Apnée du sommeil et son traitement: impact sur le risque vasculaire

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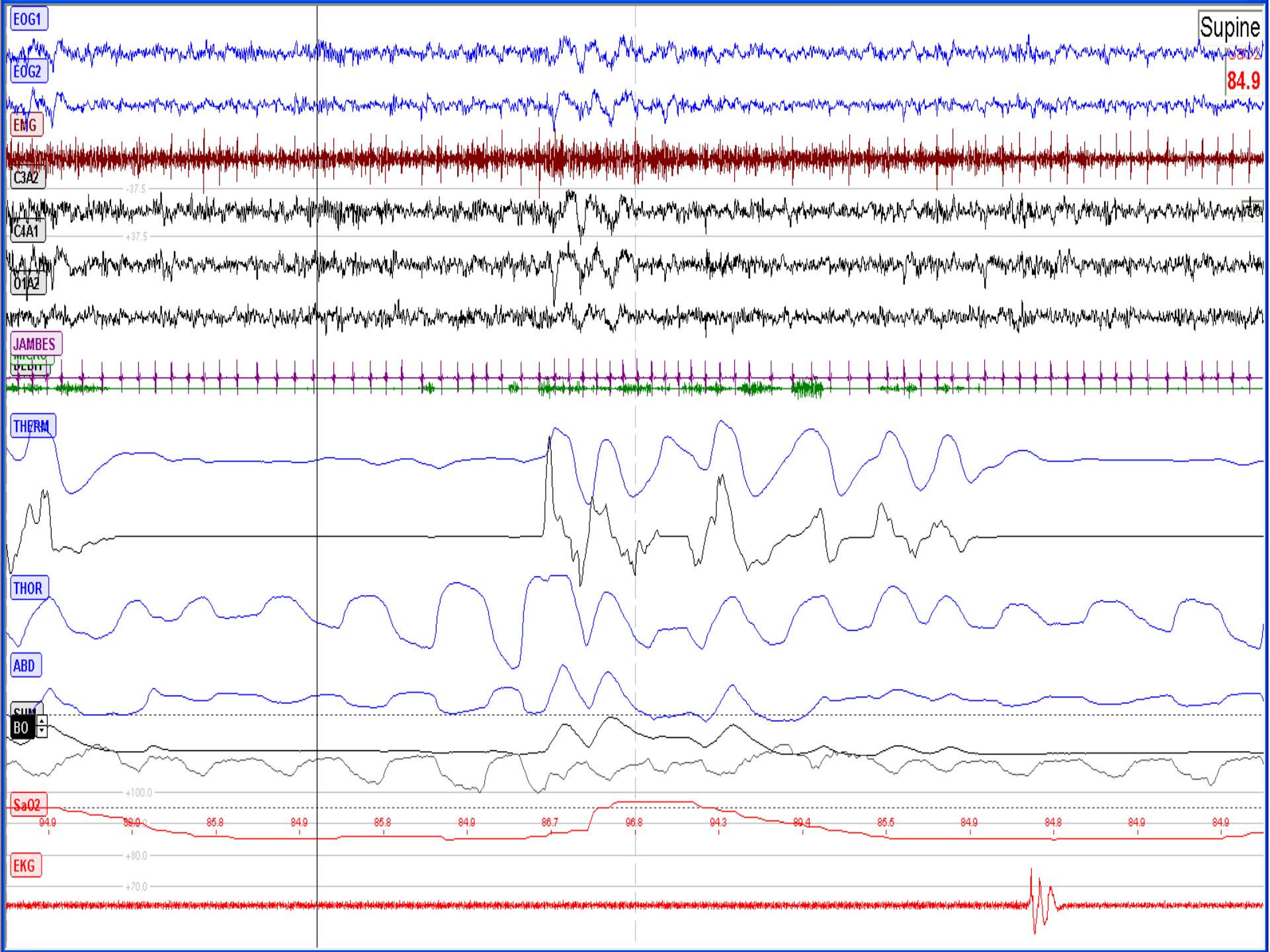
Centre de pneumologie IUCPQ
SSVQ, Novembre 2017

Aucun conflit d’intérêt


EOG1
EOG2
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JAMBES
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84.9
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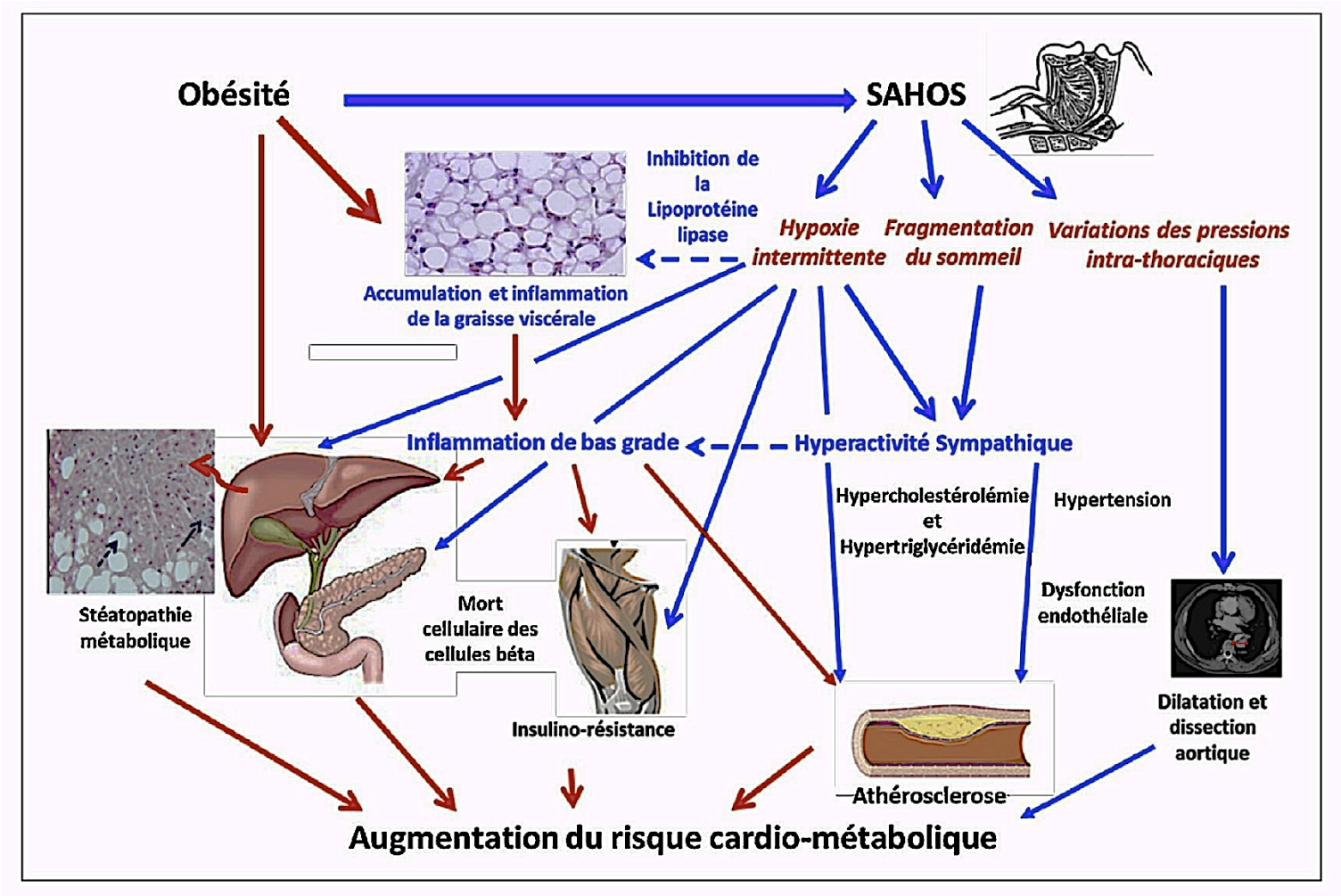
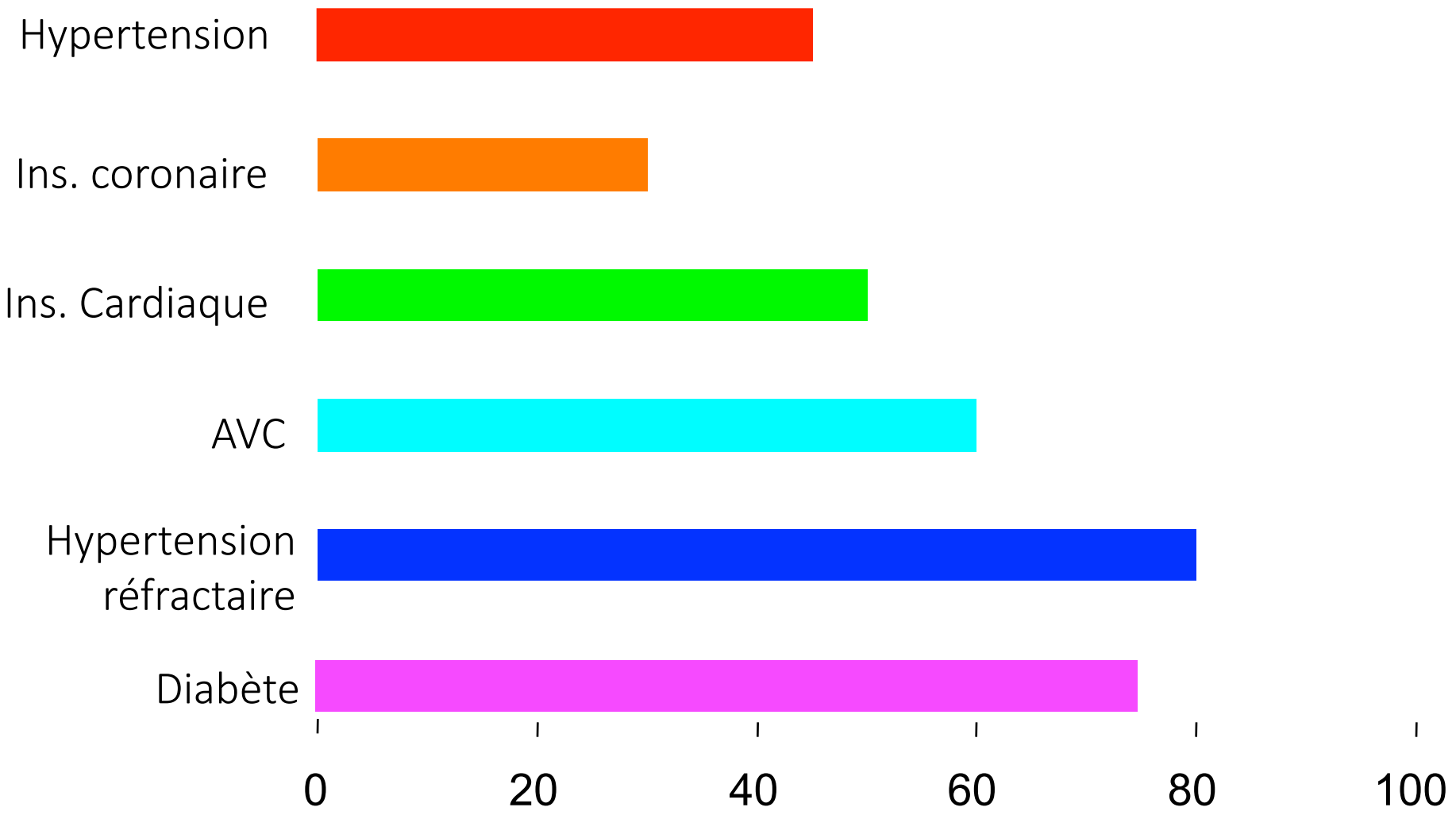
Young T, Am J Respir Crit Care Med 2003

Risque cardio-métabolique et troubles respiratoires du sommeil chez l'adulte



Destors M et al. Presse Med 2016

Prévalence du SAOS au cours des maladies cardio-métaboliques



Risque cardio-métabolique et troubles respiratoires du sommeil chez l'adulte

TABLE 3. ADJUSTED ODDS RATIOS FOR HYPERTENSION AT A FOLLOW-UP SLEEP STUDY, ACCORDING TO THE APNEA–HYPOPNEA INDEX AT BASE LINE.*

BASE-LINE APNEA–HYPOPNEA INDEX	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS AND NONMODIFIABLE RISK FACTORS (AGE AND SEX)	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS, NONMODIFIABLE RISK FACTORS, AND HABITUS (BMI AND WAIST AND NECK CIRCUMFERENCE)	ODDS RATIO, ADJUSTED FOR BASE-LINE HYPERTENSION STATUS, NONMODIFIABLE RISK FACTORS, HABITUS, AND WEEKLY ALCOHOL AND CIGARETTE USE
	odds ratio (95% confidence interval)			
0 events/hr†	1.0	1.0	1.0	1.0
0.1–4.9 events/hr	1.66 (1.35–2.03)	1.65 (1.33–2.04)	1.42 (1.14–1.78)	1.42 (1.13–1.78)
5.0–14.9 events/hr	2.74 (1.82–4.12)	2.71 (1.78–4.14)	2.03 (1.29–3.19)	2.03 (1.29–3.17)
≥15.0 events/hr	4.54 (2.46–8.36)	4.47 (2.37–8.43)	2.89 (1.47–5.69)	2.89 (1.46–5.64)
P for trend‡	<0.001	<0.001	0.002	0.002

*Hypertension was defined as a blood pressure of at least 140/90 mm Hg or the use of antihypertensive medications. Data on 893 follow-up sleep studies from 709 participants were analyzed. The odds ratios and confidence intervals were adjusted for the fact that 184 participants completed two follow-up sleep studies. BMI denotes body-mass index.

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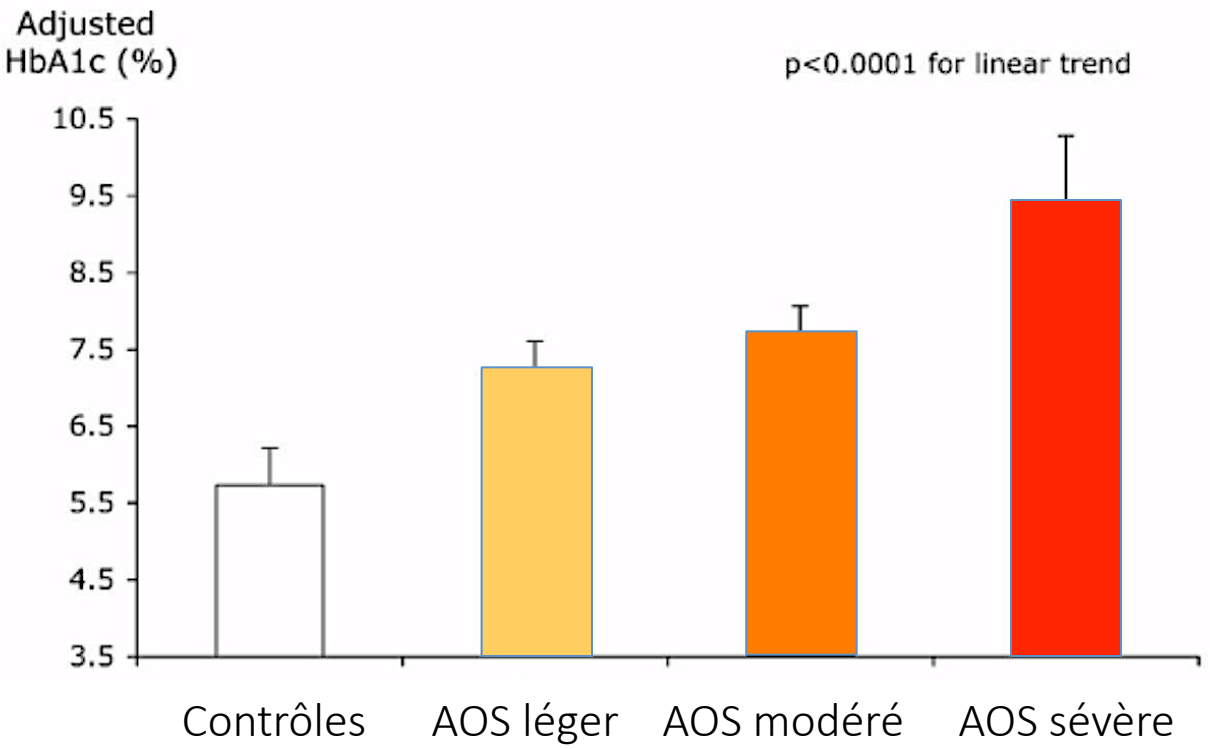
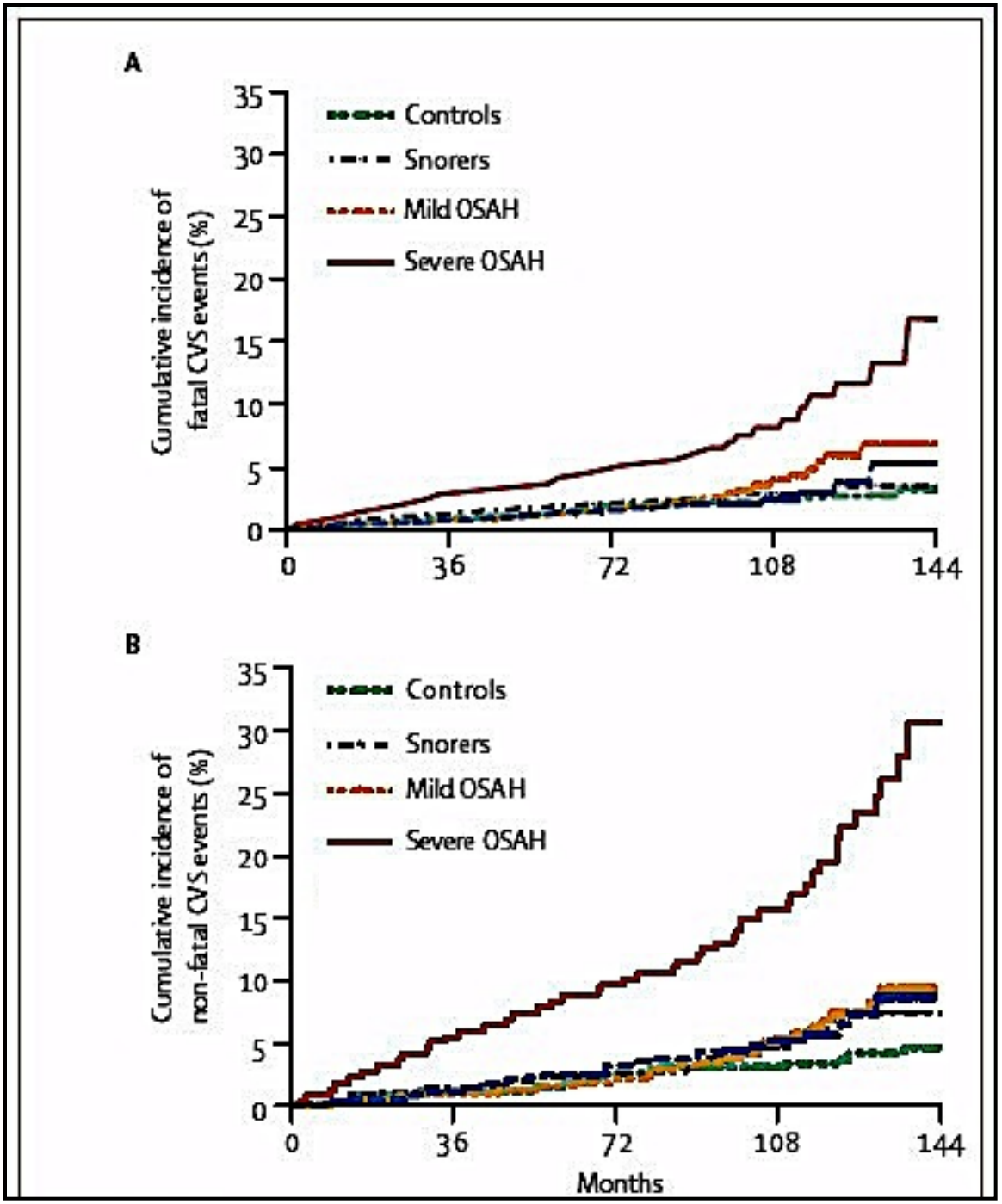
Peppard PE et al al, NEJM 2000

Dysrégulation glucidique et sévérité des troubles respiratoires du sommeil chez l'adulte



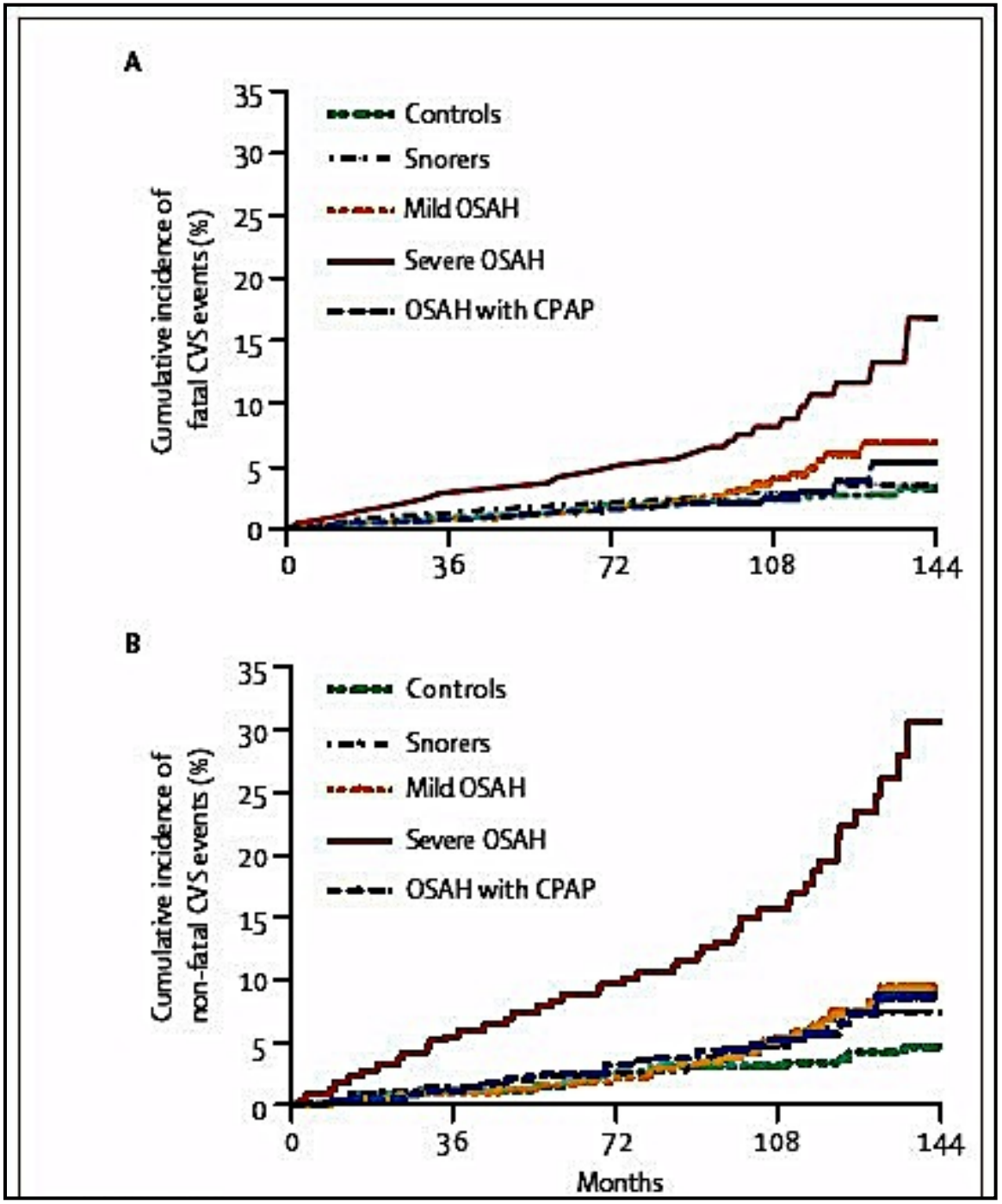
Données ajustées pour âge, sexe, ethnie, IMC, niveau d'exercice, nombre de médicaments hypoglycémiants, durée du diabète, durée de sommeil. N=60

Aronsohn RS et al, AJRCCM 2010

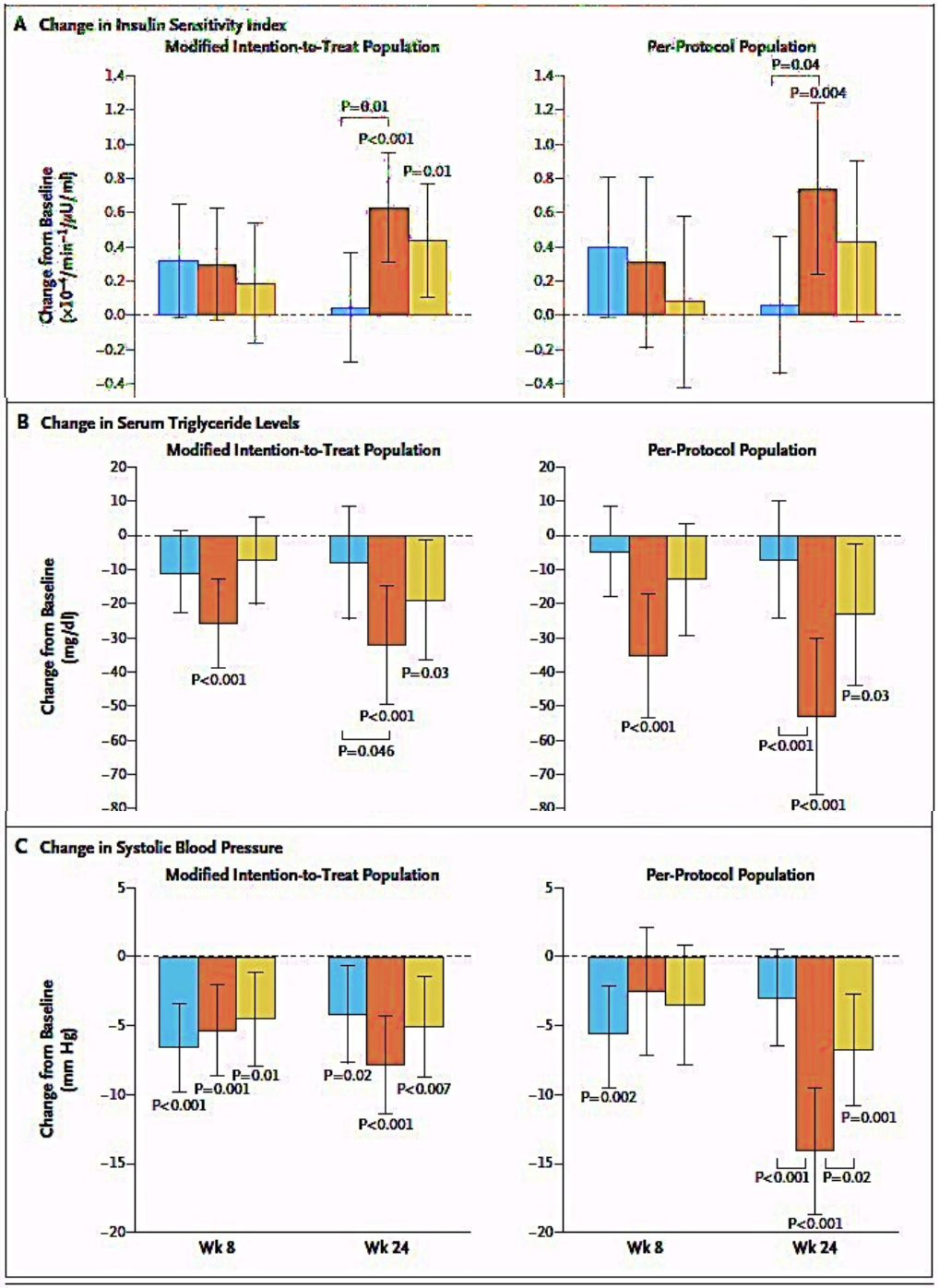


Marin JM et al, Lancet 2005

Traitement du SAOS et risque cardio-métabolique



Marin JM et al, Lancet 2005



CPAP alone | Weight loss+CPAP | Weight loss alone

RCT; 181 mod/severe OSA.

Weight loss 8 Kg in WL groups, 0 with CPAP

CPAP compliance: 4h/night

Chirinos JA et al, NEJM 2014

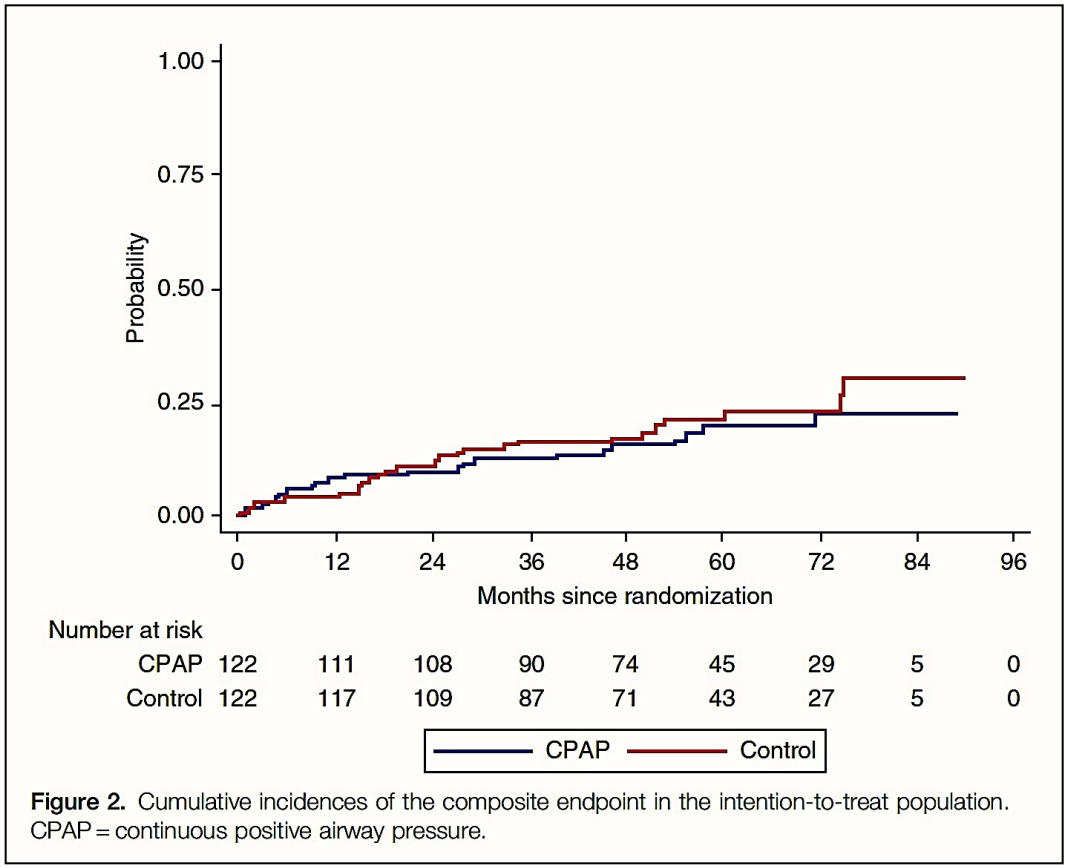


Figure 2. Cumulative incidences of the composite endpoint in the intention-to-treat population. CPAP = continuous positive airway pressure.

RCT: 244 mod/severe SAOS sans HSD avec antécédents PAC/ procédure revascularisation.

Variable: composite revascularisation, AVC, IDM, †

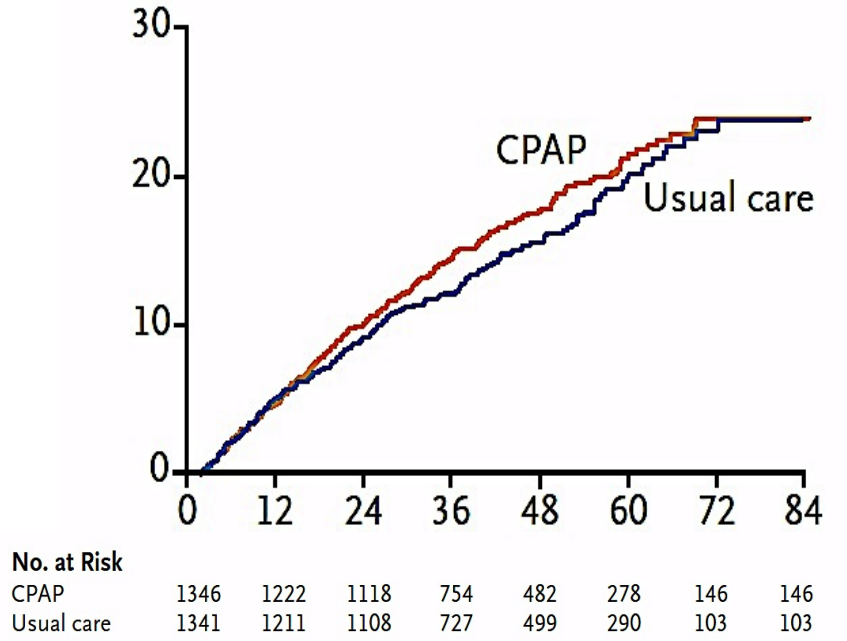
"Incidence of the composite endpoint:
CPAP usage ≥ 4 hours /night
2.31 (95% CI,0.96–5.54) /100 person-years
CPAP usage < less 4 hours per night /no CPAP
5.32 (95% CI, 3.96–7.15) /100 person-years for "

Table 3. Cox Regression Analysis of the Association between Time-Dependent CPAP Usage and Adverse Cardiovascular Outcomes in 244 Revascularized Patients with Coronary Artery Disease and Obstructive Sleep Apnea without Daytime Sleepiness (49 Patients Reached the Composite Endpoint)

	Univariate			Multivariate*		
	Hazard Ratio	95% CI	*P* Value	Hazard Ratio	95% CI	*P* Value
CPAP usage ⩾3 h/night	0.64	0.31–1.33	0.234	0.91	0.16–5.13	0.911
CPAP usage ⩾4 h/night	0.43	0.18–1.02	0.057	0.29	0.10–0.86	0.026
CPAP usage ⩾5 h/night	0.43	0.17–1.09	0.075	0.34	0.10–1.12	0.075

Definition of abbreviations: CI = confidence interval; CPAP = continuous positive airway pressure.
*Adjusted for CPAP nights per period, age, sex, body mass index, apnea–hypopnea index, current smoking, pulmonary disease, hypertension, diabetes mellitus, acute myocardial infarction, revascularization type at baseline, former revascularization, and left ventricular ejection fraction at baseline.

Peker Y et al, AJRCCM 2016



Étude SAVE

RCT: 2717 IDO ≥ 12/h avec antécédents Maladie coro ou MCV.

Variable: composite
Angor instable, AIT, AVC, IDM, †

CV outcomes for propensity score-matched CPAP adherent versus usual care patients

Outcome	CPAP + Usual care (n=561)	Usual care (n=561)	Hazard Ratio (95% CI)	P value
Composite primary outcome, no. (%)	86 (15.3)	98 (17.5)	0.80 (0.60 to 1.07)	0.13
Components of primary endpoint				
CV Death	12 (2.1)	12 (2.1)	0.90 (0.41 to 2.01)	0.81
Myocardial infarction	18 (3.2)	14 (2.5)	1.19 (0.59 to 2.39)	0.63
Stroke	19 (3.4)	31 (5.5)	0.56 (0.32 to 1.00)	0.05
Other vascular endpoints				
Composite of ischaemic CV events	77 (13.7)	87 (15.5)	0.81 (0.59 to 1.10)	0.17
Composite of major CV events	41 (7.3)	54 (9.6)	0.69 (0.46 to 1.04)	0.08
Composite for cerebral events	20 (3.6)	35 (6.2)	0.52 (0.30 to 0.90)	0.02
Composite for cardiac events	79 (14.1)	73 (13.0)	1.01 (0.74 to 1.39)	0.93

McEvoy D et al, NEJM 2016

JAMA | Original Investigation

Association of Positive Airway Pressure With Cardiovascular Events and Death in Adults With Sleep Apnea

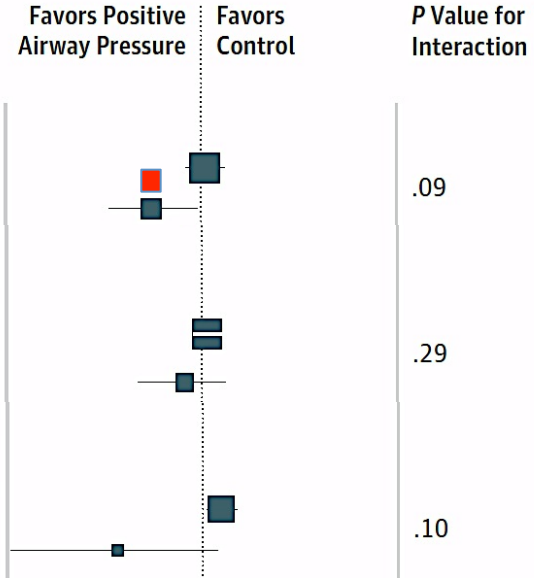
A Systematic Review and Meta-analysis

4562 patients et 356 évènements, dont 73% associés à l'étude SAVE
Analyse †, composites † CV + évènement coro ou AVC non fatal, idem + hospit pour angine instable

Durée suivi de 6 mois à 6 ans, observance PPC 3.3 h/nuit (1.6 à 6.6 h/nuit)

Figure 5. Association of Positive Airway Pressure With Vascular Outcomes and Deaths in Trial Subgroups

Subgroup	Studies, No.	Positive Airway Pressure: Events or Deaths, No.	Positive Airway Pressure: Participants, No.	Control: Events or Deaths, No.	Control: Participants, No.	Risk Ratio (95% CI)	Heterogeneity
Major adverse cardiovascular events[a]							
Adherence							
<4 h/d	3	141	1694	135	1692	1.05 (0.84-1.31)	I^2 = 0%, P = .60
≥4 h/d	4	28	578	52	598	0.58 (0.34-0.99)	I^2 = 19.70%, P = .29
Major adverse cardiovascular events plus[b]							
Adherence							
<4 h/d	3	240	1694	225	1692	1.07 (0.90-1.26)	I^2 = 0.00%, P = .59
≥4 h/d	4	75	578	95	598	0.76 (0.45-1.27)	I^2 = 52.90%, P = .09
Cardiovascular death							
Adherence							
<4 h/d	3	247	2153	198	2147	1.24 (1.05-1.46)	I^2 = 0.00%, P = .98
≥4 h/d	4	4	578	15	598	0.41 (0.14-1.18)	I^2 = 0.00%, P = .41



Yu Jet al, JAMA 2017

Traitement du SAOS et risque cardio-métabolique

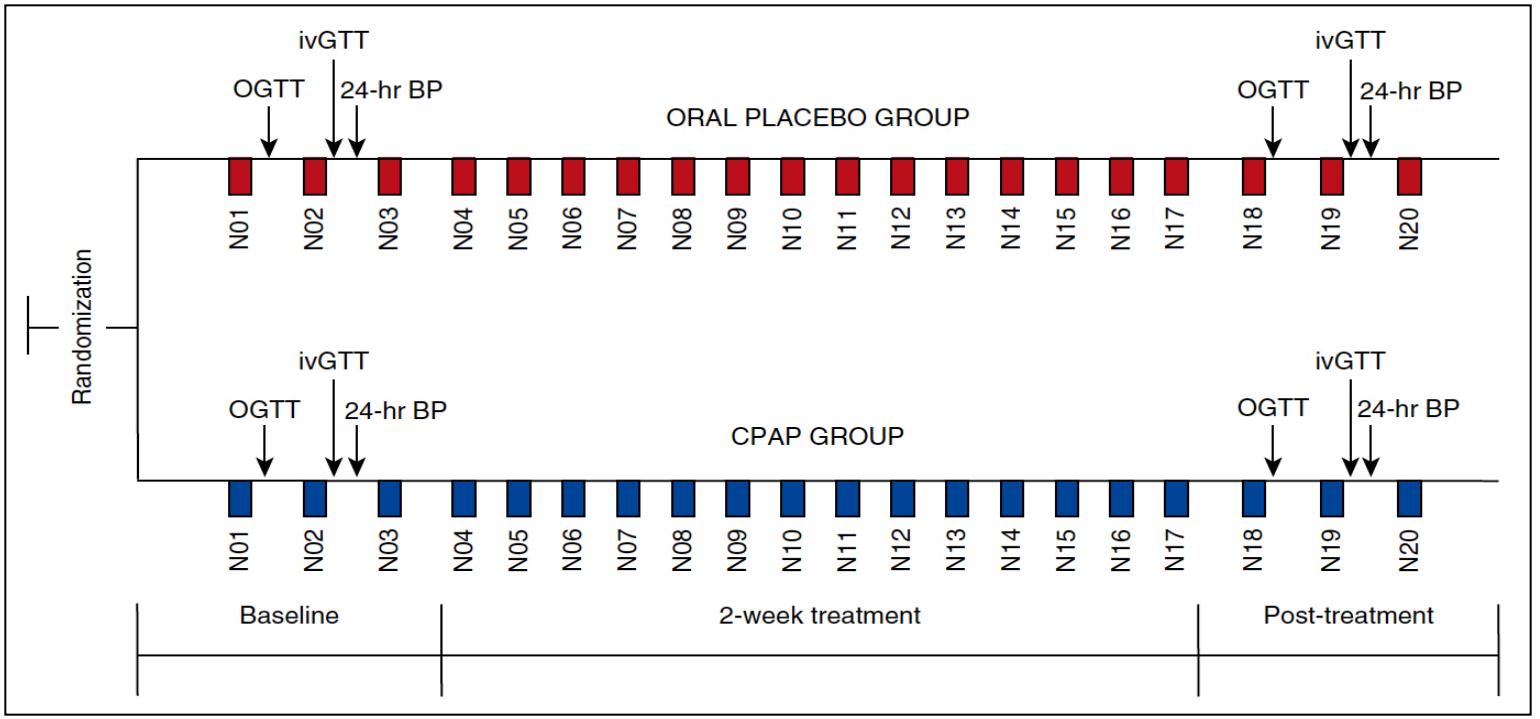
	CPAP Group		Control Group		Intergroup Crude Difference		Intergroup Adjusted Difference	
	Baseline	Follow-up	Baseline	Follow-up	Difference (95% CI)†	*P* Value	Difference (95% CI)‡	*P* Value
Hemoglobin A1c, %								
After 3 mo	7.6 ± 1.3	7.7 ± 1.2	7.6 ± 0.7	7.5 ± 1.6	0.006 (−0.6 to 0.6)	0.983	0.1 (−0.6 to 0.7)	0.873
After 6 mo		7.3 ± 1.1		7.6 ± 0.7	−0.4 (−0.7 to −0.1)	0.024	−0.4 (−0.7 to −0.04)	0.029
Fasting glucose, mg/dl								
After 3 mo	168 ± 38	162 ± 43	169 ± 40	166 ± 72	−3 (−37 to 31)	0.860	1 (−37 to 38)	0.978
After 6 mo		159 ± 38		162 ± 61	−4 (−34 to 26)	0.780	−23 (−53 to 6)	0.117
Fasting plasma insulin,§ μU/ml								
After 3 mo	17.4 ± 5.7	15.3 ± 6.0	16.7 ± 4.1	18.1 ± 6.2	−3.2 (−7.7 to 1.2)	0.150	−4.0 (−10.3 to 2.3)	0.194
After 6 mo		13.4 ± 7.1		18.8 ± 5.2	−5.7 (−10.6 to 0.9)	0.022	−5.7 (−11.5 to 0.2)	0.056
HOMA-IR†								
After 3 mo	6.73 ± 2.08	5.89 ± 2.33	6.90 ± 1.25	7.07 ± 1.72	−1.19 (−2.65 to 0.27)	0.107	−1.56 (−3.40 to 0.28)	0.092
After 6 mo		5.12 ± 2.77		6.94 ± 1.59	−1.81 (−3.47 to −0.15)	0.033	−2.58 (−4.75 to −0.41)	0.023
QUICKI†								
After 3 mo	0.494 ± 0.074	0.502 ± 0.039	0.478 ± 0.019	0.473 ± 0.027	0.024 (−0.0002 to 0.048)	0.052	0.034 (0.002 to 0.066)	0.038
After 6 mo		0.525 ± 0.059		0.469 ± 0.024	0.052 (0.017 to 0.087)	0.005	0.055 (0.013 to 0.096)	0.013

	Unstandardized Regression Coefficients		95% CI for *B*		Standardized Regression Coefficient: *B*	*P* Value	r^2	r^2 Change
	B	SE	Lower Limit	Upper Limit				
Constant	10.828	4.062	2.258	19.398	—	0.016	—	—
Mean nocturnal oxygen saturation, %	−0.120	0.044	−0.213	−0.027	−0.482	0.014	0.353	0.353
IL-1β, pg/ml	0.210	0.090	0.020	0.400	0.412	0.032	0.510	0.157

Definition of abbreviation: CI = confidence interval.

Martinez-Ceron E et al. AJRCCM 2016

Traitement du SAOS et risque cardio-métabolique



Pamidi S et al. AJRCCM 2015

Traitement du SAOS et risque cardio-métabolique

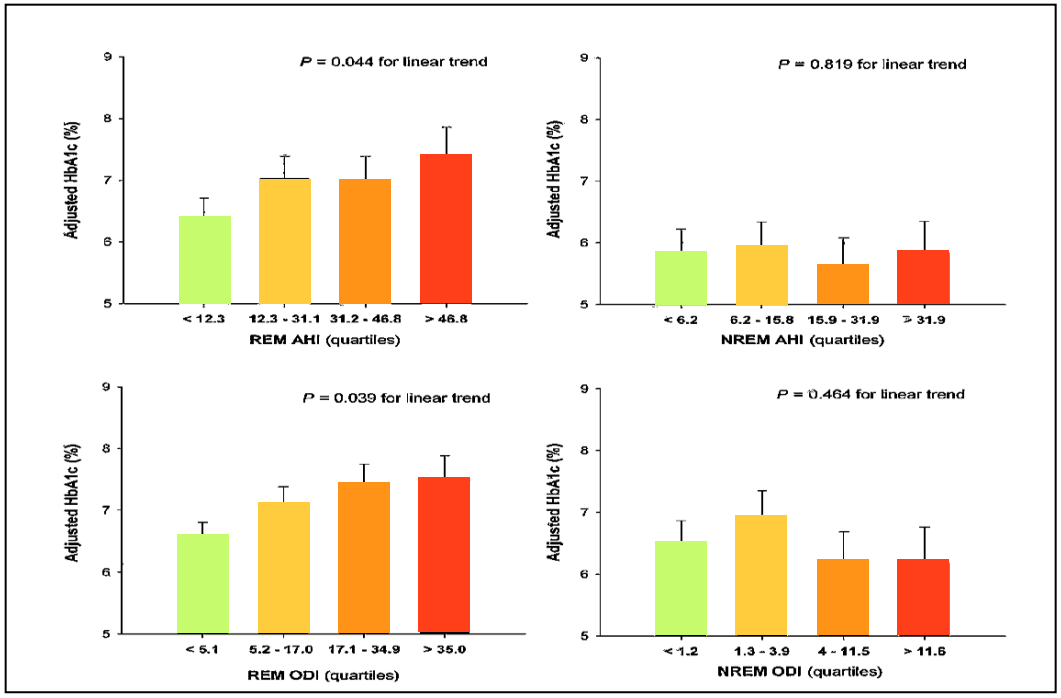
Table 3. Effect of Treatment on Measures of Glucose Metabolism for CPAP versus Oral Placebo Groups*

	CPAP Group ($n = 26$)		Oral Placebo Group ($n = 12$)			
	Baseline	Change after 2 Weeks	Baseline	Change after 2 Weeks	Treatment Difference	*P* Value†
Fasting glucose, mg/dl	104.1 (100.7 to 107.5)	−4.1 (−7.2 to −1.0)	100.9 (95.8 to 105.9)	−1.3 (−5.6 to 3.1)	−2.8 (−8.1 to 2.5)	0.30
Fasting insulin, pmol/L	73.6 (60.0 to 87.3)	−5.7 (−16.5 to 5.1)	69.7 (49.4 to 90.0)	13.0 (−2.1 to 28.1)	−18.7 (−37.3 to −0.1)	0.05
2-h glucose, mg/dl	153.4 (141.2 to 165.7)	−3.8 (−12.4 to 4.8)	147.9 (129.7 to 166.2)	10.2 (−1.7 to 22.1)	−14.0 (−28.7 to 0.6)	0.06
2-h insulin, pmol/L	766.8 (603.9 to 929.7)	−73.2 (−192.7 to 46.4)	728.0 (485.9 to 970.0)	−118.6 (−284.7 to 47.5)	45.5 (−159.1 to 250.1)	0.66
$AUC_{glucose}$, (mg/dL) · min	19,564.9 (18,548.3 to 20,581	−794.2 (−1,446.4 to −142	19,723.4 (18,212.2 to 21,234	482.7 (−422.2 to 1,387.	−1,276.9 (−2,392.4 to −161	0.03
S_I, $(mU/L)^{-1} \cdot min^{-1}$	2.3 (1.9 to 2.7)	0.31 (−0.11 to 0.74)	2.8 (2.2 to 3.4)	−0.46 (−1.07 to 0.15)	0.77 (0.03 to 1.52)	0.04

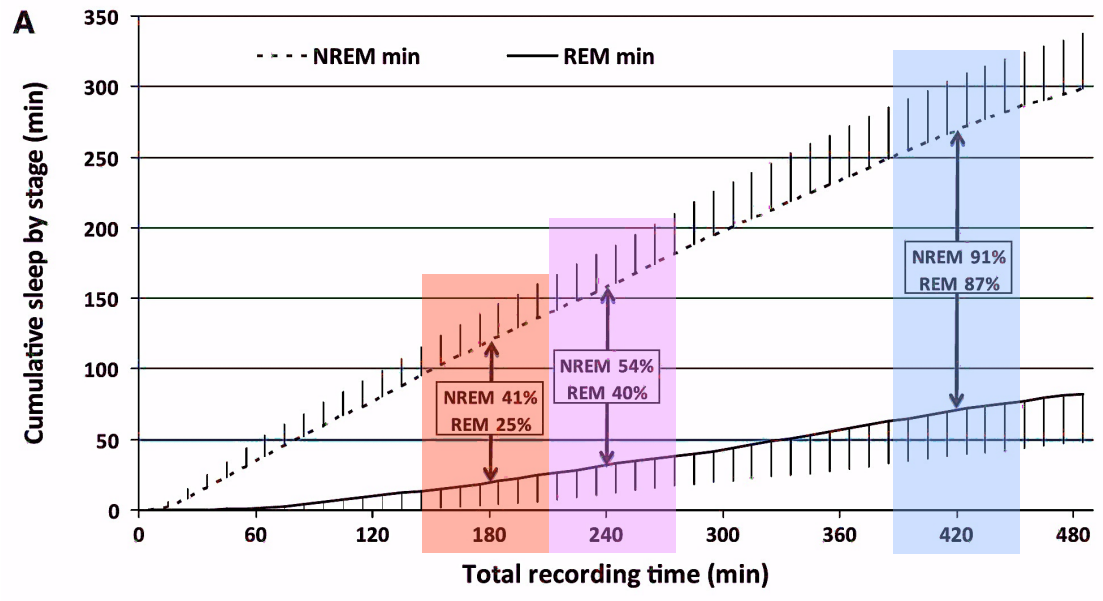
Table 4. Effect of Treatment on 24-Hour Blood Pressure for CPAP versus Oral Placebo Groups*

	CPAP Group ($n = 22$)		Oral Placebo Group ($n = 10$)			
	Baseline	Change after 2 Weeks	Baseline	Change after 2 Weeks	Treatment Difference	*P* Value†
24-h SBP, mm Hg	135.2 (129.4 to 140.	−1.9 (−6.2 to 2.3)	130.8 (122.2 to 139.4)	7.6 (1.9 to 13.3)	−9.5 (−16.6 to −2.4)	0.009
Daytime SBP, mm Hg	141.2 (135.4 to 147.	−3.8 (−8.1 to 0.5)	136.2 (127.5 to 144.8)	5.9 (0.2 to 11.6)	−9.7 (−16.8 to −2.5)	0.008
Nighttime SBP, mm Hg	122.2 (115.3 to 129.	1.7 (−4.3 to 7.7)	117.0 (106.7 to 127.4)	12.4 (4.4 to 20.4)	−10.8 (−20.7 to −0.8)	0.04
24-h DBP, mm Hg	79.3 (76.2 to 82.4)	−2.6 (−4.9 to −0.3)	75.6 (71.0 to 80.2)	4.5 (1.4 to 7.5)	−7.1 (−10.9 to −3.2)	<0.001
Daytime DBP, mm Hg	84.7 (81.3 to 88.1)	−4.7 (−7.3 to −2.1)	79.4 (74.4 to 84.4)	3.5 (0.04 to 7.0)	−8.2 (−12.5 to −3.9)	<0.001
Nighttime DBP, mm Hg	68.1 (64.6 to 71.6)	1.6 (−1.6 to 4.7)	65.7 (60.4 to 71.0)	7.7 (3.4 to 11.9)	−6.1 (−11.4 to −0.8)	0.02

Pamidi S et al. AJRCCM 2015



Results adjusted for age, sex, ethnicity , BMI, years of type 2 diabetes, insulin use



Grimaldi D et al. Diabetes Care 2014

Risque cardio-métabolique et troubles respiratoires du sommeil chez l'adulte

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Peppard PE et al al, NEJM 2000

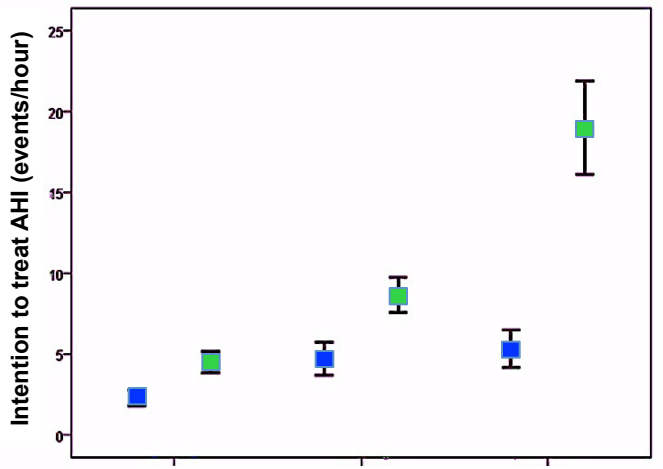
Risque cardio-métabolique et troubles respiratoires du sommeil chez l'adulte

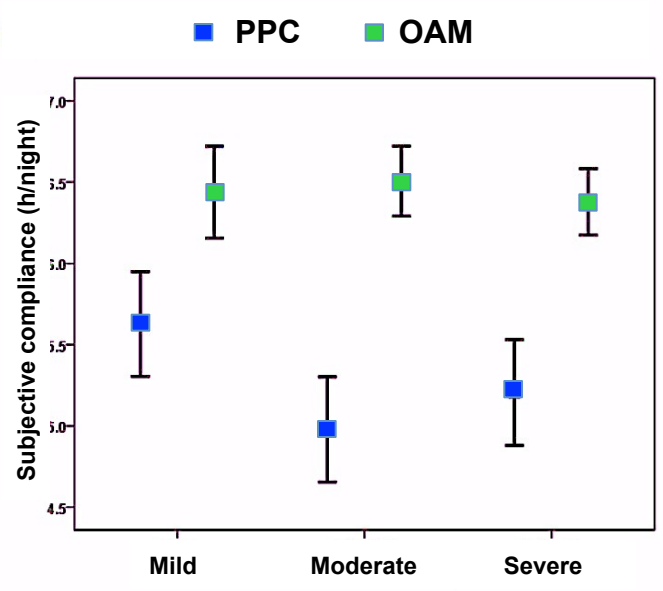
Adjusted Odds Ratios (95% CI) for Prevalent Hypertension*		
	Subset with Ambulatory Blood Pressure Monitoring	
REM AHI Severity Category	All Sleep Studies (*n = 1,085*)	non-REM AHI ⩽ 5 (*n = 779*)
<1 (reference)	NA	NA
1–4.9	1.54 (1.07–2.21)	1.70 (1.12–2.59)
5–14.9	1.28 (0.88–1.88)	1.58 (1.00–2.53)
⩾15	1.63 (1.02–2.61)	3.38 (1.70–6.72)
P trend	0.08	<0.001

Logistic Regression Models Estimating the Risk of Prevalent Hypertension by REM AHI Severity Category

‡P values are for the linear trend of the logistic-regression coefficients ($\log_e$ of the odds ratios).

Peppard PE et al al, NEJM 2000
Mokhlesi B et al. AJRCCM 2014





Phillips CL et al. AJRCCM 2013