| Apnea hypopnea index, events/h | | | |
| Total | 19.2 (22 | | |
| Obstructive | 18.7 (20. | | |
| Central | 0.0 (0.3 | | |
| Apnea hypopnea index distribution | | | |
| Mild | 30 (34.1 | | |
| Moderate | 32 (36.4%) | 26 (33.3%) | 0.68 |
| Severe | 24 (27.3%) | 23 (29.5%) | 0.75 |

**Table 2. Holter-Derived Indices of Frequency and Type of Arrhythmias in BB-Naïve and BB-Treated Groups**

| | BB-Naïve (N=88) | BB-Treated (N=78) | *P* Value |
|---|---|---|---|
| HR, bpm | 61.4 (10.6) | 59.7 (10.1) | 0.054 |
| AF/PAF (patients) | 1 (1.1%) | 6 (7.7%) | 0.52 |
| SVEB (episodes) | 7.5 (21.8) | 9.5 (53.5) | 0.41 |
| PSVT (episodes) | 0.0 (0.3) | 0.0 (0.0) | 0.73 |
| PSVT duration, s | 1.90 (2.28) | 2.35 (1.60) | 0.60 |
| VEB | | | |
| Single | 1.0 (17.3) | 2.0 (28.0) | 0.23 |
| Couples | 1.0 (1.0) | 2.0 (7.5) | 0.18 |
| Triplets | 0.0 (0.0) | 0.0 (0.0) | >0.99 |
| VT (patients) | 2 (2.3%) | 3 (2.6%) | 0.67 |
| Sinus pauses duration, s | 3.15 (0.05) | 4.10 (1.50) | 0.16 |
| Sinus pauses (patients) | 19 (21.6%) | 16 (20.5%) | >0.99 |
| Sinus pauses (episodes) | 0.0 (0.0) | 0.0 (0.0) | 0.84 |
| AVB type II–III (patients) | 7 (8.0%) | 2 (2.6%) | 0.18 |

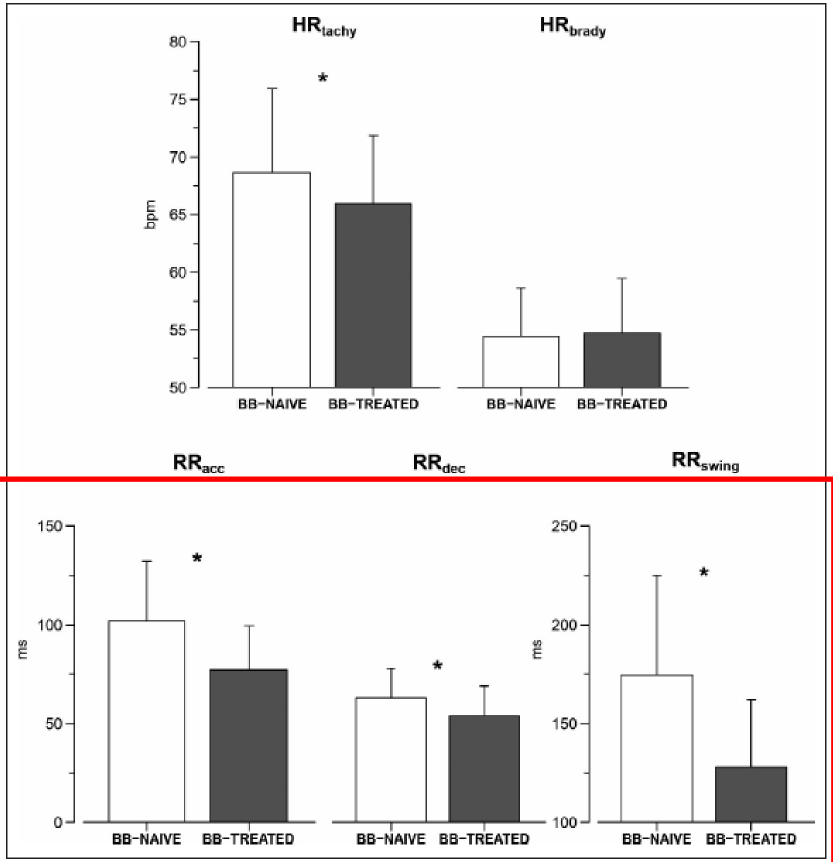



**Figure 3.** Peri-apneic HR values in BB-treated and BB-naïve patients with OSA (upper panels) and local RR changes induced by apnea in BB-treated and BB-naïve patients with OSA (lower panels).

**CONCLUSIONS:** BB appear to be safe in patients with obstructive sleep apnea because they are not associated with worse episodes of nocturnal bradyarrhythmias and even seem protective in terms of apnea-induced changes of heart rate.

> Am J Respir Crit Care Med. 2021 Jan 6. doi: 10.1164/rccm.202010-3900OC. Online ahead of print.

# The Sleep Apnea-specific Pulse Rate Response Predicts Cardiovascular Morbidity and Mortality

Ali Azarbarzin [1], Scott A Sands [2], Magdy Younes [3], Luigi Taranto-Montemurro [4 5], Tamar Sofer [6 7], Daniel Vena [4 5], Raichel M Alex [2], Sang-Wook Kim [2], Daniel J Gottlieb [5], David P White [2], Susan Redline [8 9], Andrew Wellman [4 5]

Affiliations + expand

PMID: 33406013 DOI: 10.1164/rccm.202010-3900OC

FULL TEXT LINKS

AJRCCM Full Text

ACTIONS

Cite

Favorites

SHARE

PAGE NAVIGATION

< Title & authors

## Abstract

**Rational:** Randomized controlled trials have been unable to detect a cardiovascular benefit of continuous positive airway pressure (CPAP) in unselected patients with obstructive sleep apnea (OSA). We hypothesize that deleterious cardiovascular outcomes are concentrated in a subgroup of patients with heightened apnea/hypopnea-related pulse rate response.

pulse rate response to apneas/hypopneas (ΔHR) in the Multi-Ethnic Study of Atherosclerosis (MESA, N=1395) and the Sleep Heart Health Study (SHHS, N=4575).

The risk associated with high ΔHR
was particularly high in those with substantial hypoxic burden (non-fatal: 1.93 [1.36-2.73]; fatal:
3.50 [2.15-5.71]; all-cause: 1.84 [1.40-2.40]) and was exclusively observed in non-sleepy individuals.

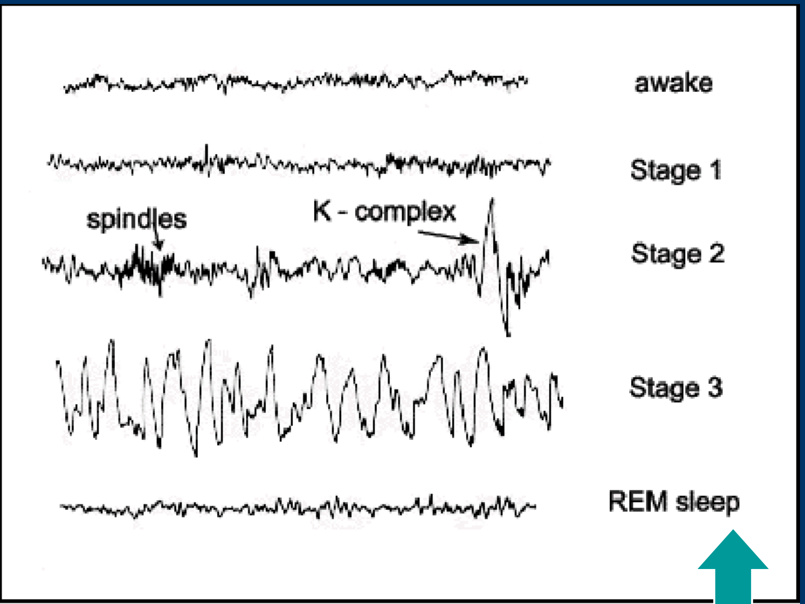
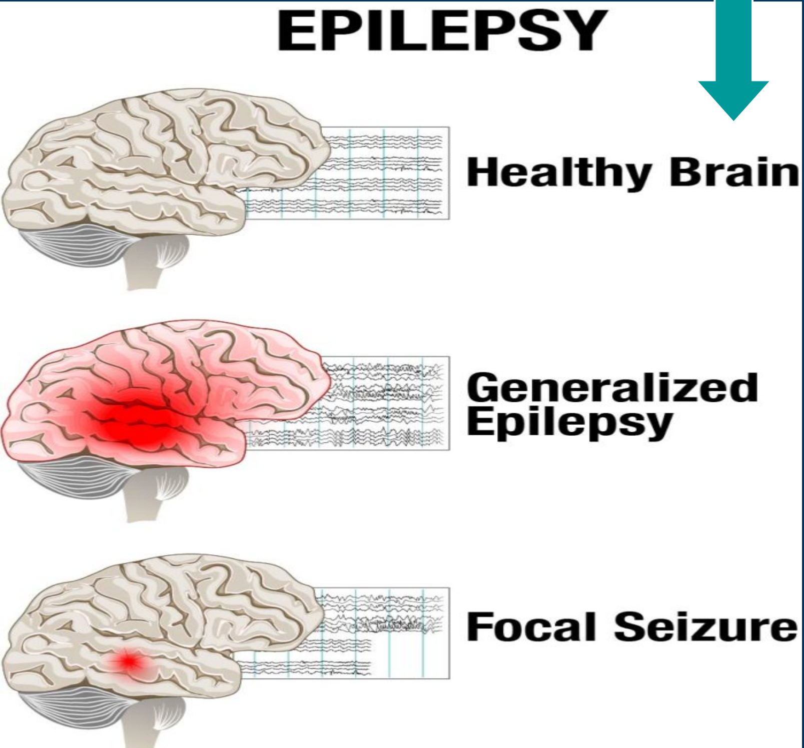
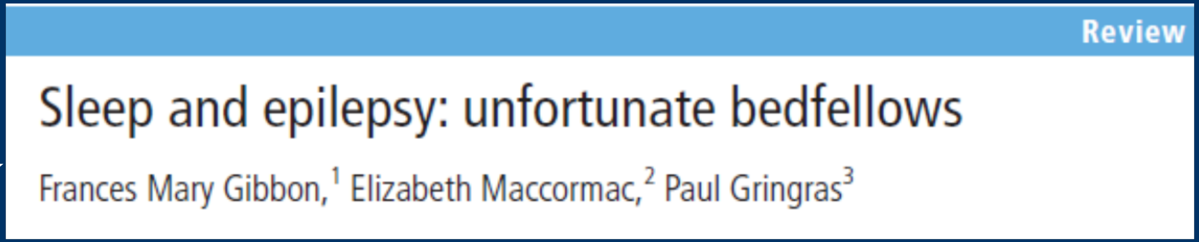



Figure 3: Wave pattern of different sleep Stages





Review

# Sleep and epilepsy: unfortunate bedfellows

Frances Mary Gibbon,[1] Elizabeth Maccormac,[2] Paul Gringras[3]

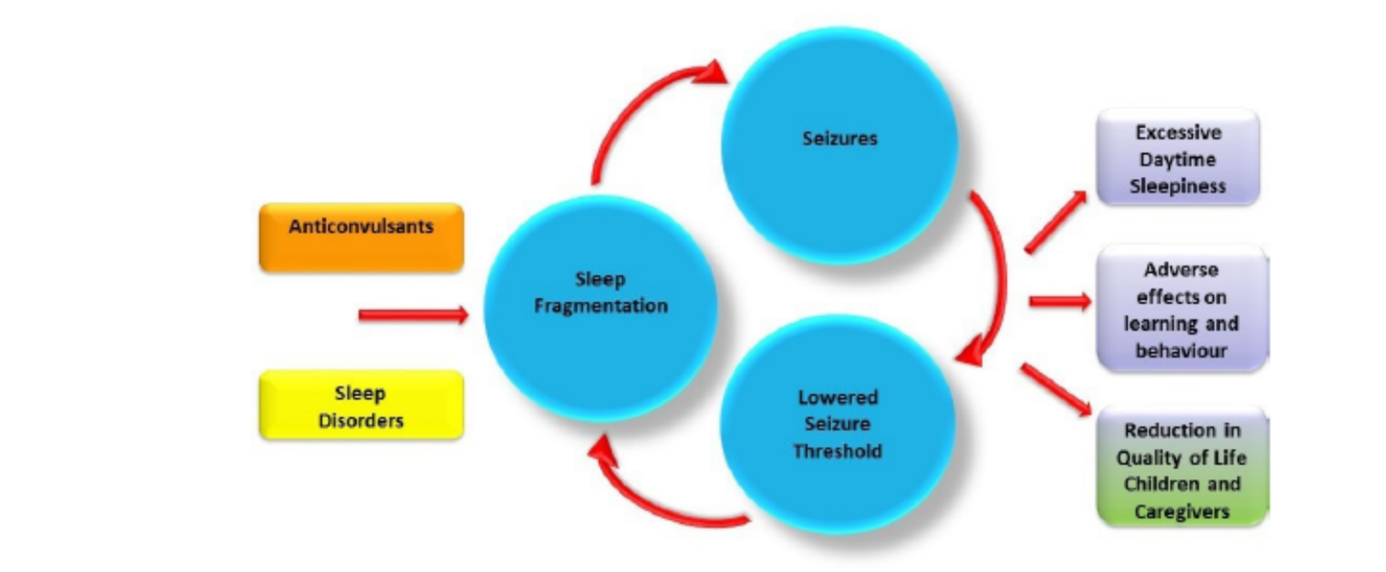
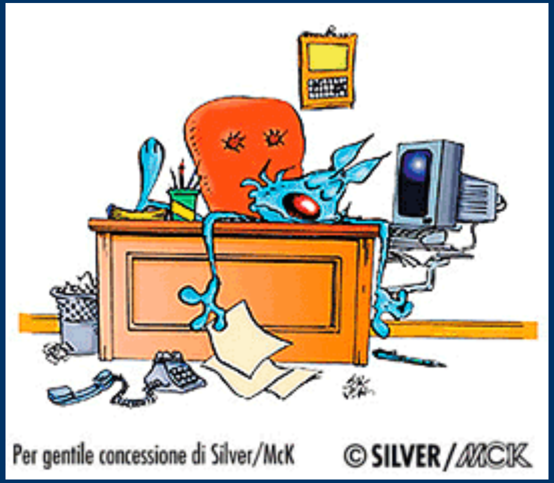



**Figure 1** Sleep and epilepsy—a vicious cycle.

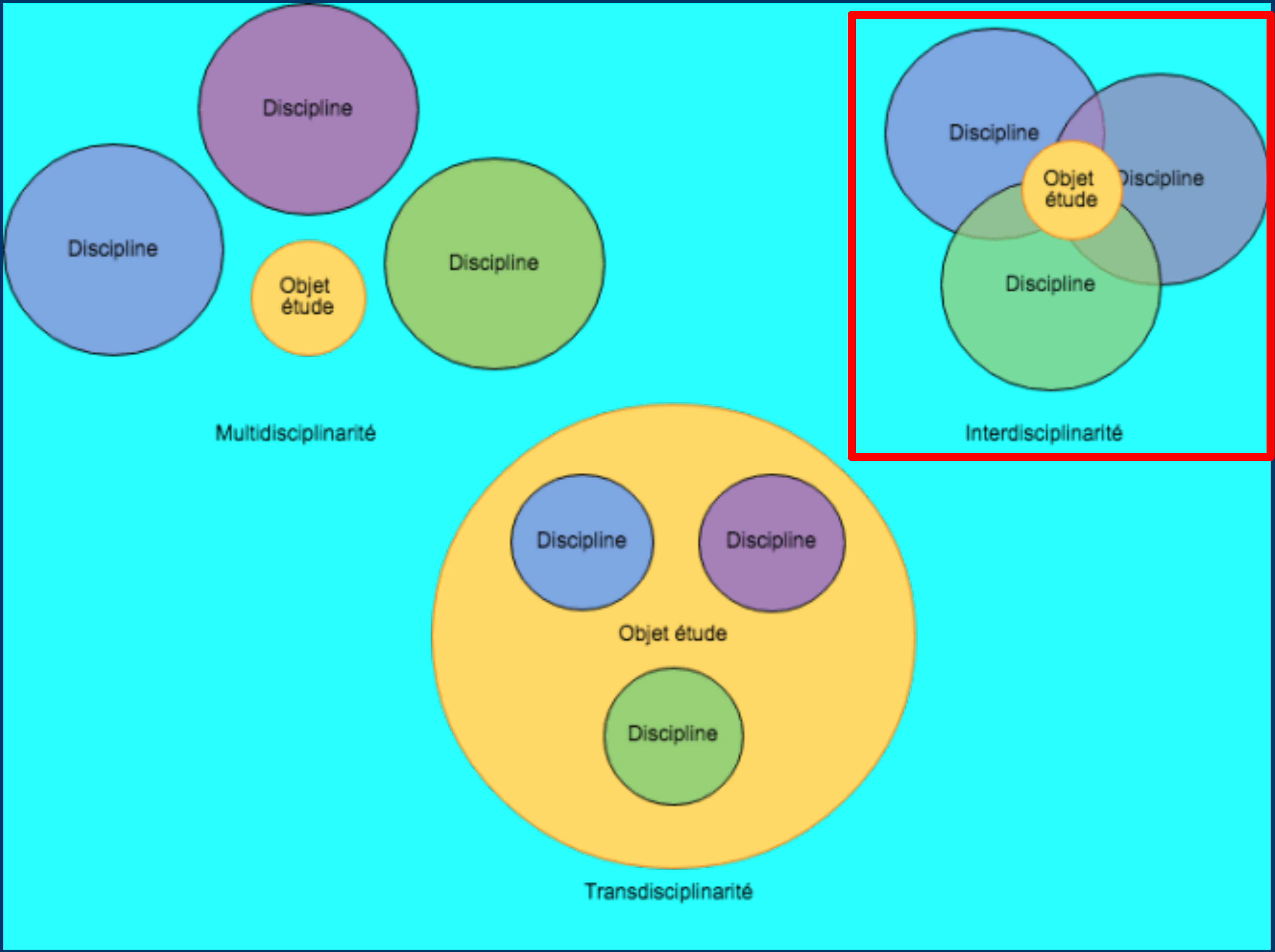
Gibbon FM, *et al. Arch Dis Child* 2019;**104**:189–192.

# NARCO-CATAPLESSIA




Attacchi di sonno


CATAPLESSIA

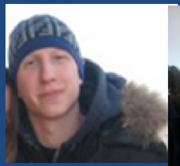


Discipline
Discipline
Objet
étude
Discipline
Multidisciplinarité
Discipline
Objet
étude
Discipline
Discipline
Interdisciplinarité
Discipline
Discipline
Objet étude
Discipline
Transdisciplinarité

# «SLEEP TEAM»

Prof. G.Parati

Prof.ssa Lombardi Carolina
Direttore

Students and fellows:

Dott.ssa Mattaliano
Dott. Pengo
Dott.ssa Perger
Dott. Foresi
( Fisiopatologia Respiratoria)




Segreteria
Sig.ra Lucci Elena

Statistician:
Dott. Davide Soranna

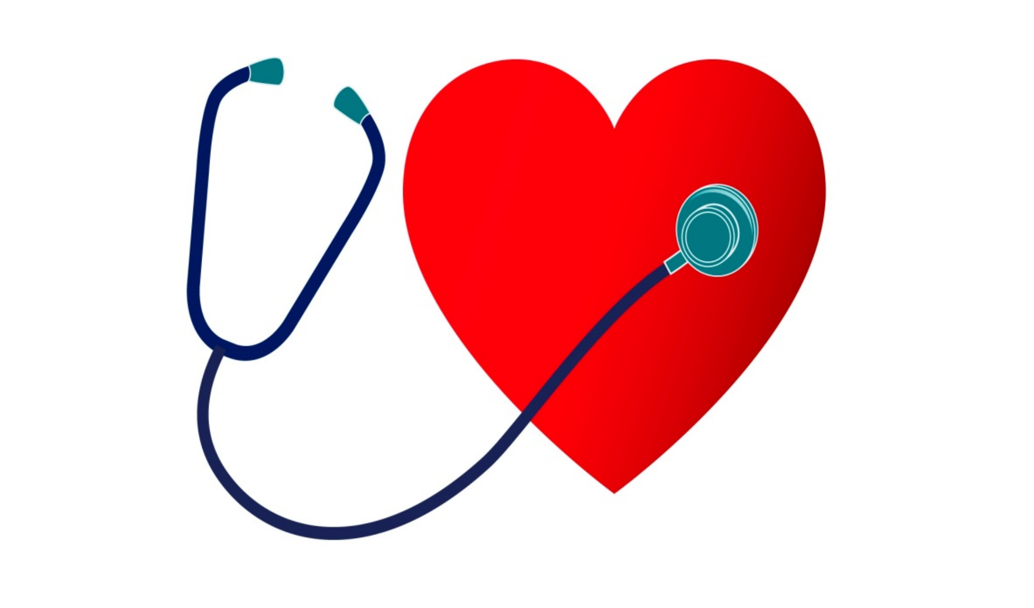
TNFP
- Barbara Riccardi
- Francesca Gregorini
- Anna Motta
- Valeria De Stefano
- Aurora Cremonesi
- Davide Reggi
- Margherita Scandiffio



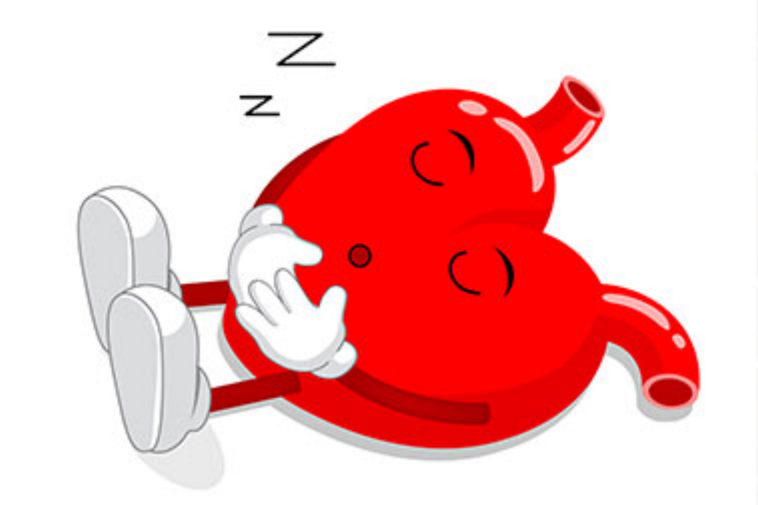

Ing. Faini Andrea
Ing.Castiglioni Paolo
Ing. Meriggi Paolo



Data and trial Manager:
Dott.ssa Beretta Ada



# THANK YOU FOR YOUR ATTENTION

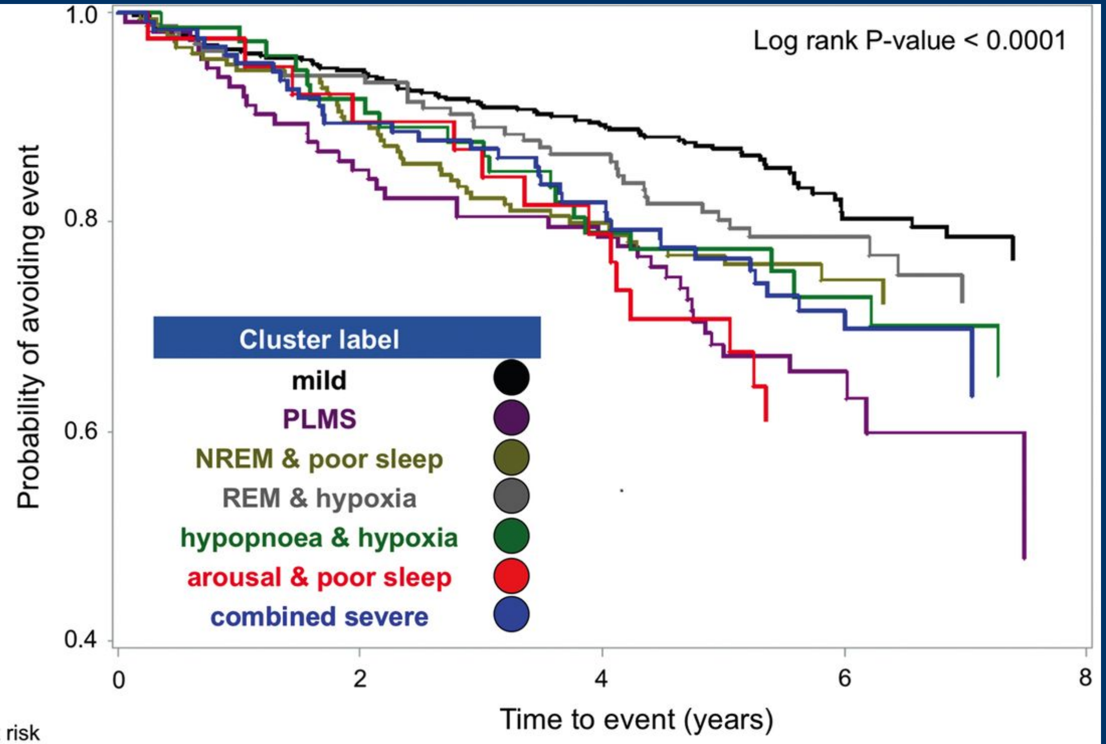


# Polysomnographic phenotypes and their cardiovascular implications in obstructive sleep apnoea.

Zinchuk AV1, Jeon S2, Koo BB3, Yan X1, Bravata DM4, Qin L5, Selim BJ6, Strohl KP7, Redeker NS2, Concato J1,8, Yaggi HK1.

*Thorax. 2017 Sep 21.*

**COMORBIDITY**



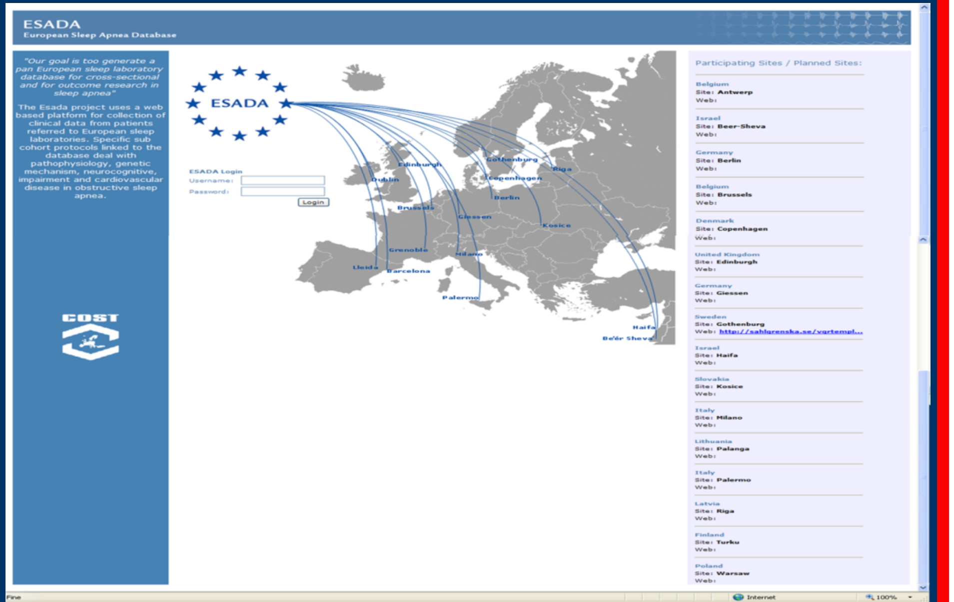

| Cluster / number at risk | 0 | 2 | 4 | 6 | 8 |
|---|---|---|---|---|---|
| mild | 517 | 478 | 407 | 129 | 17 |
| PLMS | 114 | 96 | 82 | 27 | 1 |
| NREM & poor sleep | 181 | 162 | 130 | 42 | 5 |
| REM & hypoxia | 167 | 154 | 129 | 61 | 8 |
| hypopnoea & hypoxia | 74 | 67 | 51 | 26 | 5 |
| arousal & poor sleep | 41 | 34 | 29 | 14 | 0 |
| combined severe | 124 | 110 | 95 | 40 | 3 |

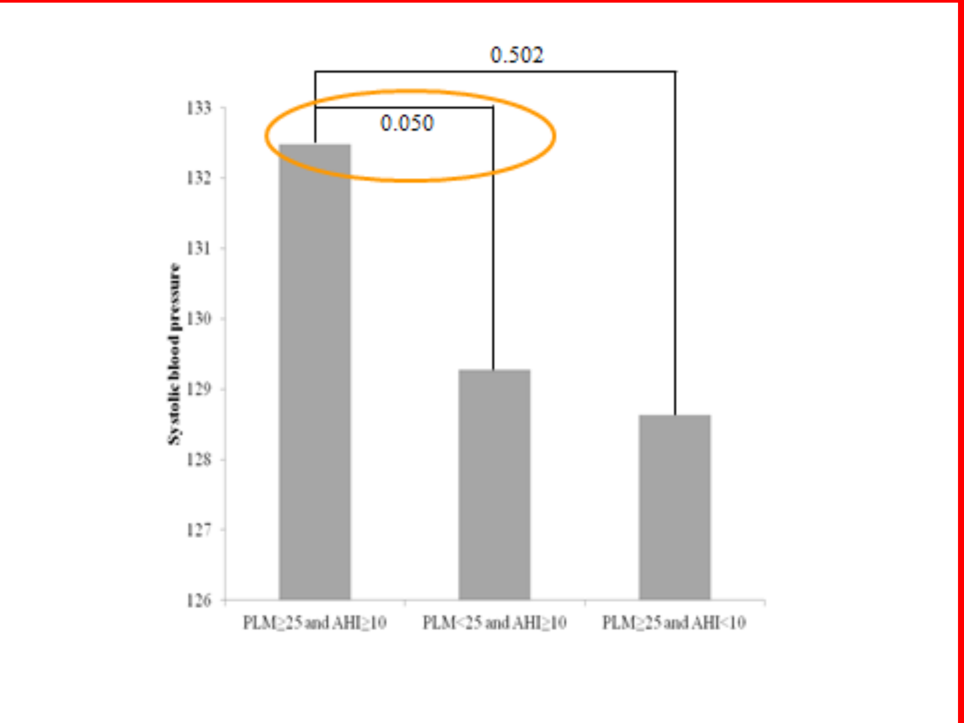
Official Journal of the Asian Pacific Society of Respirology
Respirology

ORIGINAL ARTICLE

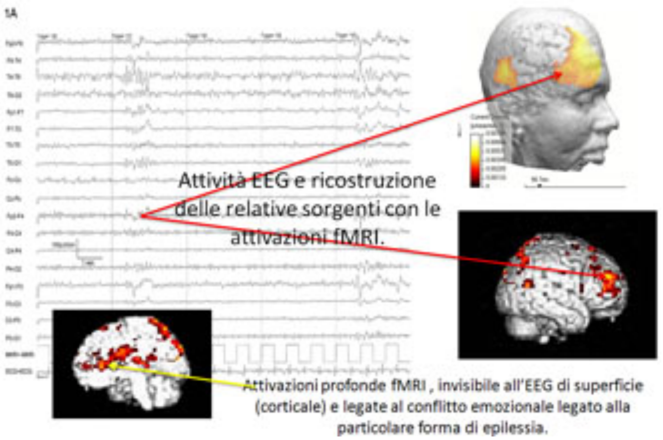
# Periodic limb movements during sleep and blood pressure changes in sleep apnoea: Data from the European Sleep Apnoea Database

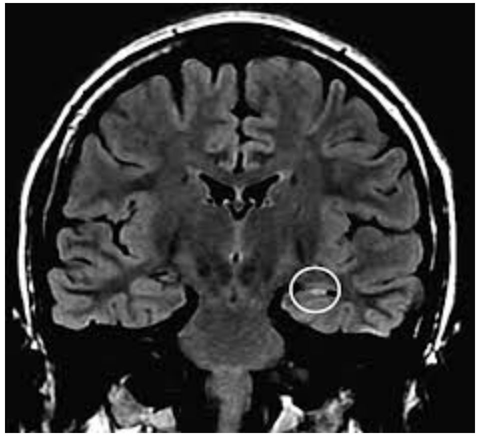
CAROLINA LOMBARDI,[1,2] GIANFRANCO PARATI,[1,2] DAVIDE SORANNA,[1] ANTONELLA ZAMBON,[1,3] PAWEŁ SLIWINSKI,[4] GABRIEL ROISMAN,[5] JEAN-LOUIS PEPIN,[6,7] SOPHIA SCHIZA,[8] RENATA RIHA,[9] PAVOL JOPPA,[10] INGO FIETZE,[11] JAN HEDNER,[12,13] LUDGER GROTE[12,13] AND ON BEHALF OF THE EUROPEAN SLEEP APNOEA DATABASE (ESADA) COLLABORATORS




Università degli Studi di Siena


Attività EEG e ricostruzione delle relative sorgenti con le attivazioni fMRI.
Attivazioni profonde fMRI , invisibile all'EEG di superficie (corticale) e legate al conflitto emozionale legato alla particolare forma di epilessia.



A.I.M.S.

AIMS

*Associazione Italiana di Medicina del Sonno*

# XX CORSO RESIDENZIALE DI MEDICINA DEL SONNO

## I DISTURBI DEL SONNO DELL'ADULTO E DEL BAMBINO

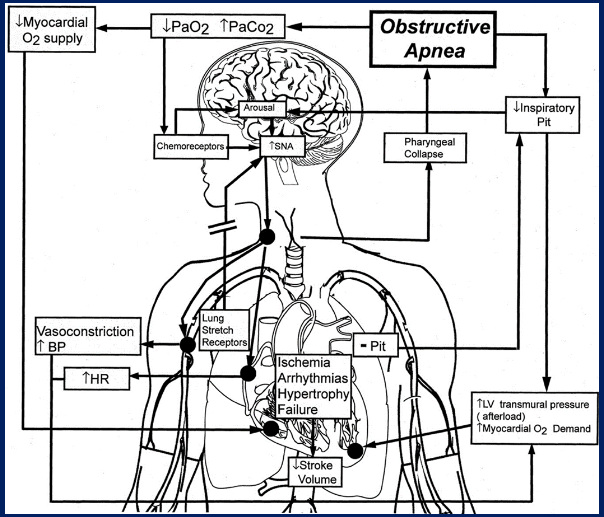
*Bertinoro (FC) 16 - 21 Aprile 2016*

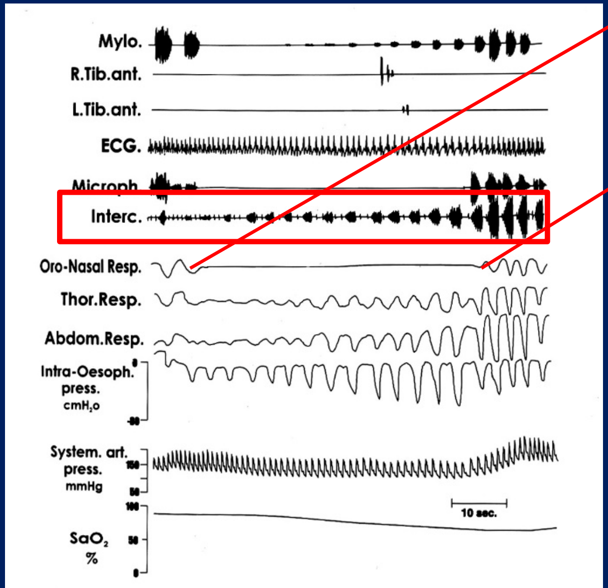
CENTRO RESIDENZIALE UNIVERSITARIO DI BERTINORO

ALMA MATER STUDIORUM
UNIVERSITÀ DI BOLOGNA

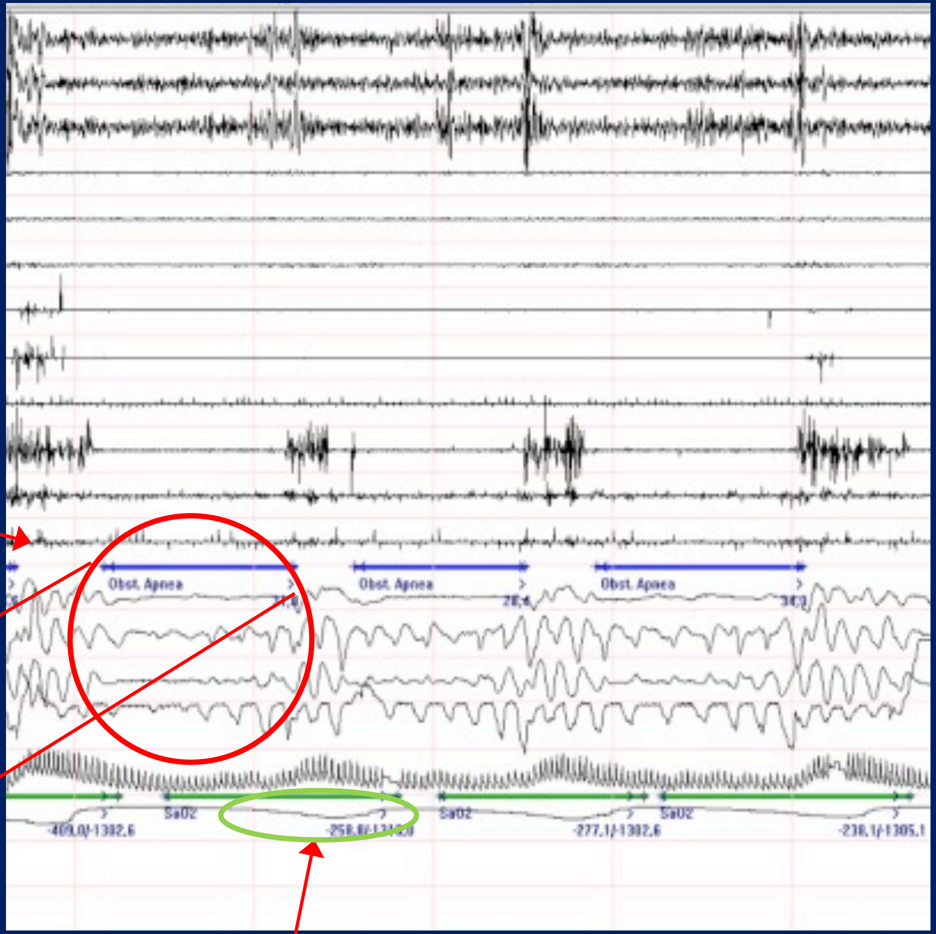

ISTITUTO AUXOLOGICO ITALIANO
Istituto di Ricovero e Cura a Carattere Scientifico
Per una
scienza
dello sviluppo
umano


AHI




Obstructive apnea




O2 and CO2 changes

# The HIGHCARE team

# HIGHCARE

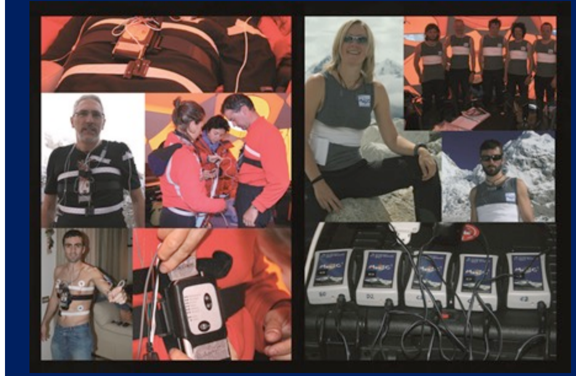
## HIGH altitude CArdiovascular REsearch

*J Sleep Res.* (2013) Regular Research Paper

# High-altitude hypoxia and periodic breathing during sleep: gender-related differences

CAROLINA LOMBARDI[1], PAOLO MERIGGI[2], PIERGIUSEPPE AGOSTONI[3,4], ANDREA FAINI[1], GRZEGORZ BILO[1,6], MIRIAM REVERA[1,6], GIANLUCA CALDARA[1], MARCO DI RIENZO[2], PAOLO CASTIGLIONI[2], BUSSOTTI MAURIZIO[7], FRANCESCA GREGORINI[1], GIUSEPPE MANCIA[1,6], GIANFRANCO PARATI[1,6] and ON BEHALF OF THE HIGHCARE INVESTIGATORS

[1]Department of Cardiology, S.Luca Hospital, Istituto Auxologico Italiano, IRCCS, Milan, Italy, [2]Polo Tecnologico, Biomedical Technology Department, Fondazione Don Carlo Gnocchi Onlus, Milano, Italy, [3]Centro Cardiologico Monzino, IRCCS, Milan, Italy, [4]Department of Cardiovascular Sciences, University of Milan, Milan, Italy, [5]Division of Critical Care and Respiratory Medicine, University of Washington, Seattle, WA, USA, [6]Department of Health Sciences, University Milano-Bicocca, Milan, Italy, [7]Cardiologia Riabilitativa, Istituto di Riabilitazione, Fondazione Salvatore Maugeri, IRCCS, Milan, Italy



ISTITUTO AUXOLOGICO ITALIANO
Istituto di ricovero e cura a carattere scientifico

UNIVERSITÀ DEGLI STUDI DI MILANO BICOCCA

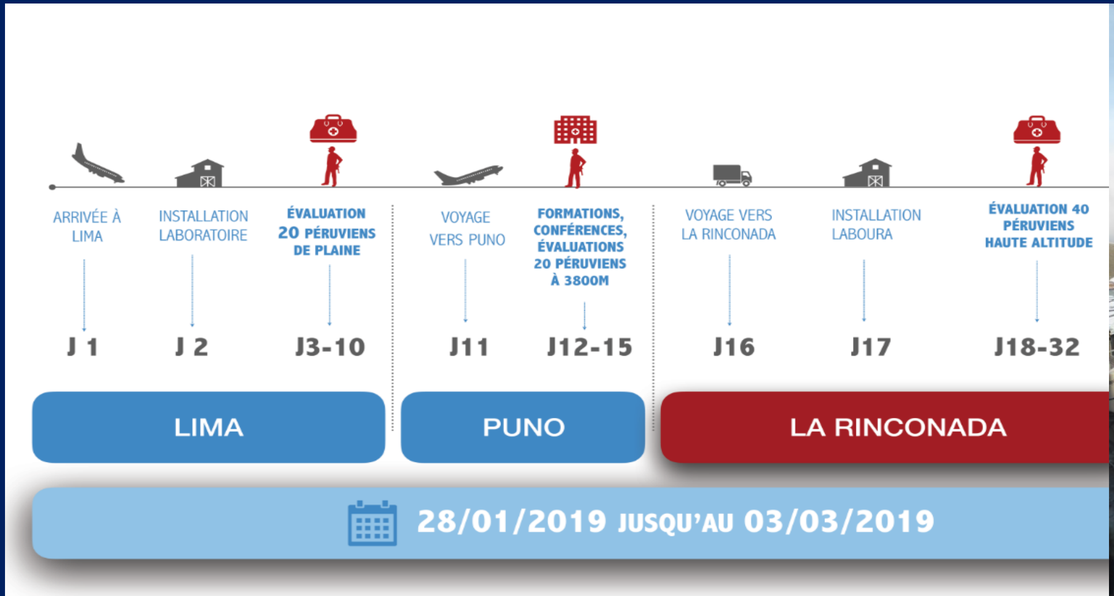


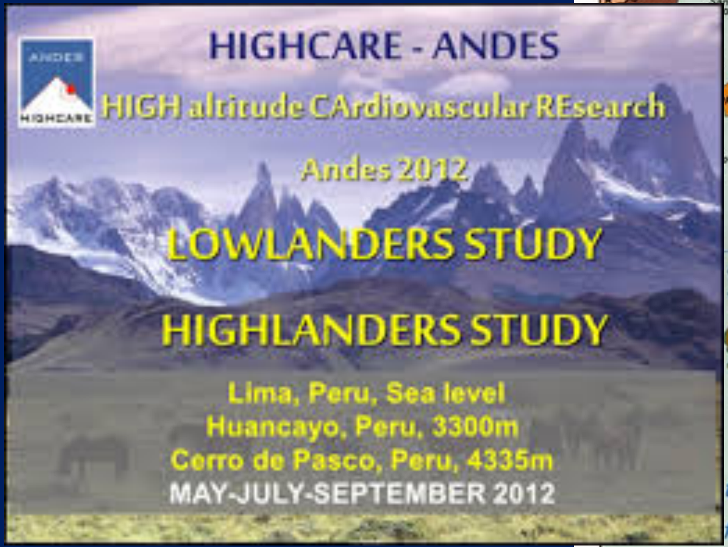




# EXPEDITION 5300: LA RICERCA SUL SONNO IN ALTA QUOTA

https://www.auxologico.it/news/expedition-5300-ricerca-sonno-alta-quota

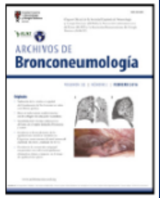




HIGHCARE - ANDES
HIGH altitude CArdiovascular REsearch
Andes 2012
LOWLANDERS STUDY
HIGHLANDERS STUDY
Lima, Peru, Sea level
Huancayo, Peru, 3300m
Cerro de Pasco, Peru, 4335m
MAY-JULY-SEPTEMBER 2012


South America
Caribbean Sea
North Atlantic Ocean
South Atlantic Ocean
Ocean
VENEZUELA
COLOMBIA
GUYANA
SURINAME
ECUADOR
PERU
BRAZIL
BOLIVIA
PARAGUAY
CHILE
ARGENTINA
URUGUAY
Caracas
Bogotá
Quito
Lima
La Paz
Asunción
Santiago
Buenos Aires
Montevideo
Brasília
Rio de Janeiro
São Paulo
Georgetown
Paramaribo
Cayenne
Manaus
Stanley
Falkland Islands (Islas Malvinas)
Strait of Magellan
South Georgia and the South Sandwich Islands

• HY

ARCHIVOS DE Bronconeumología
www.archbronconeumol.org



Special article

# Hypoxic Burden in Obstructive Sleep Apnea: Present and Future

Miguel A. Martinez-Garcia[a,b,*], Manuel Sánchez-de-la-Torre[b,c], David P. White[d], Ali Azarbarzin[d]

[a] *Respiratory Department, Hospital Universitario y Politécnico La Fe, Valencia, Spain*
[b] *Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBERES), Madrid, Spain*
[c] *Precision Medicine in Chronic Diseases, Hospital Universitari Arnau de Vilanova-Santa Maria, IRB Lleida, Department of Nursing and Physiotherapy, Faculty of Nursing and Physiotherapy, University of Lleida, Lleida, Spain*
[d] *Division of Sleep and Circadian Disorders, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, United States*



**Table 1**
Weaknesses of the apnea-hypopnea index and the oxygen desaturation index in establishing the diagnosis and quantifying the severity of obstructive sleep apnea (OSA).

| Apnea-hypopnea index (AHI) | Oxygen desaturation index (ODI) |
|---|---|
| No information on the duration and depth of respiratory events and their ensuing desaturations | No information on the duration and depth of respiratory-related desaturations |
| Apnea and hypopnea have similar weight in the AHI calculation | Arbitrary thresholds of 3% or 4% depending on the sleep lab or research study |
| Multiple definitions of hypopnea in research studies and sleep labs. Hypopneas are scored differently based on the presence/absence of arousals, and different degrees of oxygen desaturation | Inclusion of desaturations that are associated with airflow reduction not meeting scoring criteria |
| Arbitrary threshold of 10 s (9 s-events can also be associated with significant oxygen desaturation) | Desaturations due to other non-OSA cardio-respiratory diseases or obesity-related noctural hypoxemia |
| Apnea definition does not depend on oxygen desaturation, however hypopnea definition may or may not depend on the severity of oxygen desaturation | |

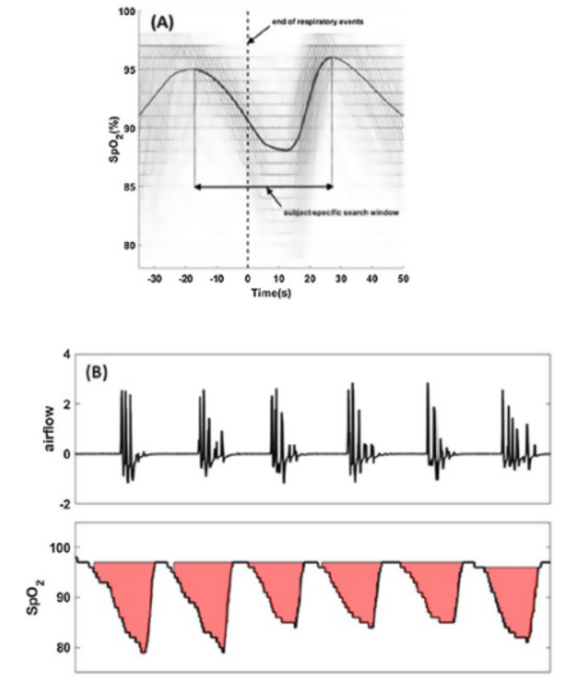



**Fig. 1.** Hypoxic burden is determined by creating a subject-specific search window (panel (A)) from all respiratory events regardless of desaturation or arousals. Overlaid oxygen saturation signals ($SpO_2$) associated with all respiratory events are synchronized at the termination of events (time zero). Synchronized $SpO_2$ signals are averaged to quantify the subject-specific desaturation curve (solid black line). The search window is the time between the two peaks. The search window will be used to determine the area under individual desaturation curves (panel (B)). Total hypoxic burden (HB) is the sum of all individuals areas normalized by sleep time.

ESC European Society of Cardiology European Heart Journal (2019) **40**, 1149–1157
doi:10.1093/eurheartj/ehy624

**CLINICAL RESEARCH**
*Prevention and epidemiology*

# The hypoxic burden of sleep apnoea predicts cardiovascular disease-related mortality: the Osteoporotic Fractures in Men Study and the Sleep Heart Health Study

**Ali Azarbarzin[1]*, Scott A. Sands[1], Katie L. Stone[2,3], Luigi Taranto-Montemurro[1], Ludovico Messineo[1], Philip I. Terrill[4], Sonia Ancoli-Israel[5,6], Kristine Ensrud[7], Shaun Purcell[1,8], David P. White[1], Susan Redline[1], and Andrew Wellman[1]**

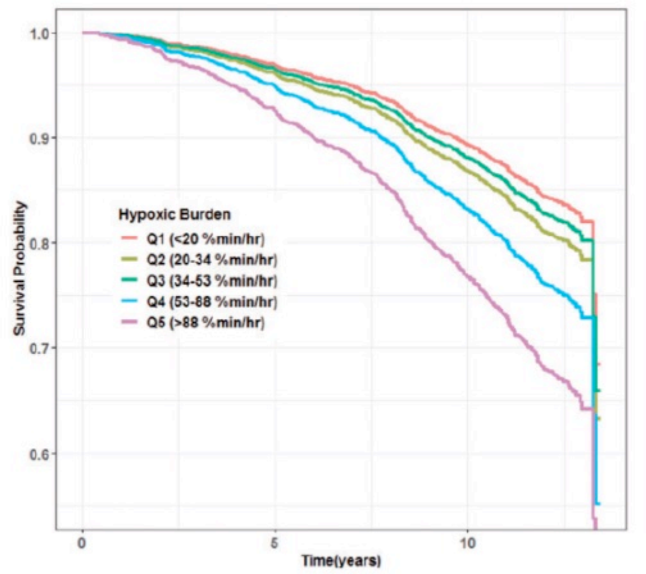
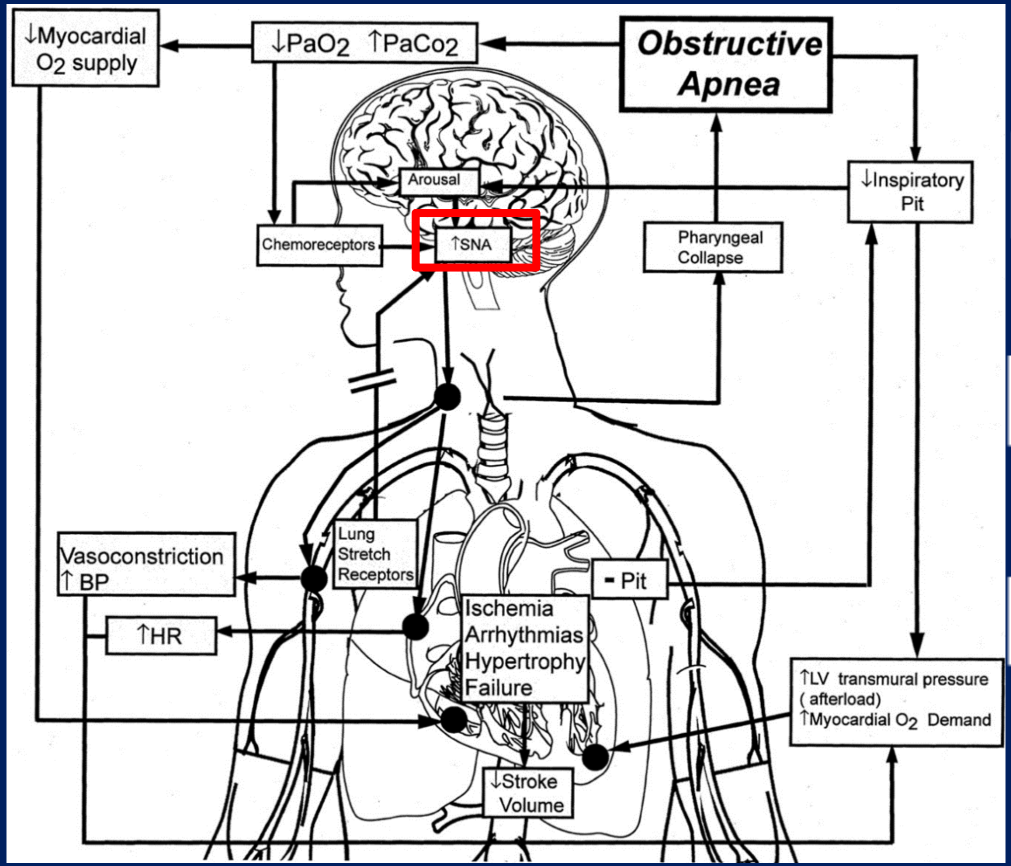
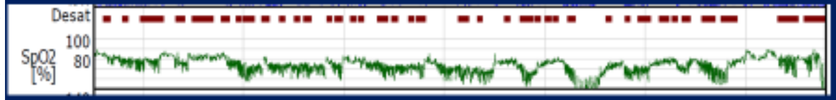
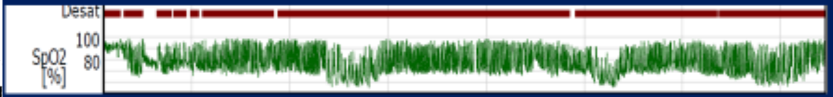



**Figure 2** Adjusted survival curves for cardiovascular mortality across categories of the hypoxic burden in MrOS. These curves were obtained from Model 4. The adjusted survival curves were obtained by averaging the predicted survival curves for every observation in MrOS study.


↓Myocardial O2 supply
↓PaO2 ↑PaCo2
Obstructive Apnea
Arousal
↓Inspiratory Pit
Chemoreceptors
↑SNA
Pharyngeal Collapse
Lung Stretch Receptors
Vasoconstriction ↑ BP
- Pit
↑HR
Ischemia Arrhythmias Hypertrophy Failure
↑LV transmural pressure ( afterload) ↑Myocardial O2 Demand
↓Stroke Volume


Desat
100
SpO2 80
[%]
62


Desat
100
SpO2 80
[%]
75


Desat
100
SpO2 80
[%]
67


WHICH IS THE LINK
WHICH ARE PREDICTORS

Cardiovascular Critical Care

# Prognostic Importance of Sleep Quality in

ıgkum Heo,
D

ıber 2016, Volume 25, No. 6

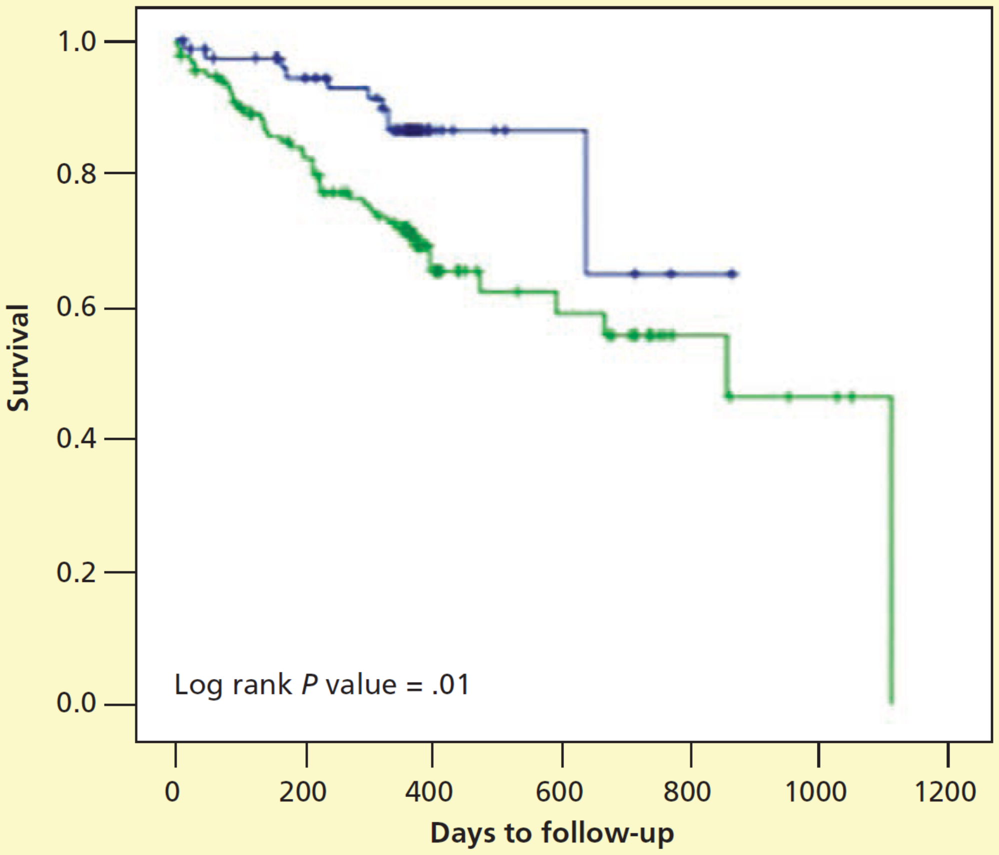



**Figure 2** Survival curves between good and poor sleepers. Blue line=good sleepers (scores ≤5 on the Pittsburgh Sleep Quality Index) and green line=poor sleepers (scores > 5 on the Pittsburgh Sleep Quality Index).

# Sleep Duration and All-Cause Mortality: A Systematic Review and Meta-Analysis of Prospective Studies

Francesco P. Cappuccio, MD, FRCP[1]; Lanfranco D'Elia, MD[2]; Pasquale Strazzullo, MD[2]; Michelle A. Miller, PhD[1]

[1]*University of Warwick, Warwick Medical School, Clinical Sciences Research Institute, Coventry, UK;* [2]*Department of Clinical and Experimental Medicine, "Federico II" University of Naples Medical School, Naples, Italy*

*SLEEP* 2010;33(5):585-592.

| First author | Year | Sample size | Deaths | Short Sleep v Reference | Relative Risk (95% CI) |
|---|---|---|---|---|---|
| Tsubono | 1993 | 4,318 | 207 | ≤6 v 7-8h | 1.26 (0.80 to 1.98) |
| Ruigomez (men) | 1995 | 395 | 224 | <7 v 7-9h | 1.06 (0.61 to 1.84) |
| Ruigomez (women) | 1995 | 594 | | | 0.66 (0.37 to 1.16) |
| Gale | 1998 | 1,299 | 1,158 | ≤7 v 9h | 1.00 (0.54 to 1.84) |
| Kojima (men) | 2000 | 2,438 | 147 | <7 v 7-8.9h | 1.93 (1.12 to 3.35) |
| Kojima (women) | 2000 | 2,884 | 109 | | 0.90 (0.50 to 1.61) |
| Heslop (men) | 2002 | 6,022 | 2,303 | <7 v 7-8h | 1.00 (0.89 to 1.12) |
| Heslop (women) | 2002 | 1,006 | 262 | | 0.98 (0.70 to 1.37) |
| Kripke (men) | 2002 | 480,841 | 45,200 | 5 v 7h | 1.11 (1.04 to 1.17) |
| Kripke (women) | 2002 | 636,095 | 32,440 | | 1.07 (1.01 to 1.14) |
| Mallon (men) | 2002 | 906 | 165 | <6 v 7h | 1.11 (0.32 to 3.80) |
| Mallon (women) | 2002 | 964 | 101 | | 1.00 (0.58 to 1.73) |
| Amagai (men) | 2004 | 4,419 | 289 | <6 v 7-7.9h | 2.41 (1.34 to 4.34) |
| Amagai (women) | 2004 | 6,906 | 206 | | 0.70 (0.21 to 2.35) |
| Patel | 2004 | 82,969 | 5,409 | ≤5 v 7h | 1.08 (0.96 to 1.22) |
| Ferrie | 2007 | 9,871 | 566 | ≤5 v 7h | 1.25 (0.93 to 1.67) |
| Hublin (men) | 2007 | 9,529 | 1,850 | <7 v 7-8h | 1.26 (1.12 to 1.42) |
| Hublin (women) | 2007 | 10,265 | 1,850 | | 1.21 (1.05 to 1.39) |
| Lan (men) | 2007 | 1,748 | 816 | <7 v 7-7.9h | 0.98 (0.76 to 1.26) |
| Lan (women) | 2007 | 1,331 | 522 | | 1.14 (0.77 to 1.69) |
| Gangwisch (32-59) | 2008 | 5,806 | 273 | ≤5 v 7h | 0.67 (0.43 to 1.05) |
| Gangwisch (60-86) | 2008 | 3,983 | 1,604 | | 1.27 (1.07 to 1.52) |
| Ikehara (men) | 2009 | 41,489 | 8,548 | ≤4 v 7h | 1.28 (1.01 to 1.62) |
| Ikehara (women) | 2009 | 57,145 | 5,992 | | 1.28 (1.04 to 1.59) |
| Stone | 2009 | 8,101 | 1,922 | <6 v 6-8h | 1.02 (0.87 to 1.19) |
| **Combined effect: P < 0.01** | | **1,381,324** | **112,163** | | **1.12 (1.06 to 1.18)** |

Heterogeneity: $I^2 = 39\%$; Q = 39.4, P = 0.02
Publication bias: Egger's test: P = 0.74

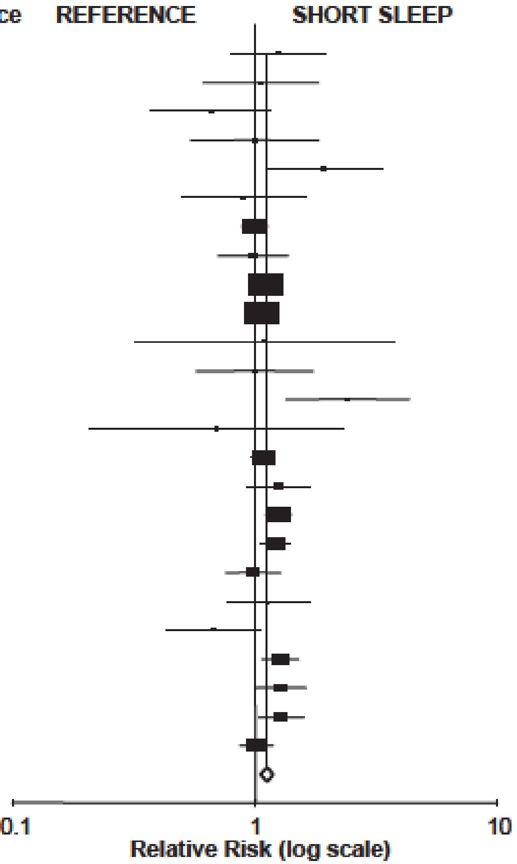



**Figure 2**—Forest plot of the risk of death associated with short duration of sleep compared to the reference group in 25 population cohorts from 15 published prospective studies including 1,381,324 participants and 112,163 events. Results are expressed as relative risk (RR) and 95% confidence intervals (95% CI). Pooled analysis P < 0.01; heterogeneity test: $I^2 = 39\%$, P = 0.02

REVIEW ARTICLES

JCSM
Journal of Clinical Sleep Medicine

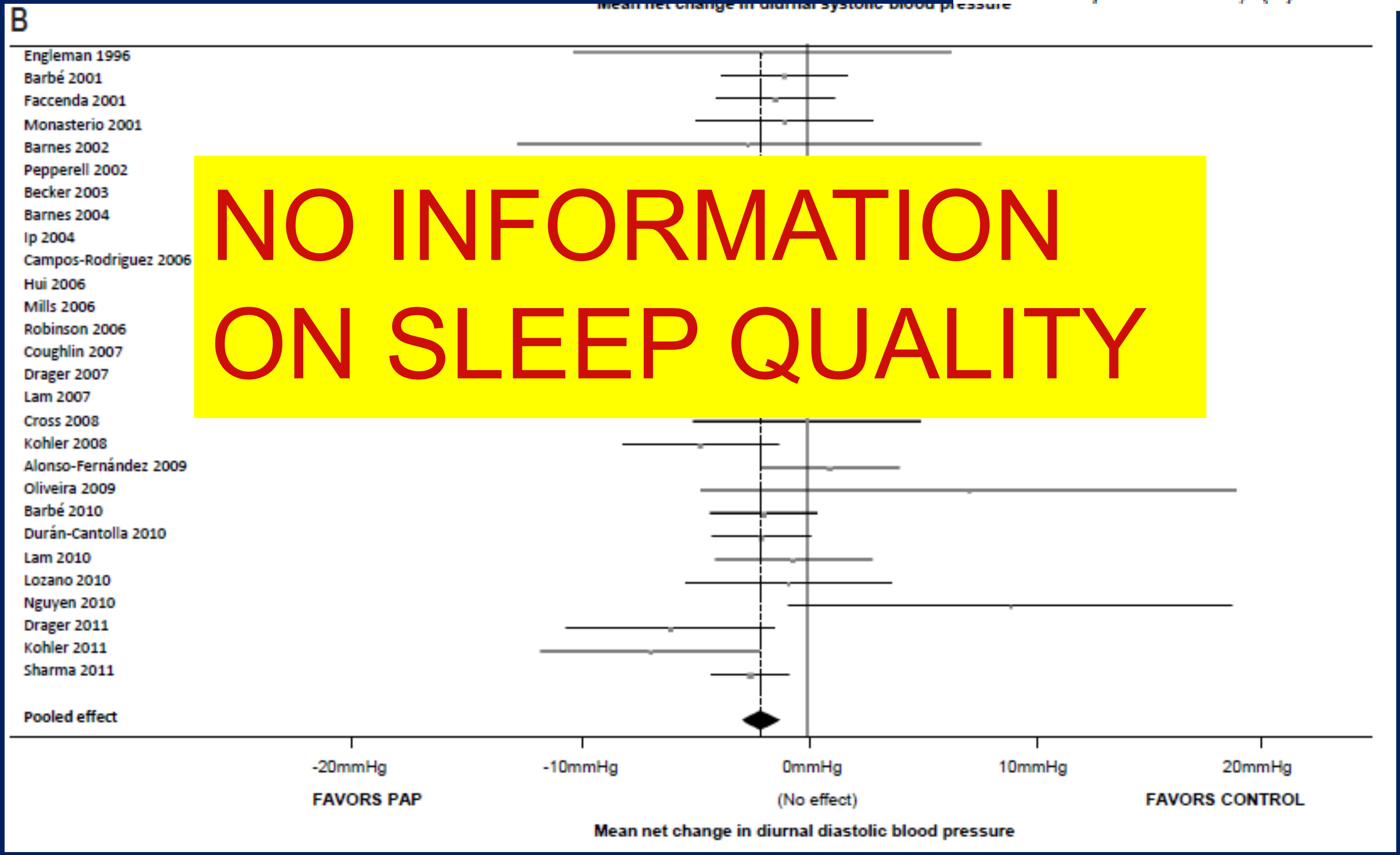
http://dx.doi.org/10.5664/jcsm.2170

# The Effect of Continuous Positive Airway Pressure Treatment on Blood Pressure: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

Sydney B. Montesi, M.D.[1,2]; Bradley A. Edwards, Ph.D.[1]; Atul Malhotra, M.D., F.A.A.S.M.[1]; Jessie P. Bakker, Ph.D.[1]

[1]Sleep Disorders Research Program, Brigham & Women's Hospital & Harvard Medical School, Boston MA; [2]Pulmonary and Critical Care Unit, Massachusetts General Hospital, Boston, MA

J Clin Sleep Med 2012;8(5):587-596.



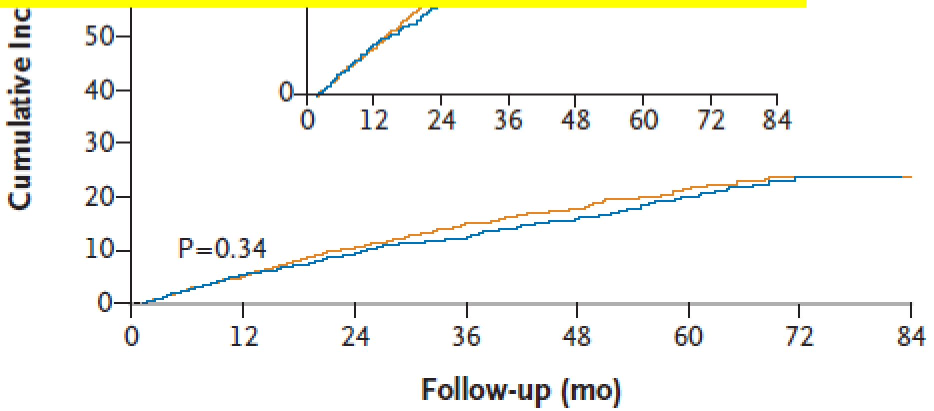
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 | SEPTEMBER 8, 2016 | VOL. 375 NO. 10

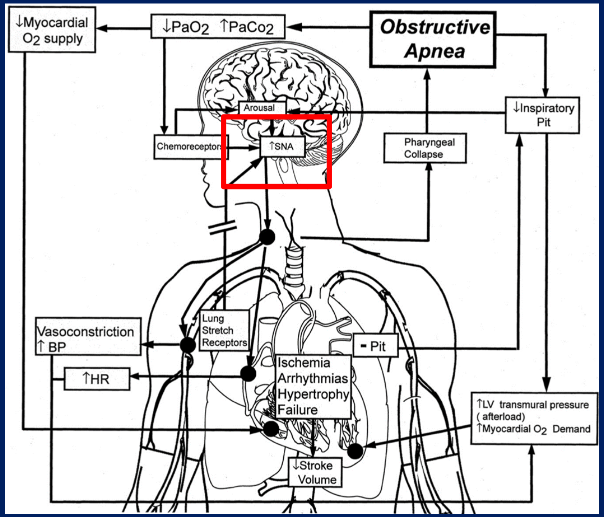
# CPAP for Prevention of Cardiovascular Events in Obstructive Sleep Apnea

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

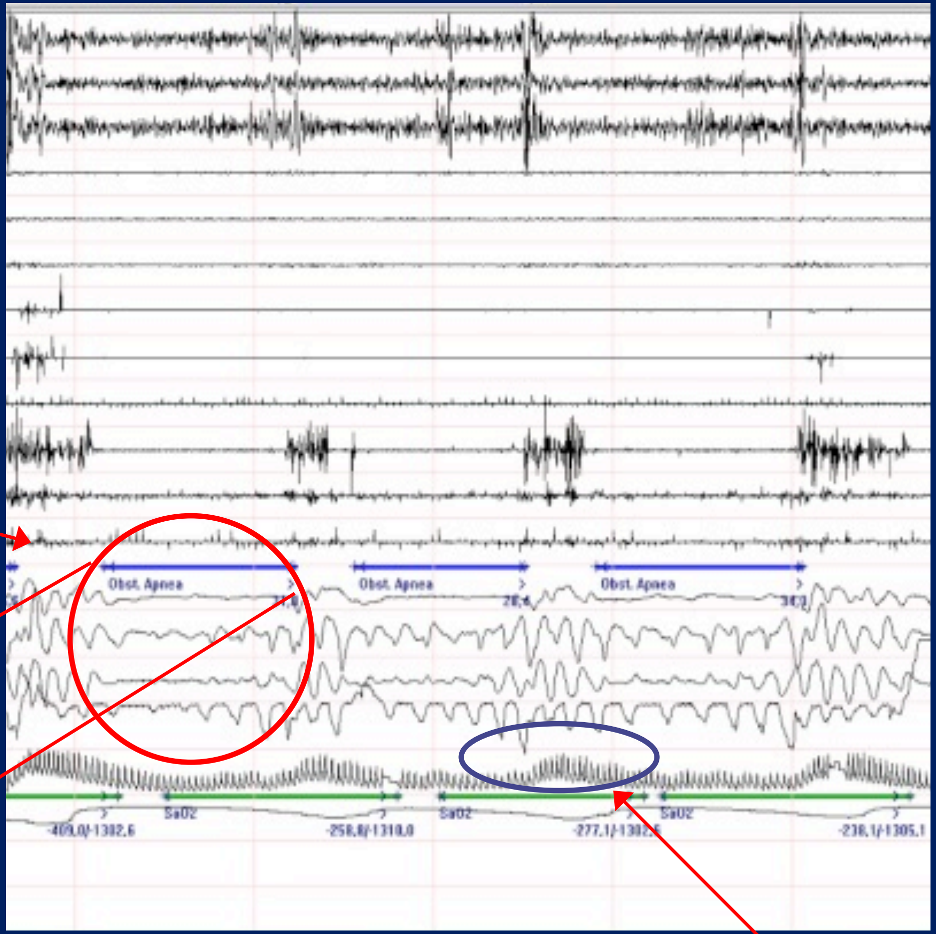
# NO INFORMATION ON SLEEP QUALITY

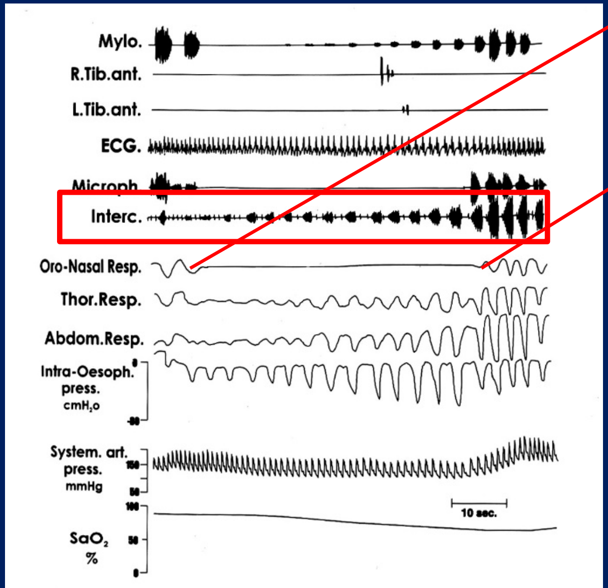



| No. at Risk | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| CPAP | 1346 | 1222 | 1118 | 754 | 482 | 278 | 146 | 146 |
| Usual care | 1341 | 1211 | 1108 | 727 | 499 | 290 | 103 | 103 |



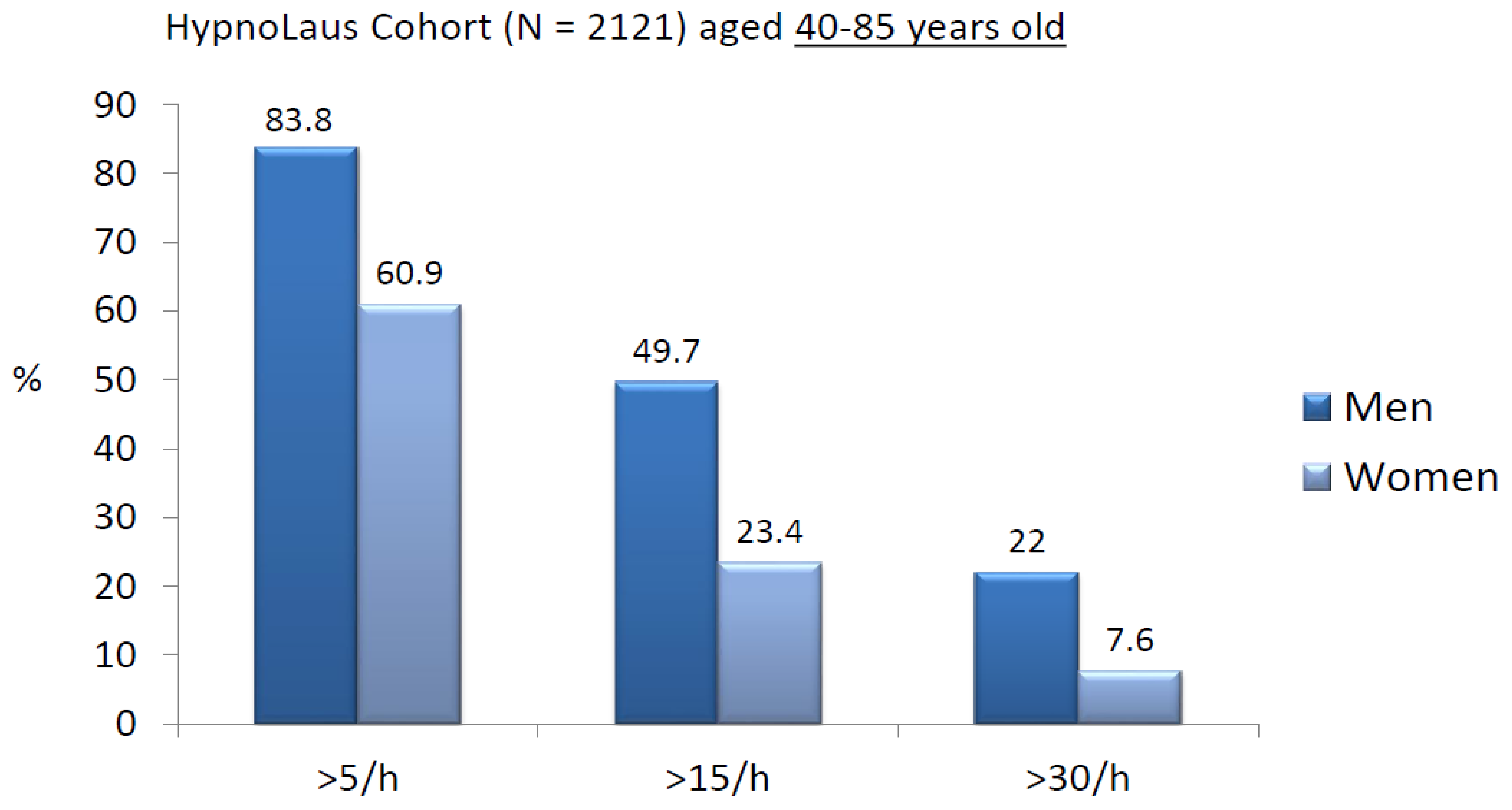

Obstructive apnea




Blood pressure and heart rate changes

# Prevalence of sleep disorderd breathing in the general population




*Heinzer et al Lancet resp med 2015*

Globally,
an estimated 936 million adults aged 30 to 69 years (men and women) have mild to severe and 425 million adults aged 30 to 69 years have moderate to severe OSA.

Benjafield AV, Ayas NT, Eastwood PR, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature based analysis. Lancet Respir Med. 2019;7(8):687-698.

26% of the US population have an apnea hypopnea index (AHI) > 5/h, using a 4% definition for hypopneas

The estimated prevalence of OSA syndrome (OSA coupled with subjective excessive daytime sleepiness [EDS], defined by Epworth Sleepiness Scale [ESS] score>10), is 15%

Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol. 2013;177(9):1006-1014.

# Association of Nocturnal Arrhythmias with Sleep-disordered Breathing

## The Sleep Heart Health Study

AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE VOL 173 2006

Reena Mehra, Emelia J. Benjamin, Eyal Shahar, Daniel J. Gottlieb, Rawan Nawabit, H. Lester Kirchner, Jayakumar Sahadevan, and Susan Redline

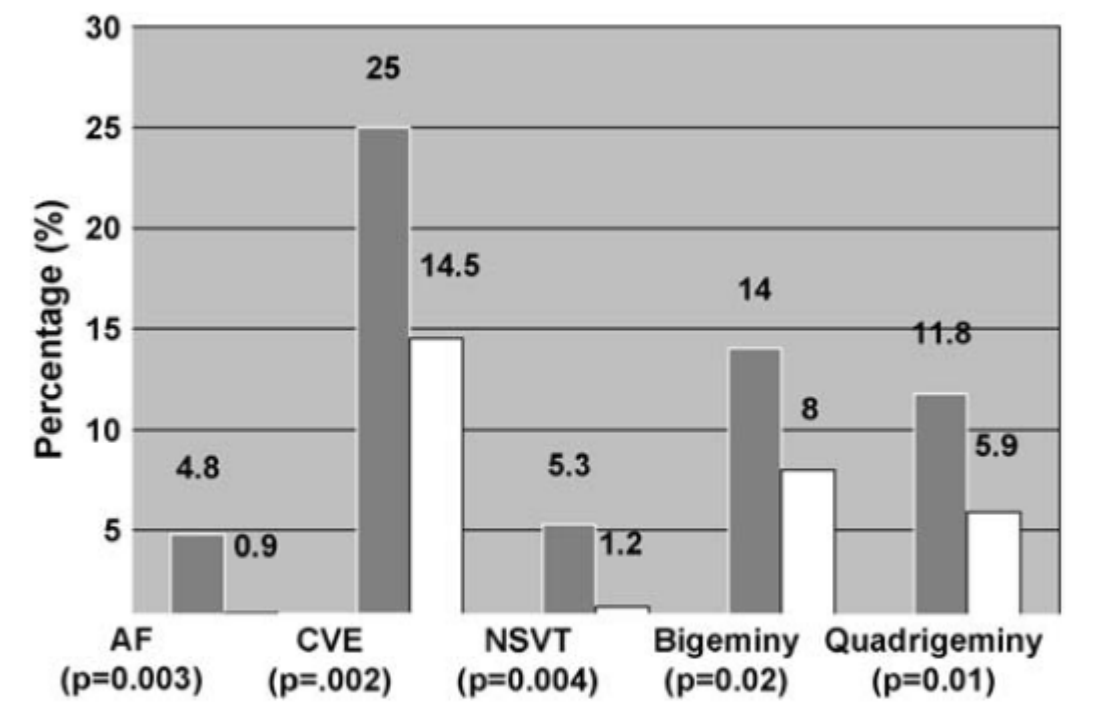



*Figure 1.* Arrhythmia prevalence (%) according to sleep-disordered breathing (SDB) status. *Shaded bars*, SDB; *open bars*, non-SDB. AF, atrial fibrillation; CVE, complex ventricular ectopy; NSVT, nonsustained ventricular tachycardia. n = 228 with SDB and n = 338 without SDB.

Pathophysiologic mechanisms:
-Intermittent hypoxiemia
-Intrathoracic pressure changes with increase wall stress
-Autonomic instability
-Diastolic dysfunction

Stroke

*Stroke*. 2021;52:00–00. DOI: 10.1161/STROKEAHA.120.030285

BRIEF REPORT

# Impact of Sleep Apnea on Cardioembolic Risk in Patients With Atrial Fibrillation

## Data From the ESADA Cohort

Martino F. Pengo, MD, PhD; Andrea Faini, Eng, PhD; Ludger Grote, MD, PhD; Ondrej Ludka, PhD; Pavol Joppa, MD, PhD; Athanasia Pataka, MD, PhD; Zoran Dogas, MD, PhD; Stefan Mihaicuta, MD, PhD; Holger Hein, MD; Ulla Anttalainen, MD, PhD; Silke Ryan, MD, PhD; Carolina Lombardi, MD, PhD; Gianfranco Parati, MD; on behalf of the ESADA Working Group

**Table 2. Main Characteristics of Patients in the 3 Different Cardioembolic Risk Categories**

| | $CHA_2DS_2$-VASc score | | | |
|---|---|---|---|---|
| | 0 | 1 | ≥2 | *P* value |
| Age, y | 51.3 (10.2) | 59.9 (7.4) | 67.9 (7.4) | 0.23 |
| BMI, kg/cm² | 29.2 (4.9) | 32.4 (6.6) | 32.6 (6.2) | <0.05* |
| SBP, mm Hg | 125.0 (11.4) | 131.6 (19.8) | 135.4 (18.8) | <0.001† |
| DBP, mm Hg | 79.9 (8.9) | 82.7 (12.4) | 80.3 (10.4) | 0.28 |
| HR, bpm | 67.2 (13.3) | 71.3 (13.5) | 69.5 (11.8) | 0.27 |
| Neck, cm | 42.4 (3.8) | 43.5 (4.2) | 41.9 (4.0) | <0.05‡ |
| AHI, events/h | 22.3 (19.9) | 29.7 (22.6) | 30.6 (22.7) | 0.08 |
| ODI4, events/h | 17.9 (17.1) | 29.6 (22.5) | 30.5 (24.1) | <0.05§ |
| Mean $Sao_2$, % | 93.2 (2.0) | 92.2 (3.1) | 92 (3.6) | 0.08 |
| Lowest $Sao_2$, % | 81.2 (9.6) | 77.8 (9.8) | 77.5 (10.3) | <0.05§ |
| Time $Spo_2$ below 90%, min | 17.2 (34.0) | 73.4 (90.1) | 58.3 (82.7) | 0.321 |

Data are expressed as mean (SD). AHI indicates apnea–hypopnea index; BMI, body mass index; and ODI4, 4% oxygen desaturation index.

*0 vs 1 and vs ≥2.

†0 vs ≥2.

‡1 vs ≥2.

§≥2 vs 0 and vs 1.

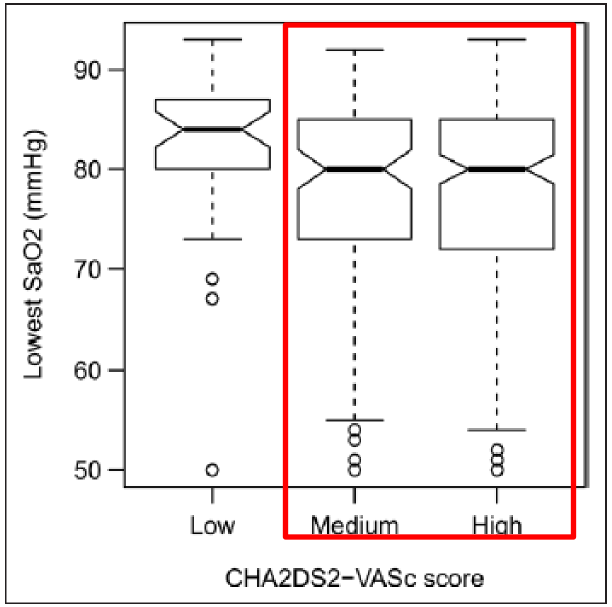



**Figure.** Bar chart showing the lowest $Spo_2$ in the 3 cardioembolic risk categories derived from $CHA_2DS_2$-VASc score.