



Institut Català de la Salut
Lleida
Hospital Universitari Arnau de Vilanova



Apnea del son i malaltia cardiovascular: de l'etiopatogènia a l'impacte clínic



Ferran Barbé

**Institut de Recerca Biomedica. IRBLleida
Hospital Univ Arnau de Vilanova. Lleida
CIBERES. Instituto de Salud Carlos III. Madrid.**

Barcelona, 29 de novembre de 2011

Definición SAHS

- Cuadro de somnolencia excesiva, trastornos cognitivo-conductuales, respiratorios, cardíacos, metabólicos o inflamatorios secundarios a episodios repetidos de obstrucción de la VAS durante el sueño.

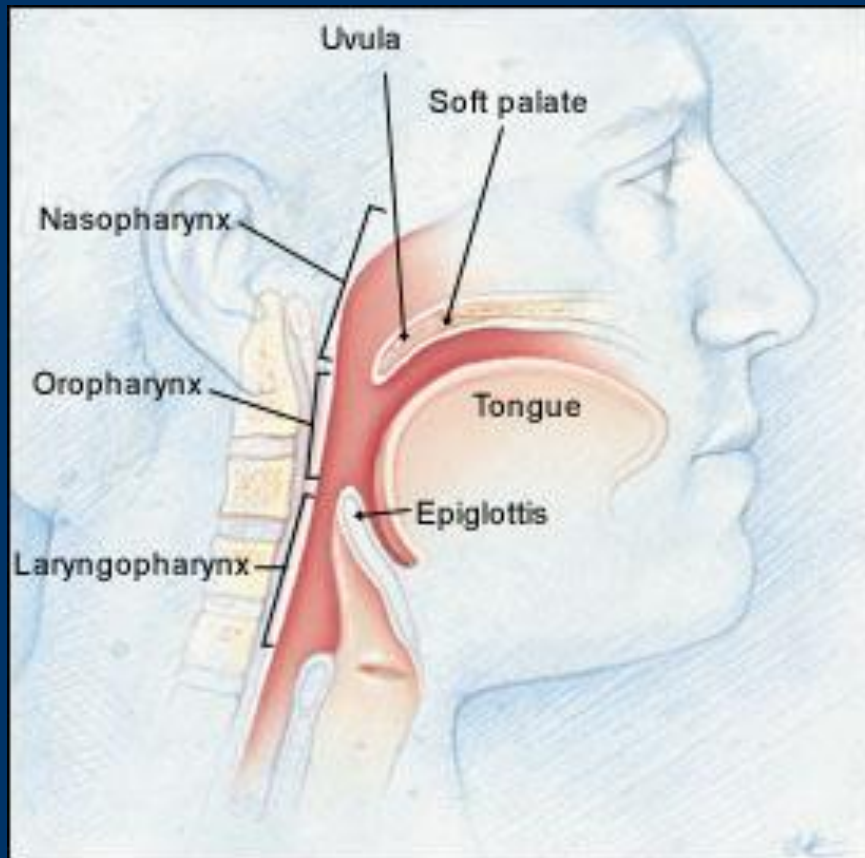


Illustration © 1999 Christy Krames

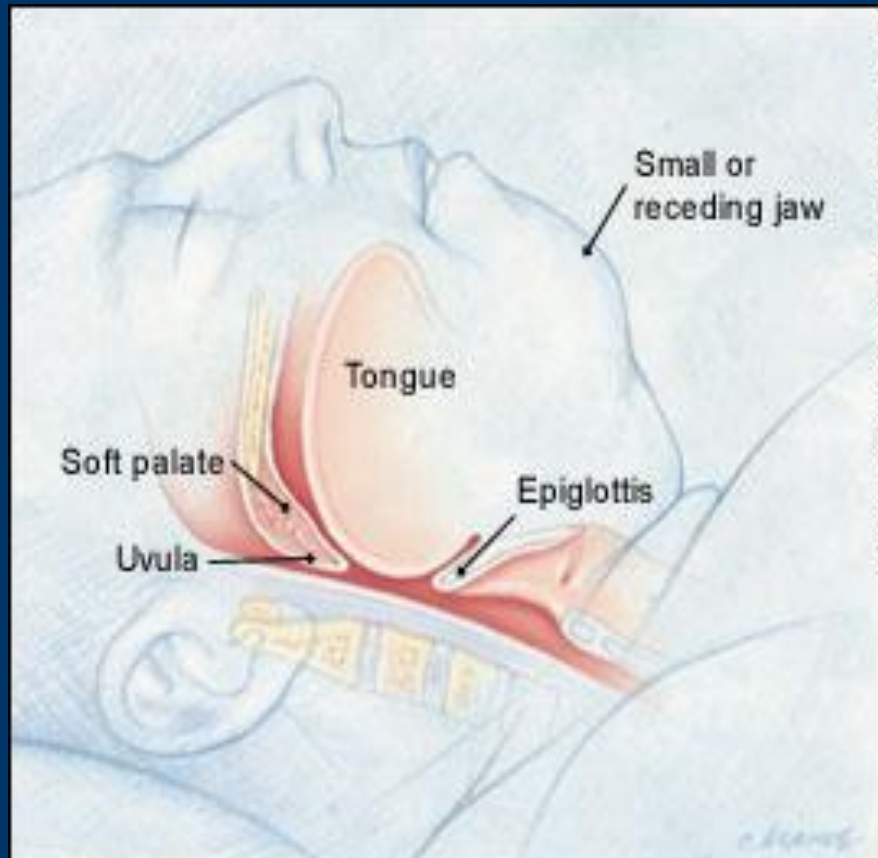
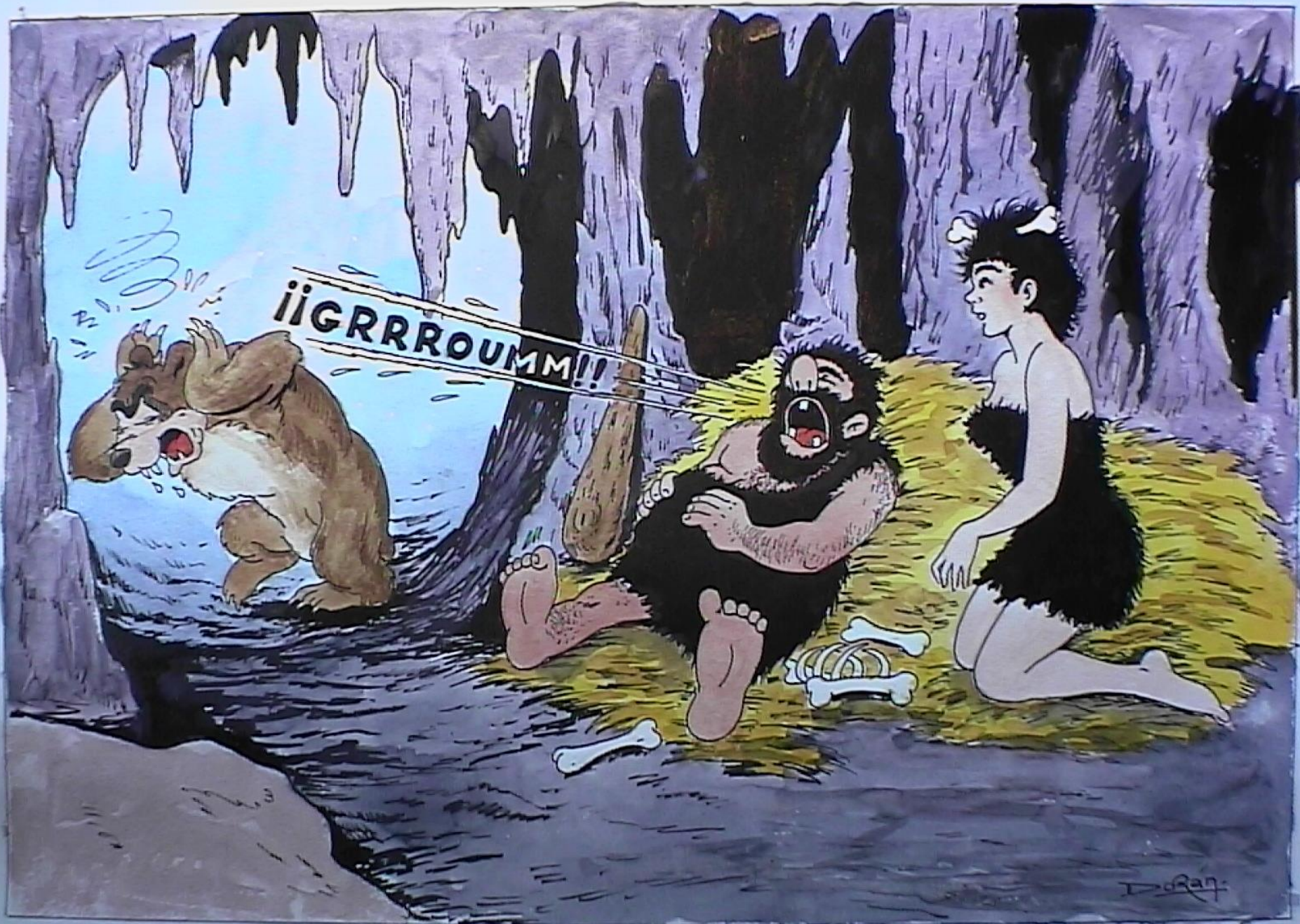


Illustration © 1999 Christy Krames

Prevalence

Workers 30-60 yr (Young et al. NEJM 1993)

	Men (n=1670)		Women (n=1843)	
AHI	%	(CI 95%)	%	(CI 95%)
≥ 5	24.0	(19-28)	9.0	(6-12)
≥ 10	15.0	(12-19)	5.0	(2-8)
≥ 15	9.1	(6-11)	4.0	(1-7)
SAHS	4.0	-	2.0	-



iiGRRROUMM!!

D. Gray

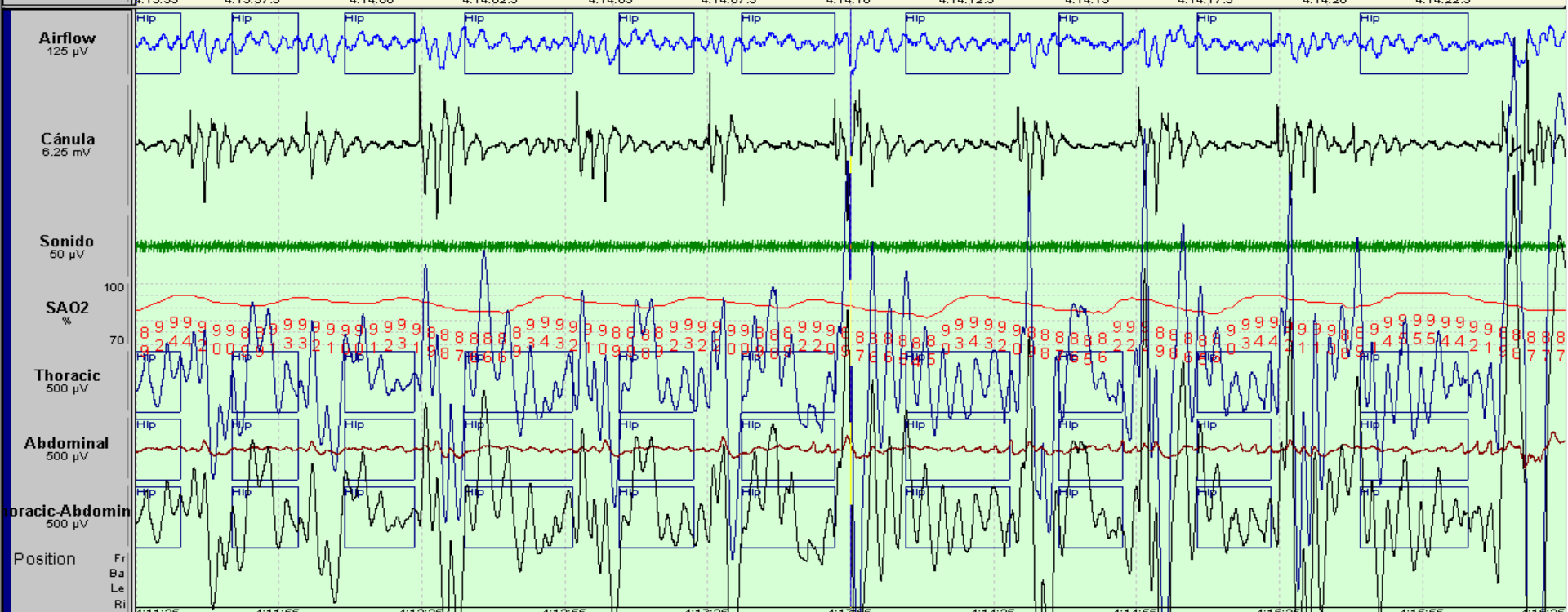
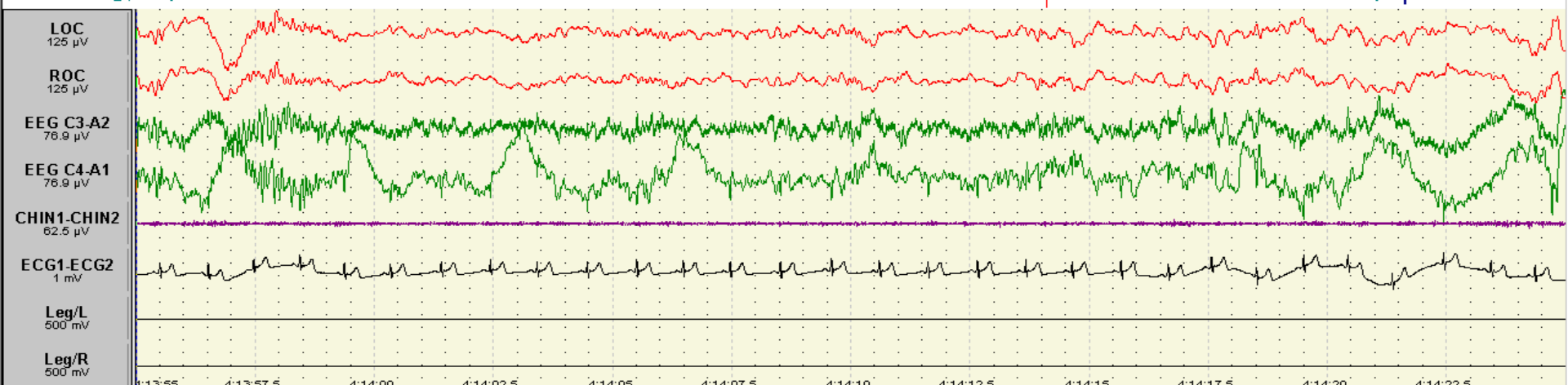


YONKIS.COM



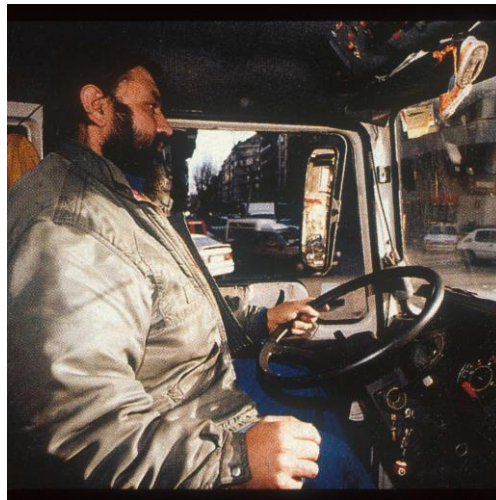
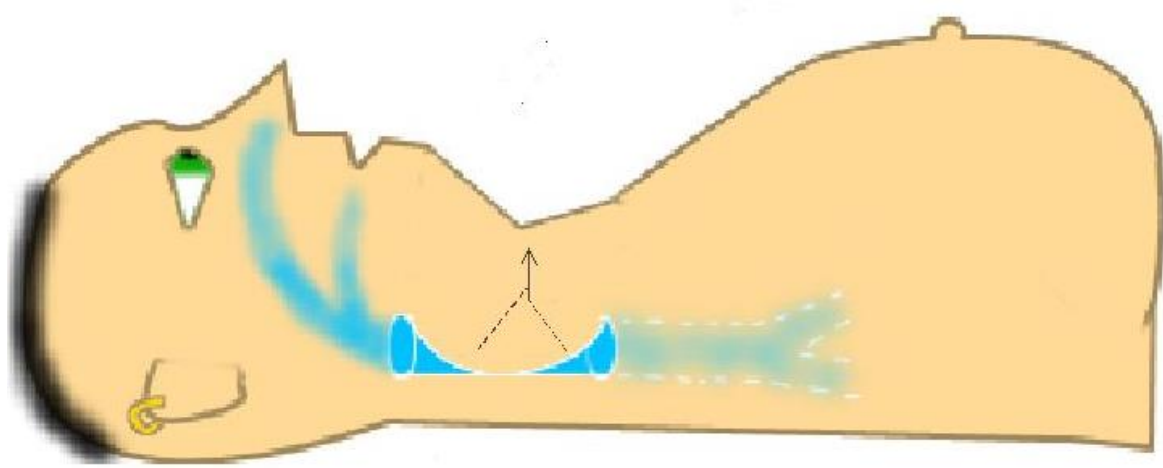
Adena por la conservacion de la fauna ibérica



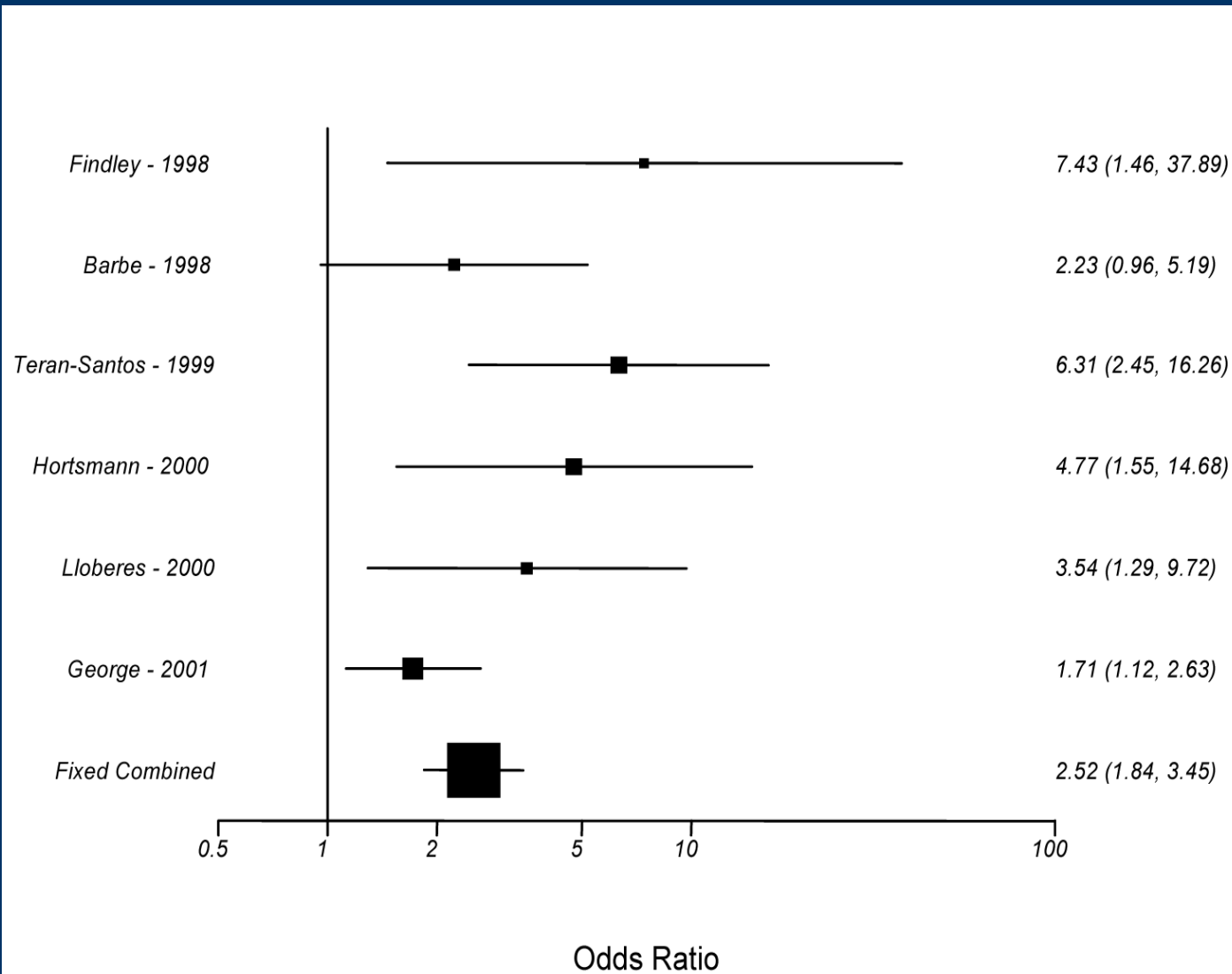




Principales consecuencias del sd. apneas del sueño



Road accidents and OSAS



The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: The JNC 7 Report

Identifiable Causes of Hypertension

Sleep apnea

Drug-induced or drug-related

Chronic kidney disease

Chronic steroid therapy

Coarctation of the aorta

.....



Chobanian AV. JAMA. 2003 May
21;289(19):2560-72





**ESTÁNDARES Y
RECOMENDACIONES
DE
UNIDADES
ASISTENCIALES**

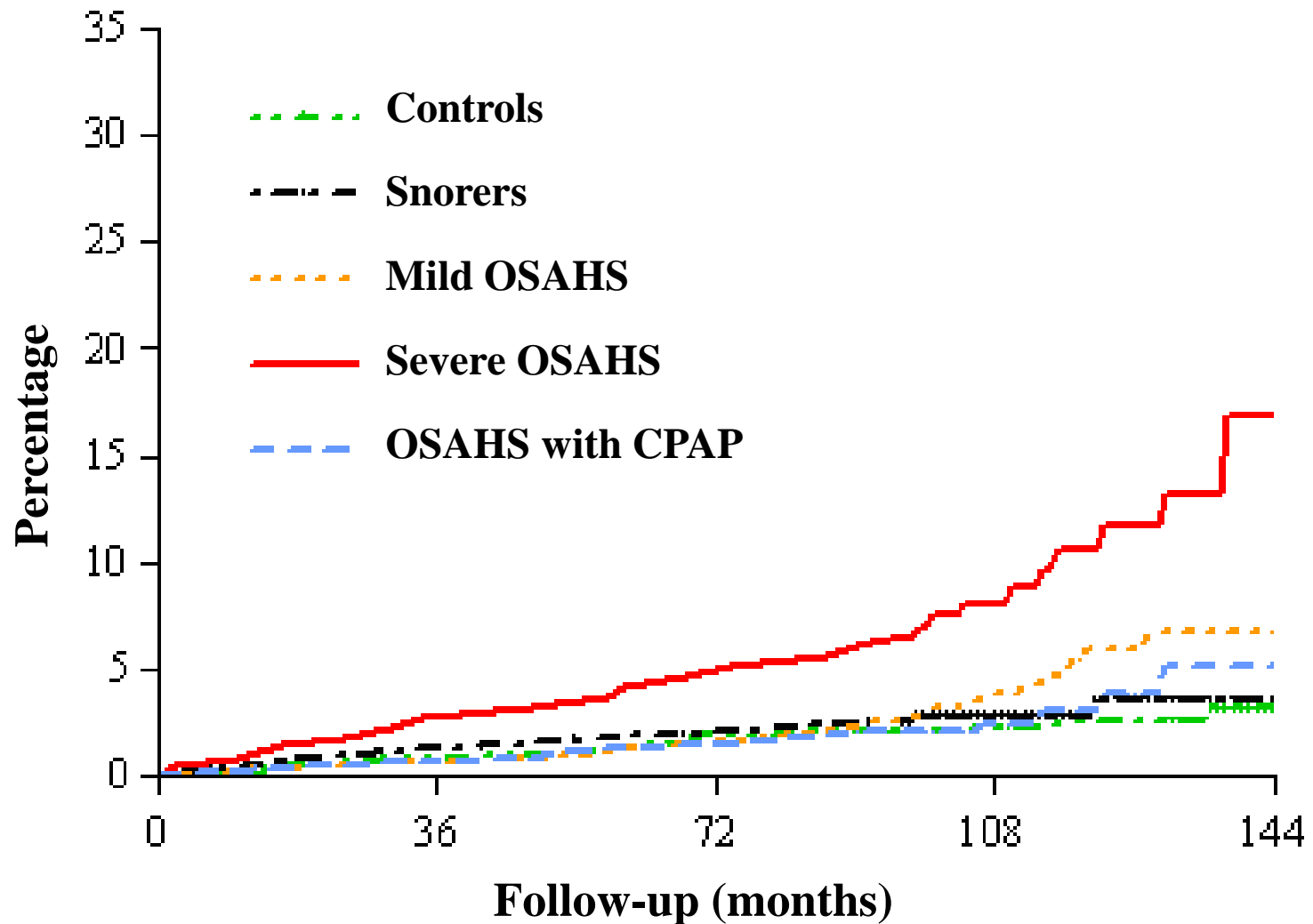
25 de mayo de 2010
UNIDAD DEL SUEÑO

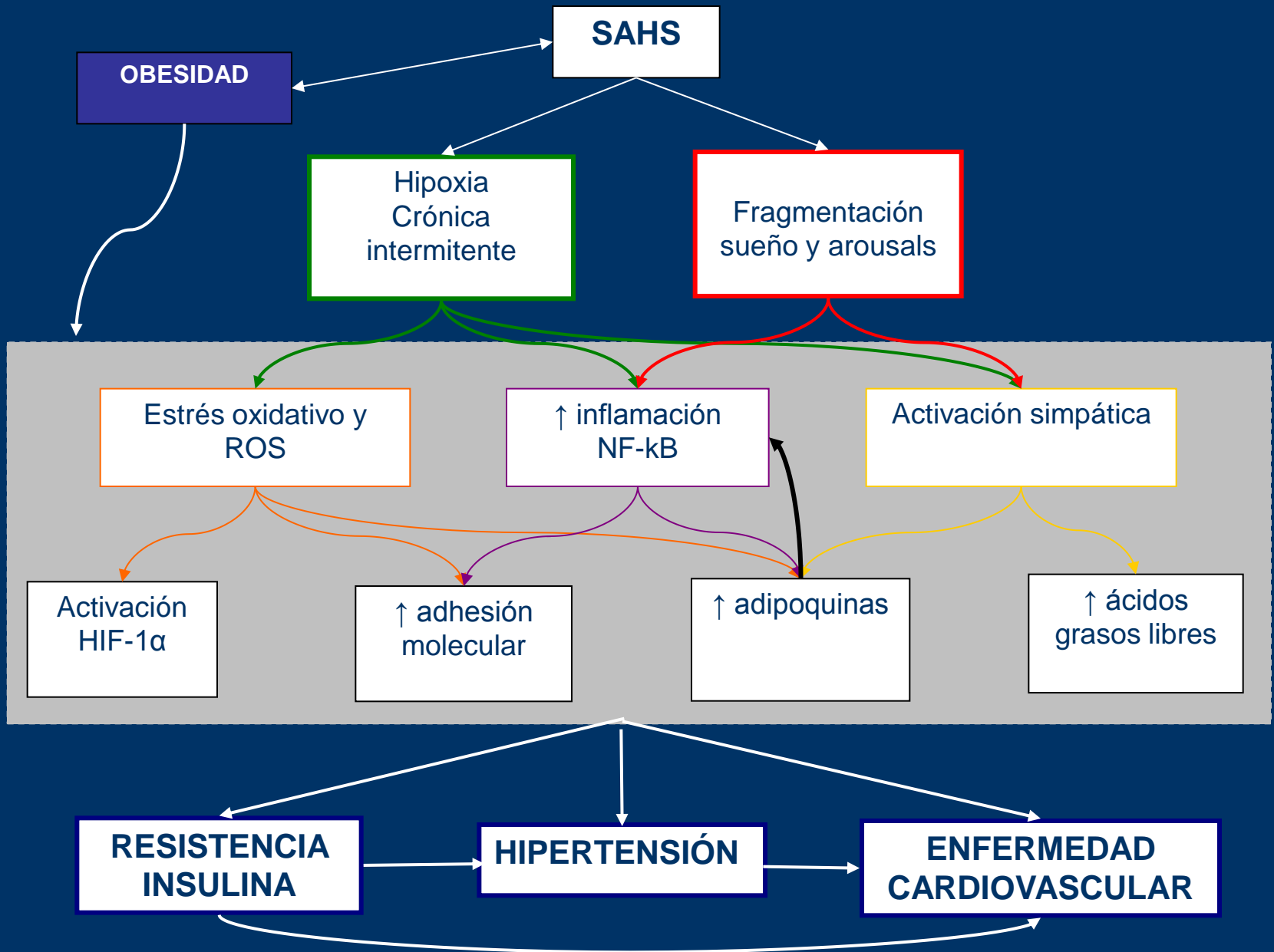


Comisión de Sanidad. Congreso de los diputados.

Cumulative incidence of fatal CV events

Marin JM *et al. Lancet* 2005





Proyectos en curso

(Investigación básica)

Sleep Breath

DOI 10.1007/s11325-011-0552-7

ORIGINAL ARTICLE

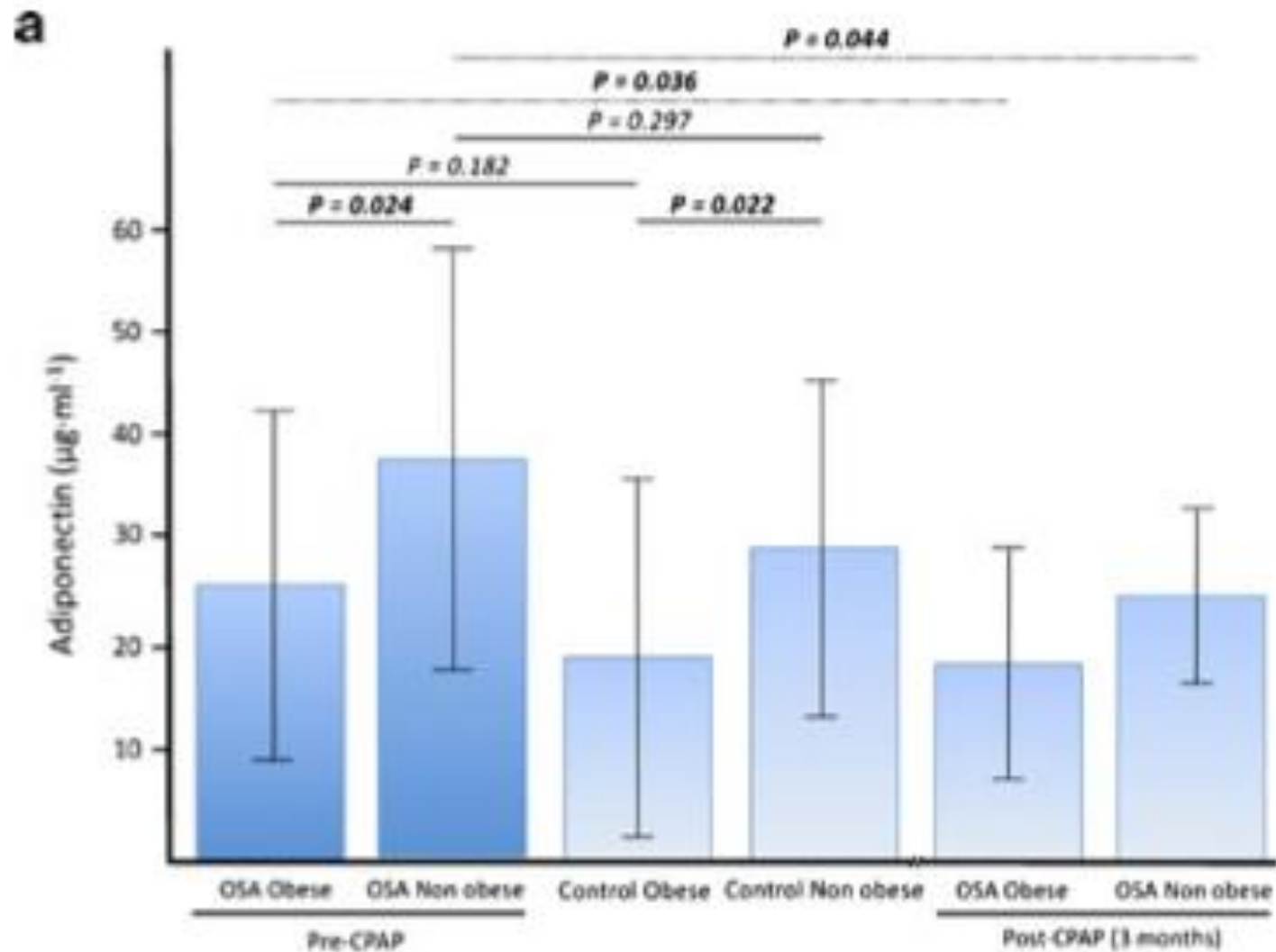
The influence of obesity and obstructive sleep apnea on metabolic hormones

**Manuel Sánchez-de-la-Torre • Olga Mediano • Antonia Barceló • Javier Piérola •
Monica de la Peña • Cristina Esquinas • Angelina Miro • Joaquin Durán-Cantolla •
Alvar G. Agustí • Francisco Capote • Jose Maria Marin • Josep Maria Montserrat •
Francisco García-Río • Ferran Barbé**

Pacients, controls, obesos, no obesos, abans i després de CPAP

Metabolic disturbances & OSA

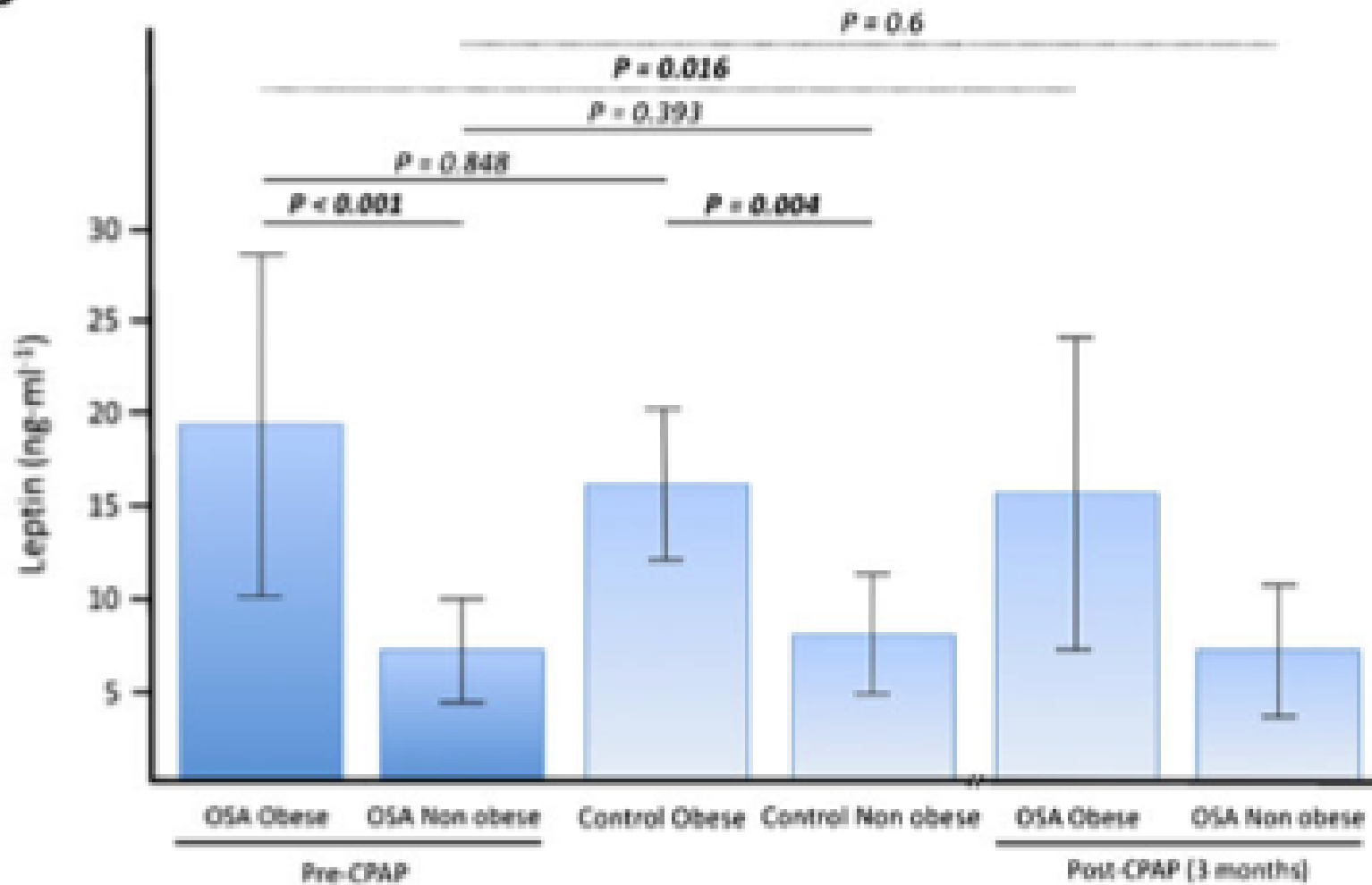
Adiponectin



Metabolic disturbances & OSA

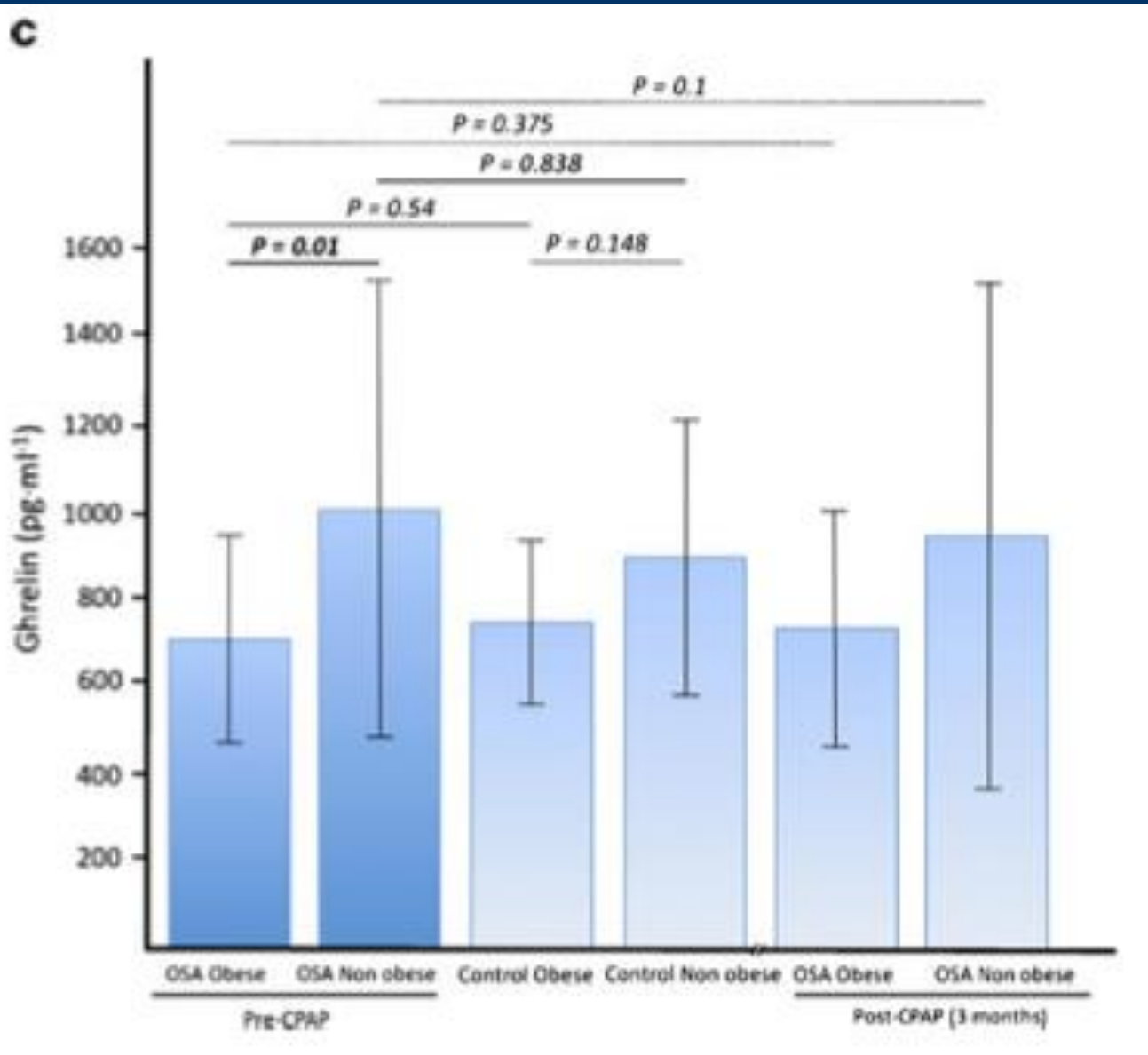
Leptin

b



Metabolic disturbances & OSA

Ghrelin



FFA, metabolic syndrome & OSA



EUROPEAN RESPIRATORY *journal*

OFFICIAL SCIENTIFIC JOURNAL OF THE ERS

Free fatty acids and the metabolic syndrome in patients with obstructive sleep apnoea

A. Barceló^{*#↓}, J. Piérola^{#¶}, M. de la Peña^{#+}, C. Esquinas[§], A. Fuster^{*},
M. Sanchez-de-la-Torre^{#§}, M. Carrera^{#+}, A. Alonso-Fernandez^{#+},
A. Ladaria⁺, M. Bosch⁺ and F. Barbé^{#§}

FFA, metabolic syndrome & OSA

Table 1. Subject characteristics

	Controls (n=119)	OSAS (n=119)	p value
Age (years)	45 ± 11	46 ± 12	0.635
Men (%)	87 (73%)	88 (74%)	0.883
BMI (Kg.m ⁻²)	28 ± 4	28 ± 4	0.727
Waist circumference	101±11	101±11	0.889
Hypertension (%)	22 (21%)	26 (22%)	0.470
Diabetes (%)	4 (4%)	9 (8%)	0.169
Current smoker (%)	36%	36%	0.951
Metabolic Syndrome (%)	21 %	38 %	0.006
AHI (hour ⁻¹)	3.2 (1.8-4.5)	39 (23.2-53.5)	< 0.001
Arousal index	22 ± 13	47 ± 18	< 0.001
Mean Sat O ₂ (%)	94±3	93 ± 2	< 0.001
Minimal Sat O ₂ (%)	86±9	83±8	0.061
Epworth scale	7 (5-10)	11 (6-14)	< 0.001

FFA, metabolic syndrome & OSA

Table 2. Metabolic and biochemical markers

	Controls (n=119)	OSAS (n=119)	p value
Glucose (mg/dL)	94 ± 4	103 ± 22	0.001
Triglycerides (mg/dL)	124 ± 51	147 ± 94	0.079
Cholesterol (mg/dL)	207 ± 41	212 ± 39	0.398
HDLc (mg/dL)	56 ± 15	55 ± 16	0.505
Creatinine (mg/dL)	0.88 ± 0.2	0.96 ± 0.3	0.692
Uric acid (mg/dL)	6.2 ± 4.7	6.1 ± 3.2	0.336
AST (U/L)	22 ± 7	21 ± 7	0.387
ALT (U/L)	27 ± 15	27 ± 13	0.809
GGT (U/L)	32 ± 27	37 ± 29	0.048
CRP (mg/L)	1.4 (0.5-3.2)	2.0 (0.9-3.6)	0.01
8-isoprostanes (ng/dL)	4.3 (1.2-9.1)	11.4 (6.1-22.5)	0.001
FFA (mg/dL)	10.5 ± 5	12.2 ± 5	0.009

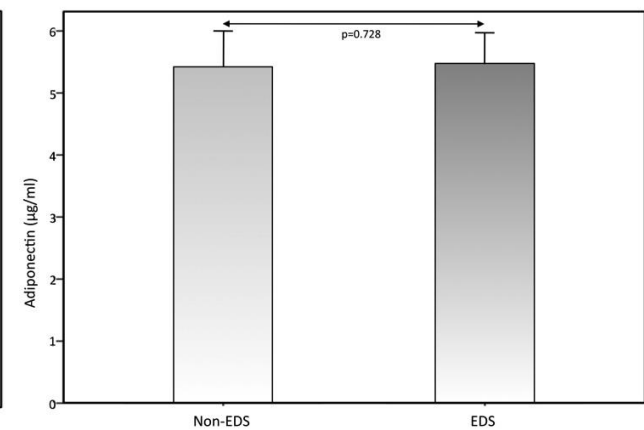
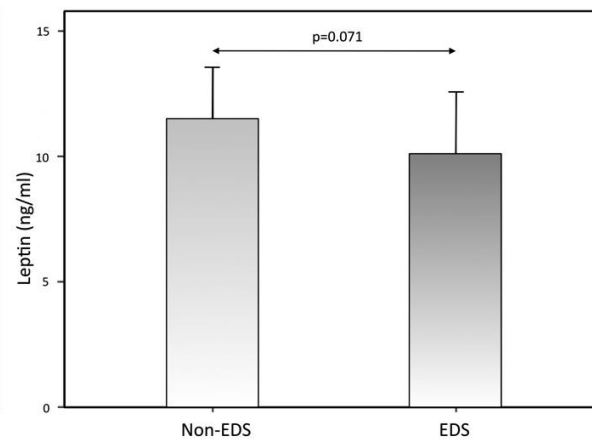
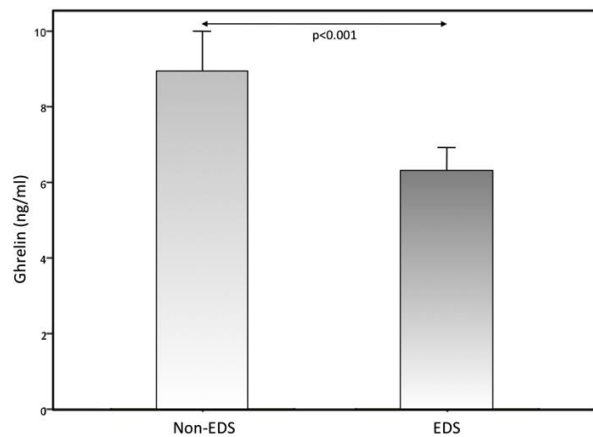
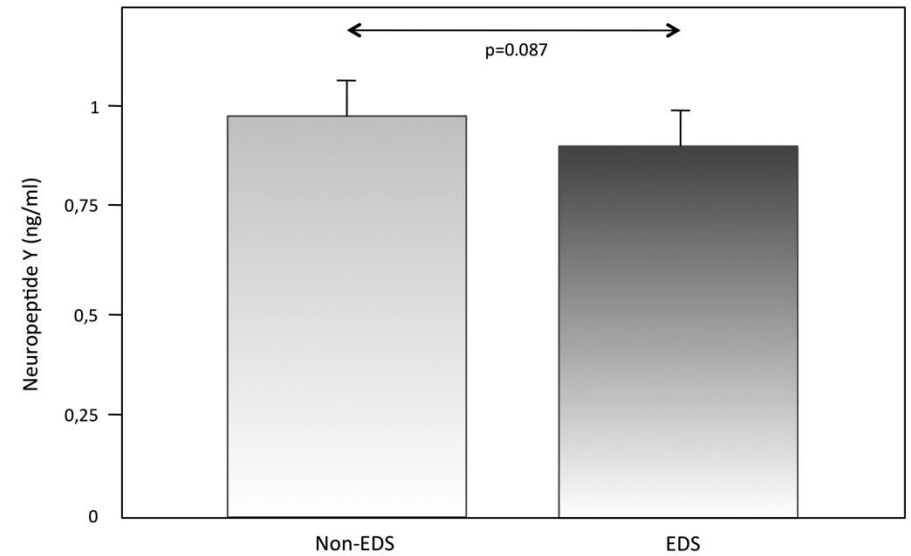
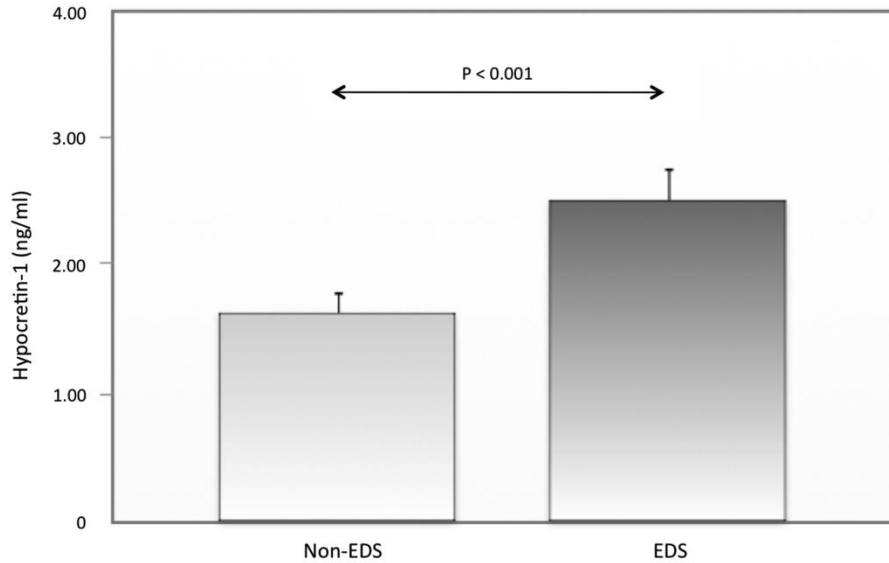
Sympathetic activity, metabolism, sleepiness & OSA

respiratoryMEDICINE

Plasma levels of neuropeptides and metabolic hormones, and sleepiness in obstructive sleep apnea

[M. Sánchez-de-la-Torre](#), [A. Barceló](#), [J. Piérola](#), [C. Esquinas](#), [M. de la Peña](#), [J. Durán-Cantolla](#), [F. Capote](#), [J.F. Masa](#), [J.M. Marin](#), [M. Vilá](#), [G. Cac](#), [M. Martinez](#), [L. de Lecea](#), [D. Gozal](#), [J.M. Montserrat](#), [F. Barbé](#)

Sympathetic activity, metabolism, sleepiness & OSA



Endothelial dysfunction markers and haemostatic factors & OSA



EUROPEAN RESPIRATORY *journal*

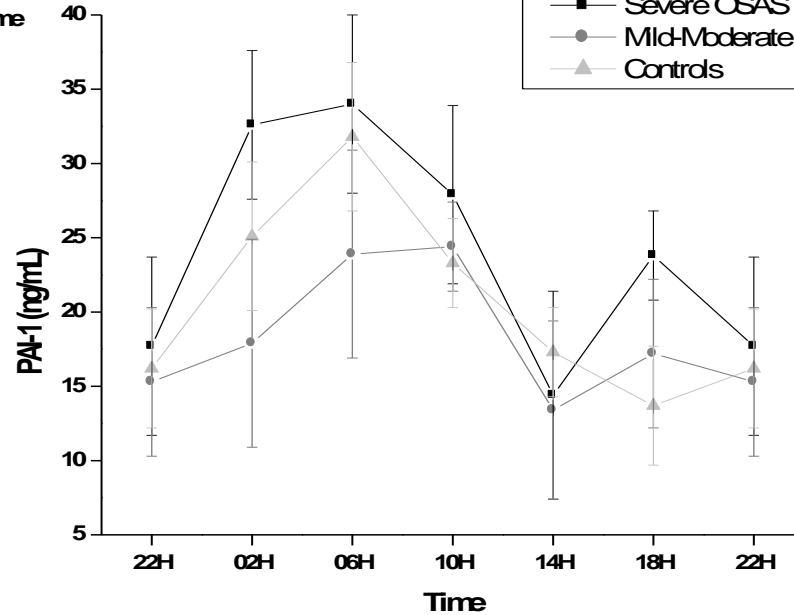
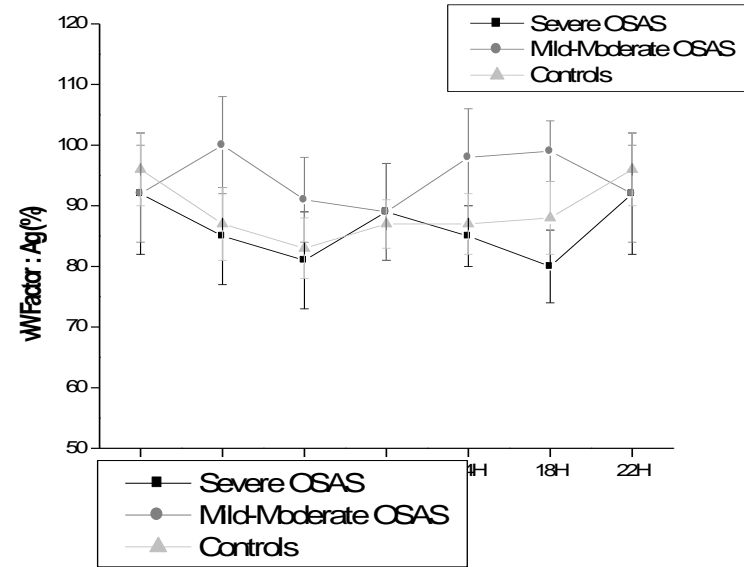
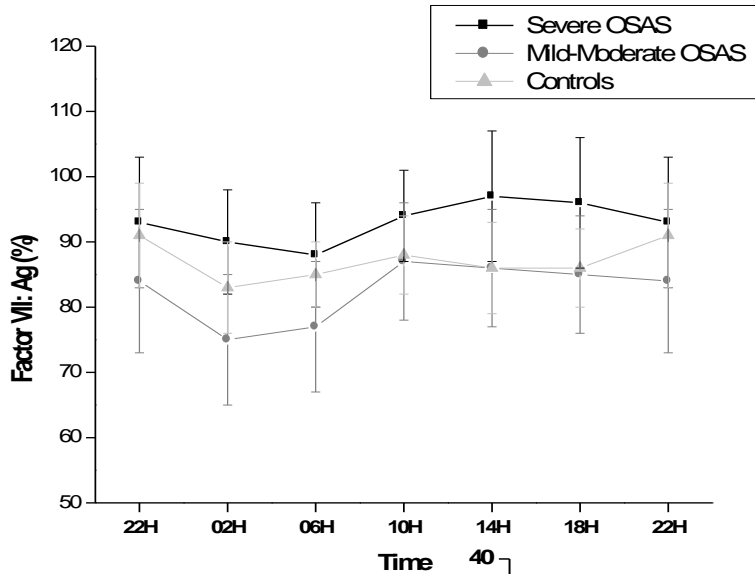
OFFICIAL SCIENTIFIC JOURNAL OF THE ERS

Day- night variations in endothelial dysfunction markers and haemostatic factors in sleep apnoea

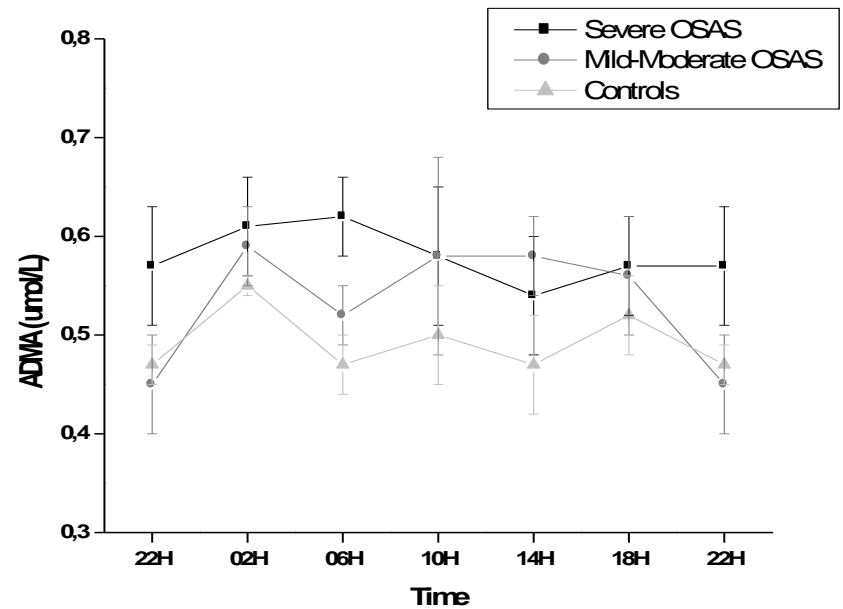
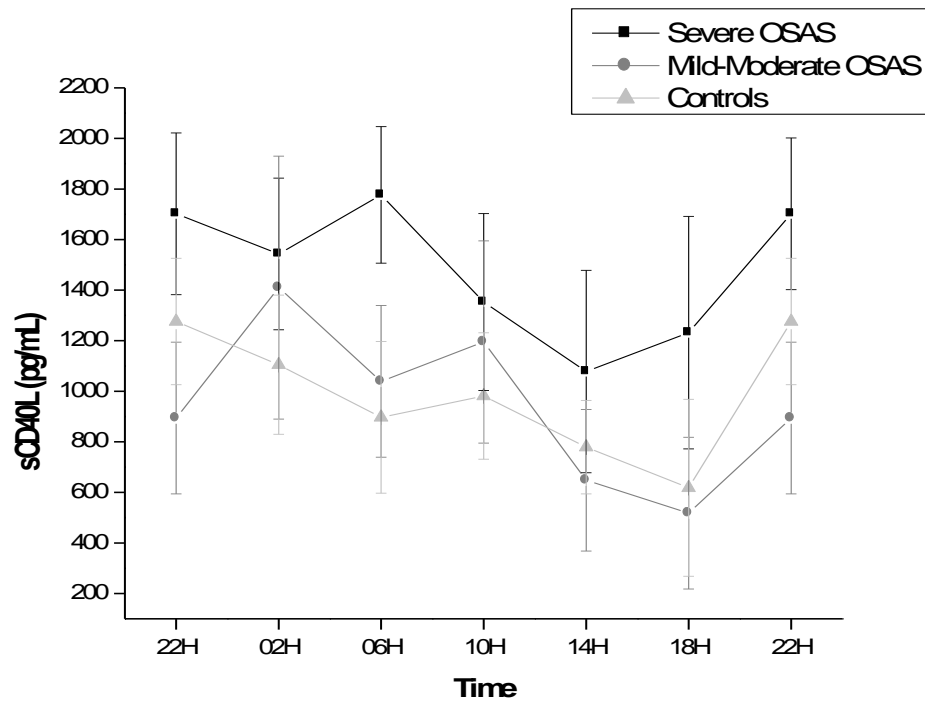


A. Barceló^{*+↓}, J. Piérola^{†+}, M. de la Peña^{#+}, C. Esquinas^f,
M. Sanchez-de la Torre^{+f}, O. Ayllón^{*}, A. Alonso^{#+}, A.G.N. Agusti^{+§**}
and F. Barbè^{+f}

Endothelial dysfunction markers and haemostatic factors & OSA



Endothelial dysfunction markers and haemostatic factors & OSA



CPAP in non-sleepy OSA

- **Objective:** To evaluate the long term effect of CPAP on blood pressure in hypertensive patients with sleep apnea and no daytime sleepyness
- **Methods:** RCT 374 hypertensive patients with OSA



Methods

DESIGN: Randomized prospective controlled study

POPULATION: Patients with AHI ≥ 20 and Epworth scale < 10 and hypertension

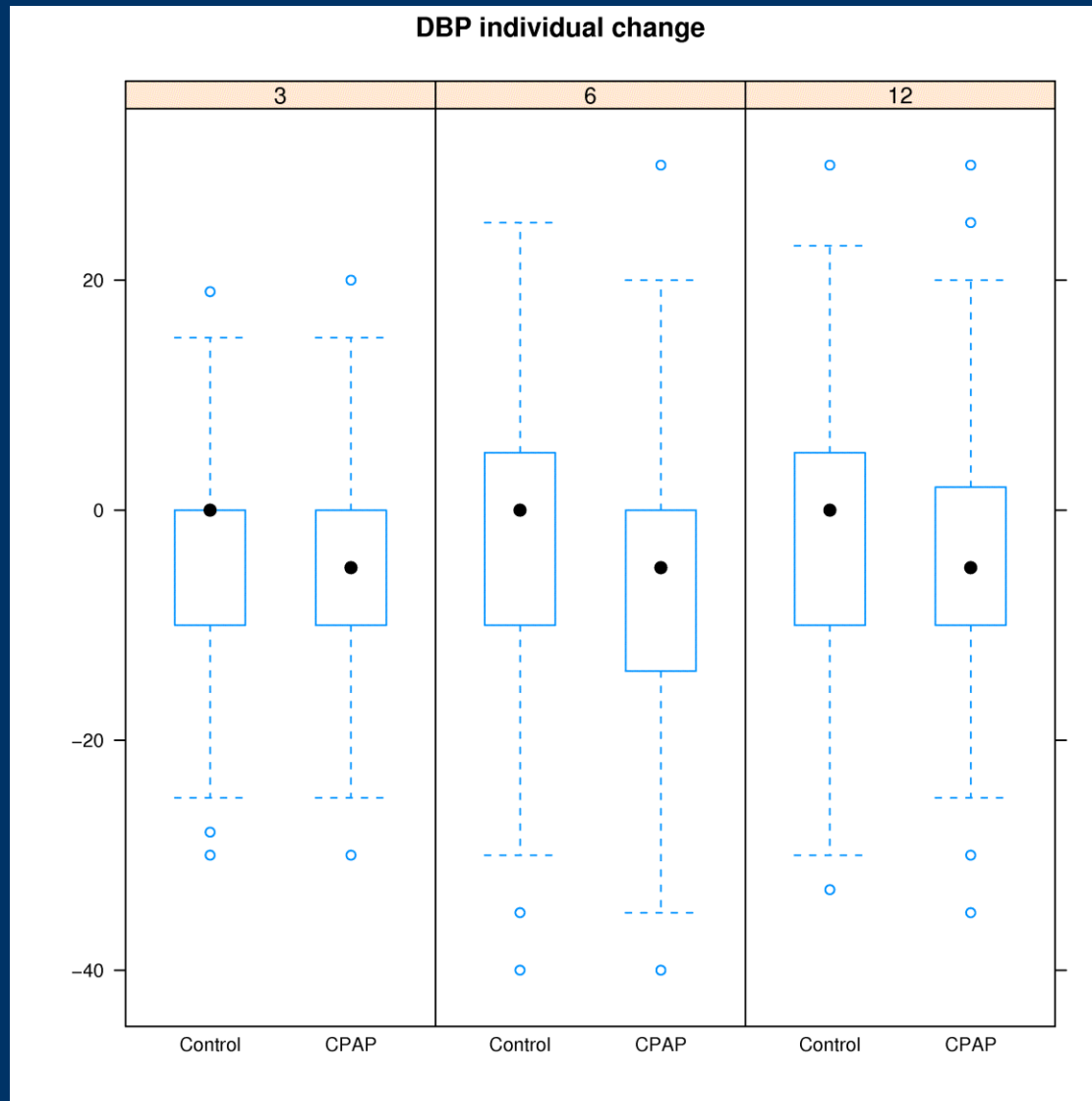
MEASUREMENTS:

- Sleep study (polysomnography or partial study)
- CPAP titration by auto-CPAP
- Office blood pressure measurement

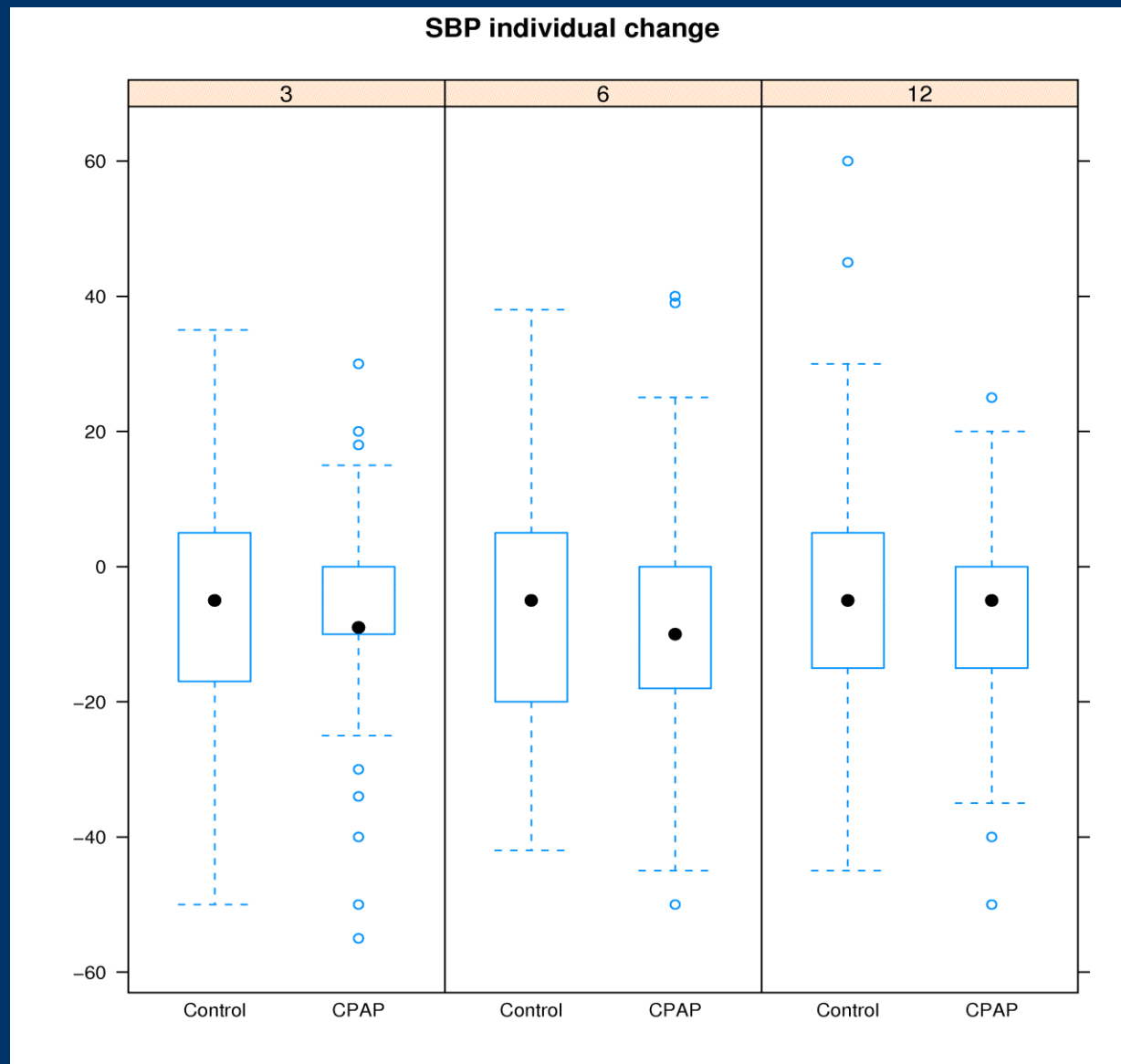
EVALUATIONS: Basal, at 3, 6 and 12 month

STATISTICS: Linear regression models

Differences diastolic blood pressure



Differences systolic blood pressure



Long-term Effect of Continuous Positive Airway Pressure in Hypertensive Patients with Sleep Apnea

Ferran Barbé^{1,2}, Joaquín Durán-Cantolla^{2,3}, Francisco Capote⁴, Monica de la Peña^{2,5}, Eusebi Chiner⁶, Juan F. Masa^{2,7}, Mónica Gonzalez⁸, Jose M. Marín^{2,9}, Francisco Garcia-Rio¹⁰, Josefa Diaz de Atauri¹¹, Joaquín Terán^{2,12}, Mercedes Mayos^{2,13}, Carmen Monasterio^{2,14}, Felix del Campo¹⁵, Sivia Gomez¹, Manuel Sanchez de la Torre^{1,2}, Montse Martinez^{1,2}, and José M. Montserrat^{2,16}, on behalf of the Spanish Sleep and Breathing Group*

¹Coordinating Center, Institut de Recerca Biomèdica Lleida, Lleida; ²Centro de Investigación Biomédica en Red Enfermedades Respiratorias (CIBERES), Madrid; ³Sleep Unit, Hospital Txagorritxu, Vitoria; ⁴Respiratory Department, Hospital Virgen del Rocío, Sevilla; ⁵Respiratory Department, Hospital Universitario Son Dureta, Palma de Mallorca; ⁶Respiratory Department, Hospital Sant Joan, Alacant; ⁷Respiratory Department, Hospital San Pedro de Alcántara, Cáceres; ⁸Respiratory Department, Hospital Marques de Valdecilla, Santander; ⁹Respiratory Department, Hospital Miguel Servet, Zaragoza; ¹⁰Respiratory Department, Hospital La Paz, Madrid; ¹¹Respiratory Department, Hospital 12 de Octubre, Madrid; ¹²Respiratory Department, Hospital General Yagüe, Burgos; ¹³Respiratory Department, Hospital Sant Pau, Barcelona; ¹⁴Respiratory Department, Hospital de Bellvitge, Barcelona; ¹⁵Respiratory Department, Hospital Rio Hortega, Valladolid; ¹⁶Respiratory Department, Hospital Clinic, Barcelona, Spain

AT A GLANCE COMMENTARY

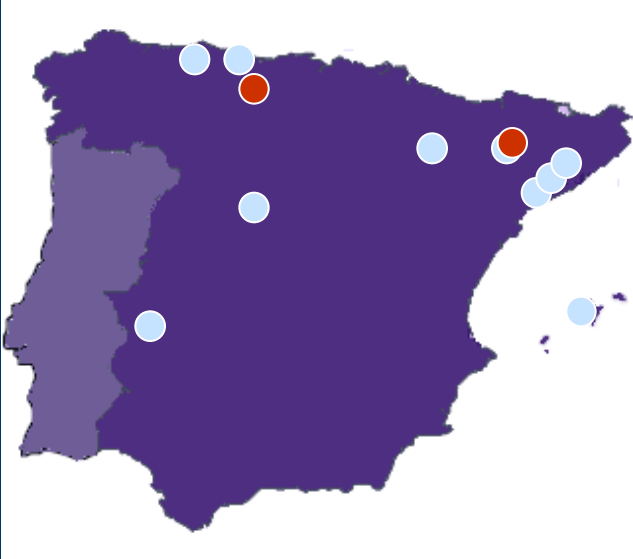
Scientific Knowledge on the Subject

Continuous positive airway pressure (CPAP) is the current treatment for patients with symptomatic obstructive sleep apnea (OSA). The effects of CPAP on blood pressure are moderate and variable. Short-term studies performed in subjects with severe OSA but without daytime sleepiness failed to show any effect of CPAP on 24-hour ambulatory blood pressure. These studies infer that CPAP is not useful in nonsleepy patients.

What This Study Adds to the Field

This study shows that, in hypertensive patients with severe obstructive sleep apnea but without daytime hypersomnolence, 1 year of CPAP treatment slightly reduces blood pressure.

- Objective: To explore the effects of CPAP on systemic blood pressure in subjects with hypertension (new diagnostic) and have an apnea-hypopnea index $>15 \text{ h}^{-1}$
- Design: RCT, placebo control



Patients with systemic hypertension recently diagnosed by primary care physician
All of them between 18-75 yr. and habitual snorers

Fullfill all inclusion and exclusion criteria and signed the informed consent

Nocturnal Standard Polysomnography
If $AHI \geq 15$ are included in the study

Blood samples, questionnaires, explorations and 24 hours blood pressure monitoring

Randomization

Optimal CPAP

SHAM CPAP

Blood samples, questionnaires, explorations and 24 hours blood pressure monitoring
At 6 and 12 weeks

Results of 24 hr. BPM

VARIABLE	BLOOD PRESSURE		Difference	P
	Basal	3 month		
SHAM CPAP				
Diurnal SBP	133 ± 11	132 ± 13	-0.8 ± 8.1	0.2
Nocturnal SBP	122 ± 14	121 ± 15	-0.8 ± 9.6	0.3
Diurnal DBP	85 ± 8	85 ± 9	-0.2 ± 2.4	0.7
Nocturnal DBP	76 ± 10	76 ± 10	-0.9 ± 7.2	0.1
OPTIMAL CPAP				
Diurnal SBP	134 ± 11	132 ± 12	-2.7 ± 9.7	0.001
Nocturnal SBP	124 ± 12	119 ± 13	-4.6 ± 12.5	<0.001
Diurnal DBP	85 ± 8	84 ± 9	-1.5 ± 6.2	0.006
Nocturnal DBP	76 ± 8	74 ± 9	-2.7 ± 7.6	<0.001

Continuous positive airway pressure as treatment for systemic hypertension in people with obstructive sleep apnoea: randomised controlled trial

Joaquín Durán-Cantolla, respiratory physician,^{1,2} Felipe Aizpuru, epidemiologist,^{3,4} Jose María Montserrat, respiratory physician,^{5,6} Eugeni Ballester, respiratory physician,^{5,6} Joaquín Terán-Santos, respiratory physician,^{6,7} Jose Ignacio Aguirregomoscorta, respiratory physician,⁸ Mónica Gonzalez, respiratory physician,⁹ Patricia Lloberes, respiratory physician,^{6,10} Juan Fernando Masa, respiratory physician,^{6,11} Mónica De La Peña, respiratory physician,^{6,12} Santiago Carrizo, respiratory physician,^{6,13} Mercedes Mayos, respiratory physician,¹⁴ Ferrán Barbé, respiratory physician,^{2,6} on behalf of the Spanish Sleep and Breathing Group

CPAP in non-sleepy OSA

- Title: Effect of CPAP on the incidence of hypertension or cardiovascular events in patients with sleep apnea and no daytime sleepiness (NCT 00127348)
- Design: RCT. 725 patients included,



Methods

DESIGN: Randomized prospective controlled study

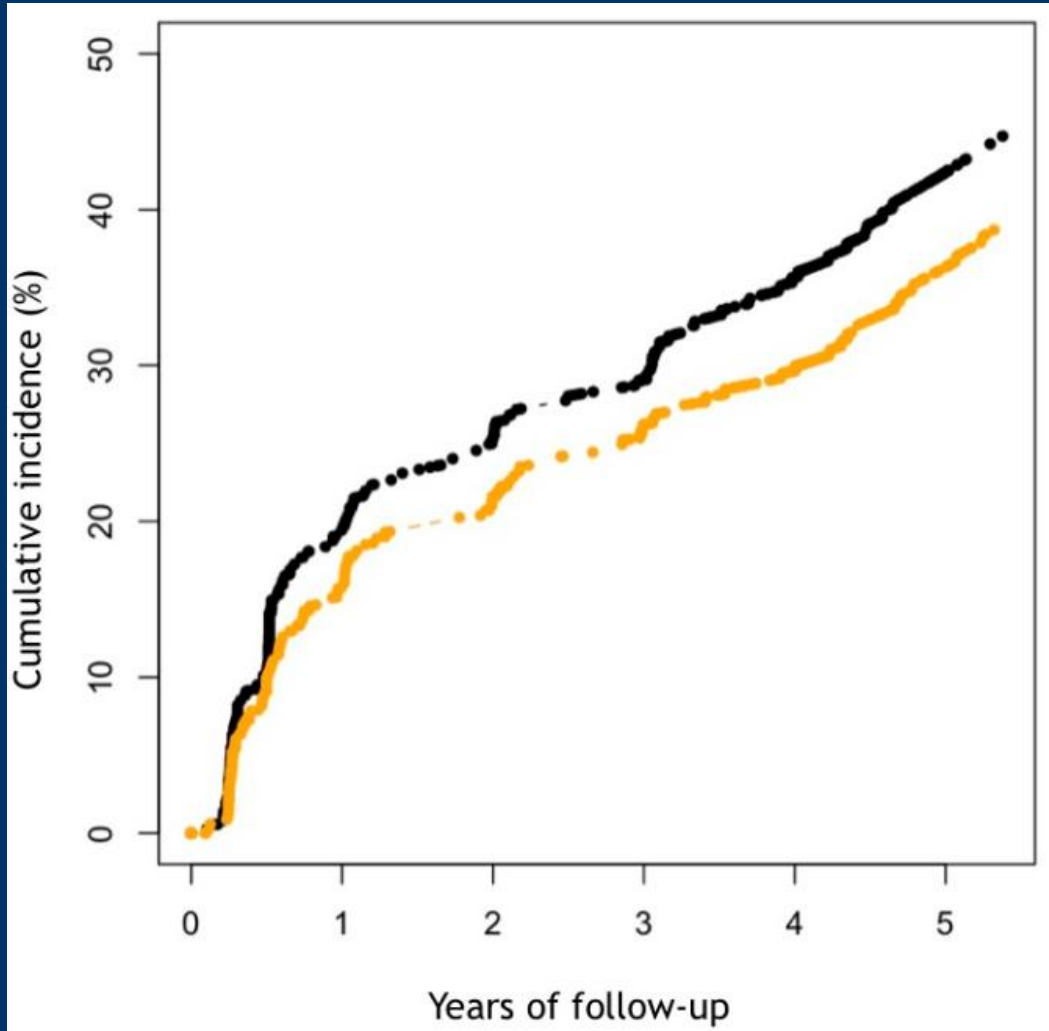
POPULATION: Patients with AHI ≥ 20 and Epworth scale < 10

MEASUREMENTS:

- Sleep study (polysomnography or partial study)
- CPAP titration by auto-CPAP
- Office blood pressure measurement
- Cardiovascular events

EVALUATIONS: Basal, 3, 6, 12, 24, 36, 48 month

Incidence of CVE or HT (ITT)

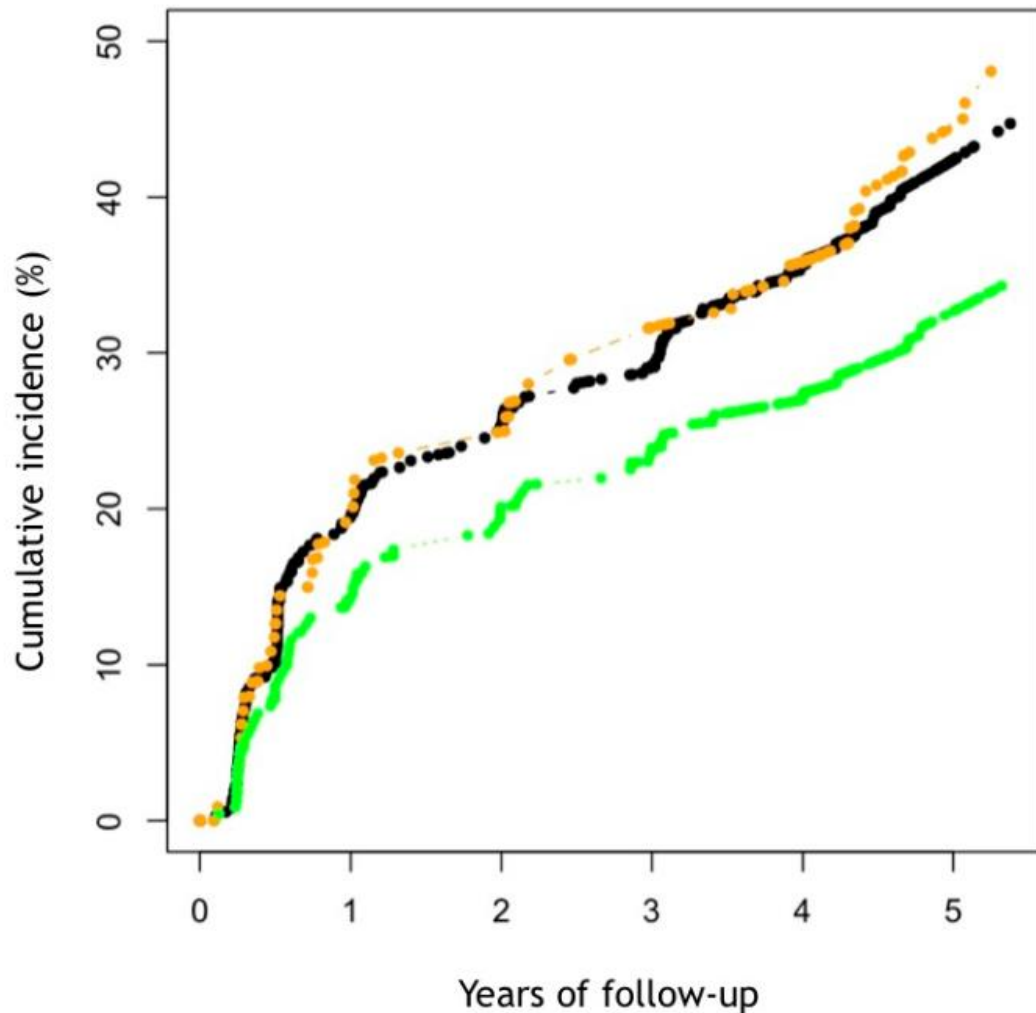


CPAP

Conservative

IDR: 0.83; 95% CI (0.63,1.1)
p=0.195

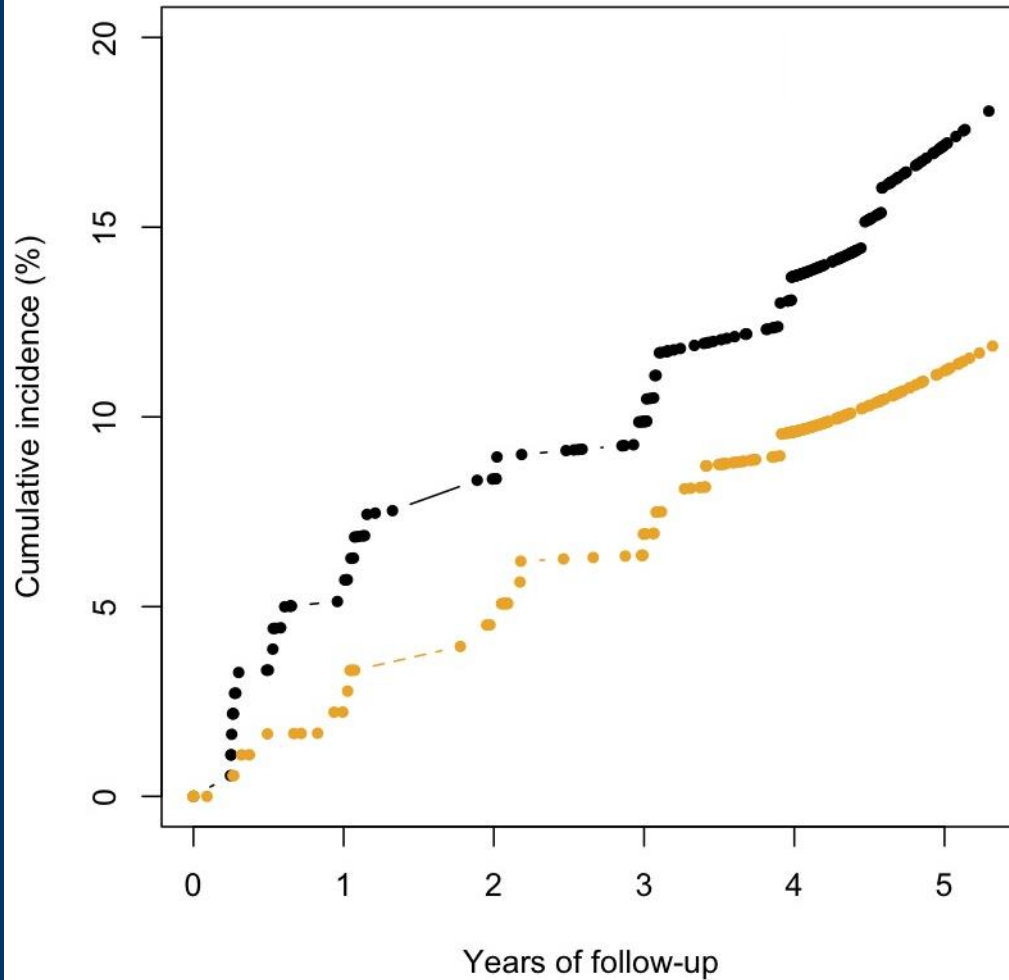
Incidence of CVE or HT (PP)



CPAP <4h
CPAP ≥4h
Conservative

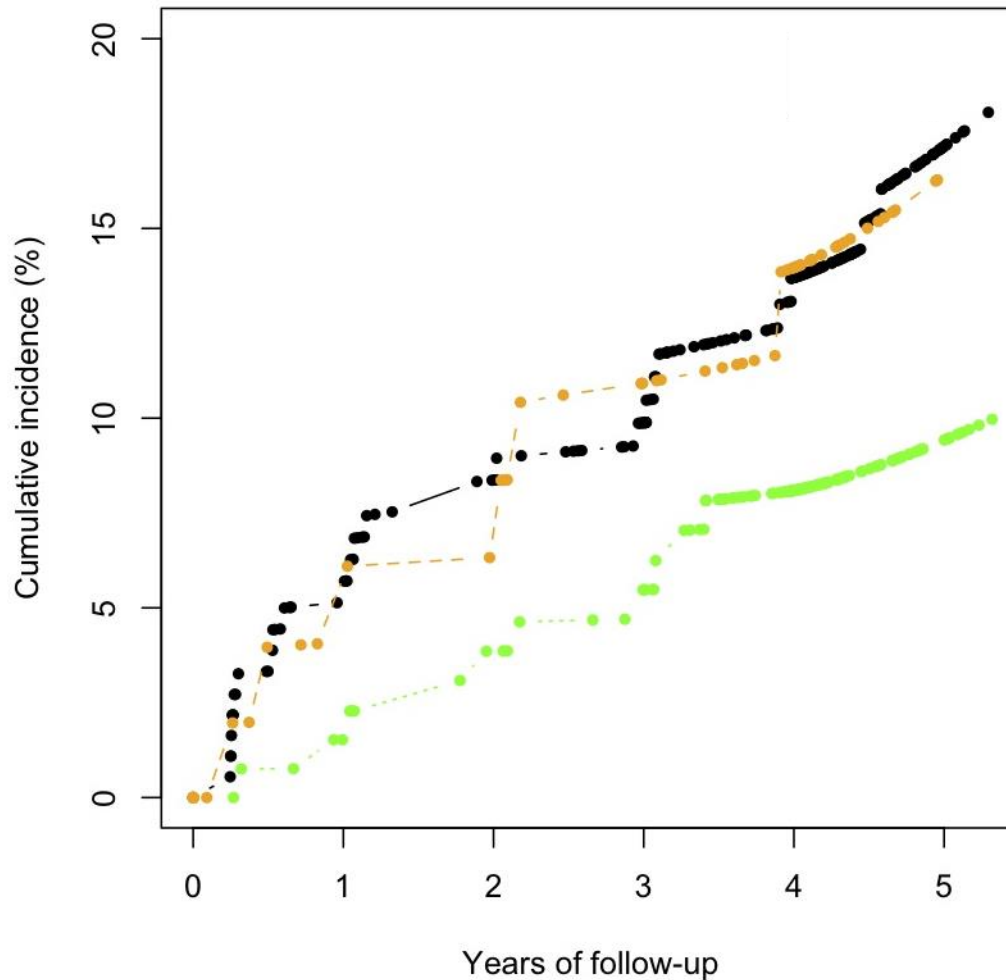
IDR: 0.72; 95% CI (0.52,0.98)
p=0.039

Incidence of CVE (ITT)



IDR: 0.52; 95% CI (0.25,1.1)
p=0.089

Incidence of CVE (PP)



CPAP <4h

CPAP ≥4h

Conservative

IDR: 0.47; 95% CI (0.22,1.01)
p=0.052

Proyectos en curso

(Investigación clínica)

- **Ámbito nacional**
 - Estudio ISAACC
- **Ámbito internacional**
 - Estudio SAVE (Australia)
 - Estudio ADVENT-HF (Canadá)

Estudio ISAACC

Impacto del síndrome de apneas-hipopneas del sueño en la evolución del síndrome coronario agudo. Efecto de la intervención con presión positiva continua (CPAP). Estudio prospectivo aleatorizado. Estudio ISAACC.

(Clinical Trials Registration Number: NCT00738170)



Estudio ISAACC



16 centros participantes

Centro coordinador: Hospital Arnau de Vilanova de Lleida.

Fecha de inicio: 2011

Estudio ISAACC

HIPOTESIS:

El síndrome de apneas del sueño es una condición infradiagnosticada entre los pacientes con Síndrome Coronario Agudo (SCA). Las repercusiones del SAHS (episodios de hipoxia-reoxigenación, arousals, cambios en la presión intrapleurales) empeoran el pronóstico clínico de los sujetos con SCA reciente. El tratamiento con presión de aire positiva continua (CPAP) revierte las repercusiones del SAHS y mejora el pronóstico del paciente con SCA.

Proyectos en curso (Ámbito internacional)

Objective: To determine the effectiveness of treatment with continuous positive airways pressure (CPAP) in addition to standard care in reducing cardiovascular (CV) morbidity and mortality in patients with co-existing CV disease and moderate-severe obstructive sleep apnea (OSA). An international, multi-centre, open, parallel group, prospective, randomised, controlled trial (Clinical Trials Registration Number: NCT00738170)



Proyectos en curso (Ámbito internacional)

Objective: The Effects of Adaptive Servo Ventilation (ASV) on Survival and Frequency of Cardiovascular (CV) Hospital Admissions in Patients with Heart Failure (HF) and Sleep Apnea (SA): (Registration Number: ISRCTN67500535)

The ADVENT-HF Trial

Grup de Medicina Respiratòria

- **Dr. Ferrán Barbé. Investigador Principal**

- **Dr. Manuel Sánchez.** Doctor en Biología. Investigador CIBERes.
- **Sra. Cristina Esquinas. DUE.** Diplomada en Estadística.
- **Dr. Gerard Torres.** Médico adjunto.
- **Sr. Oriol Capdevila.** Ingeniero Telecomunicaciones.
- **Sra. Monste Martínez.** Estadística.
- **Sr. Gonzalo Cao.** Farmacéutico.
- **Dra. Nuria Roure.** Psicóloga.
- **Dra. M^a Jesús Muniesa,** médico adjunto.
- **Dra. Silvia Gómez.** Médico adjunto.
- **Dra. Marina Lumbierres.** Médico adjunto.
- **Grupo 35 del CIBERes (Madrid).**

Personal Técnico:

- **Sra. Ana Martinez.** Técnico de laboratorio.
- **Olga Minguez,** Técnico de Sueño.
- **Lydia Pascual,** Enfermera.

Soporte Administrativo:

- **Sra. Maricel Arbonés.**



Spanish Sleep and Breathing Group

