



1^E EDITION DU SÉMINAIRE SAODA Sommeil France / Benin à Cotonou



**Du 25 au 29 Mai 2022
Palais des congrès de Cotonou**

Sujet : SAOS SNA ET SCM

Orateurs : DR THOIN FABRICE

SAOS SNA SCM

RISQUE CARDIOMETABOLIQUE

1 / EPIDEMIOLOGIE ET PUBLICATIONS

LE REM

2 / UN LIEN PHYSIOPATHOLOGIQUE PRECOCE ! LE SNA

3/SAOS AU TRAVERS DE 2 TRAJECTOIRES : FEMME ENCEINTE ET BARIATRIQUE

4/ PHENOTYPE

LE COMISA

5 / PRISE EN CHARGE MULTIMODALE

KINE et RHD TCC PPC /SNA

DR THOIN FABRICE



MORTALITY AND MORBIDITY IN OBSTRUCTIVE SLEEP APNOEA-HYPOPNOEA SYNDROME: RESULTS FROM A 30-YEAR PROSPECTIVE COHORT STUDY

SOPHIE DODDS 2020

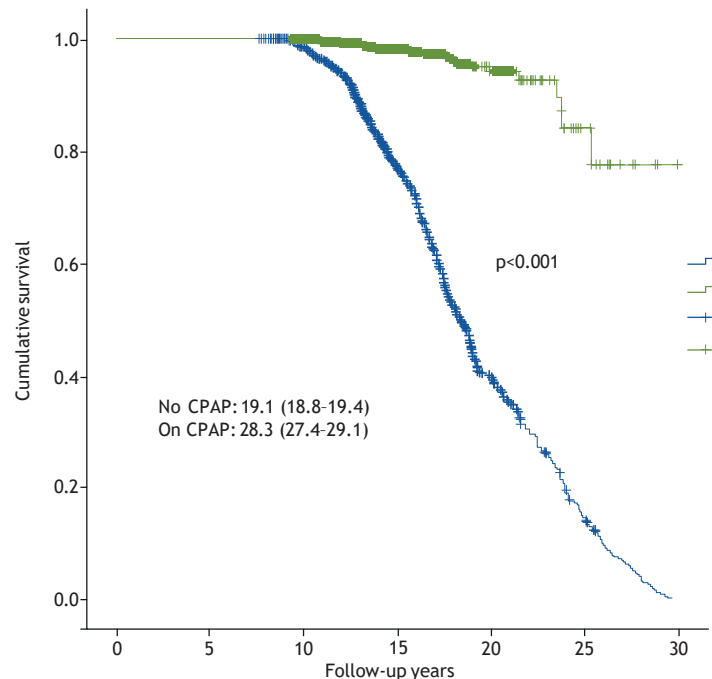
OBSERVANCE EN REM

prospective, cohort study comprised 4502 patients

Cohort arm No
CPAP On CPAP
No CPAP, censored
On CPAP, censored

SOPHIE DODDS 2020 ERJ

MYOCARDIAL INFARCTION 29/659 (4.4%) 35/198 (17.7%) <0.001



BAISSE DE 30 À 39 % INCIDENCE DIABETE TYPE II SOUS PPC

27.9% versus 18.7%, p=0.003

Results of imputation analysis of CPAP use and long-term survival in 4502 patients

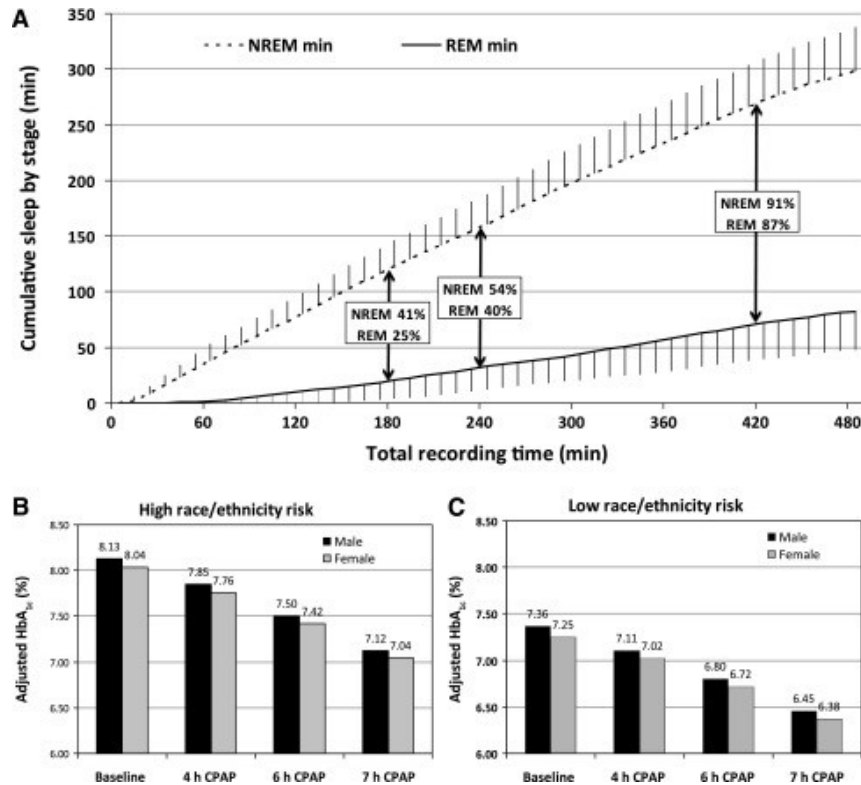
CPAP use ratio	Relative risk of mortality ratio	Lower 95% CI	Upper 95% CI	p-value
No use/short-term use	3.14	2.69	3.66	<0.001
No use/long-term use	5.63	4.83	6.58	<0.001
Short-term us/ long-term use	1.74	1.49	2.02	<0.001

long-term CPAP users (>5 years) were 5.63 times more likely to be alive at study end than non-CPAP users



IAH EN REM CORRELE A L HG GLYQUEE ET AU RCV

multivariate linear regression model



4 H CPAP USE WOULD LEAVE **60% OF REM SLEEP** UNTREATED AND WOULD BE ASSOCIATED WITH A DECREASE IN **HBA_{1c} 0.25%**.
7 H CPAP USE WOULD COVER MORETHAN **85% OF REM SLEEP** AND WOULD BE ASSOCIATED WITH A DECREASE IN **HBA_{1c} BY AS 1%**.

BAISSE DE 1.9 mmhg SBP et 1 mmhg DBP / 1 H PPC

[Sleep](#). 2021 Feb; 44(2): zsaa229.

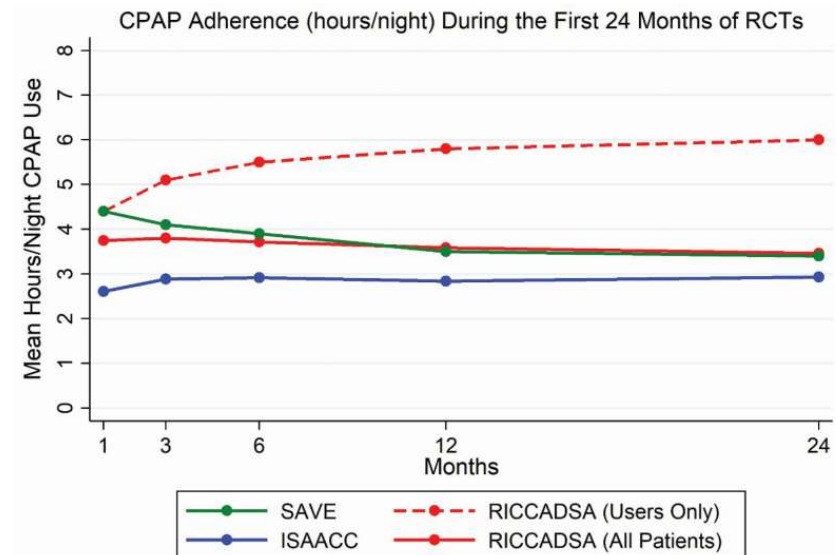
Published online 2020 Nov 9. doi: [10.1093/sleep/zsaa229](#)

PMCID: PMC7879410

PMID: [33165616](#)

Randomized clinical trials of cardiovascular disease in obstructive sleep apnea: understanding and overcoming bias

[Allan I Pack](#),¹ [Ulysses J Magalang](#),² [Bhajan Singh](#),³ [Samuel T Kuna](#),⁴ [Brendan T Keenan](#),^{1,5} and [Greg Maislin](#)^{1,5}



SAOS FDR PRIMAIRE DES MALADIES CV ET MÉTABOLIQUES ? RÔLE DU SOMMEIL PARADOXAL

- Cohorte de la Wisconsin Sleep Cohort Study.
- PSG, 1453 patients, étude du métabolisme glucidique
- $AHI_{NREM} < 8,3/h$

**Résistance à
l'insuline associée
à IAH REM**

**IAH REM $\geq 30/h$
FDR à 9,5 ans
MACES OR 2,41**

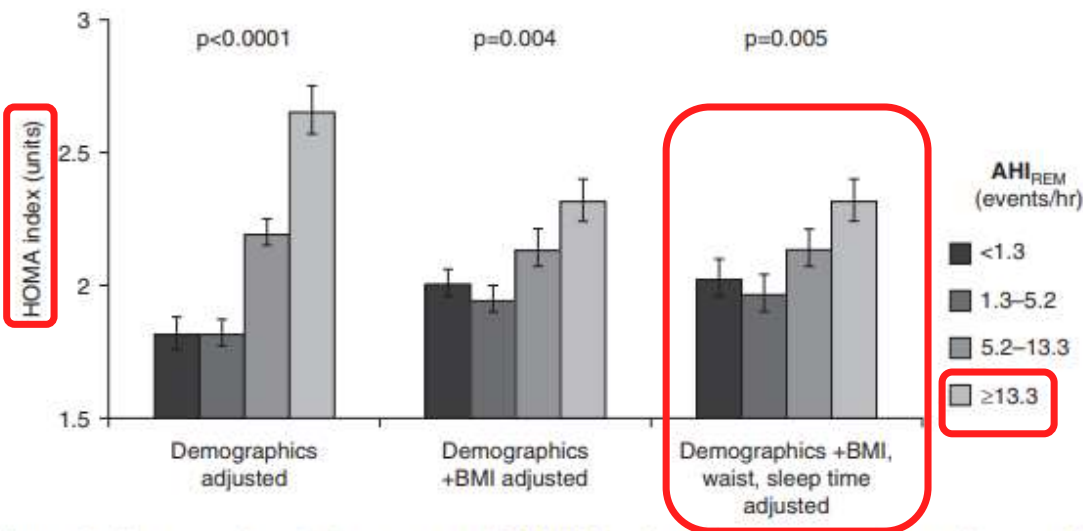
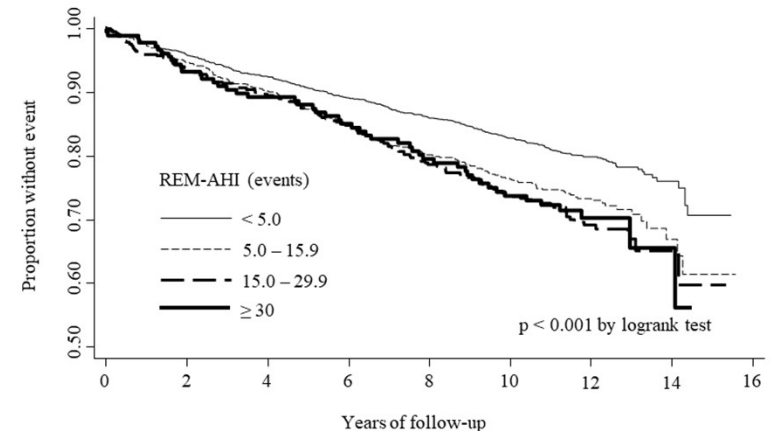


Figure 1. Homeostatic model assessment (HOMA) index by AHI_{REM} category, in participants with $AHI_{NREM} < 8.3$ events/h, $n = 1,177$. Demographic variables: age, sex, race, study site. AHI = apnea-hypopnea index; BMI = body mass index; sleep time = self-reported usual sleep time; waist = waist circumference.

AHIREM was only associated with **HOMA-IR** ($\beta = 0.04$; 95% CI, 0.1-0.07; $P = 0.01$),

Chami. Am J Respir Crit Care 2015

1. COHORTE DE LA SLEEP HEART HEALTH STUDY.
2. PSG, 3265 PATIENTS AVEC IAH NON-REM $< 5/H$
3. SUIVI MEDIAN DE 9,5 ANS (ÉVÉNEMENTS DÉCÈS CV OU IDM, REVASCULARISATION CORONAIRE, IC, AVC)



Aurora. Am J Respir Crit Care 2018

A Systematic Review and Meta-analysis of Randomized Controlled Trials

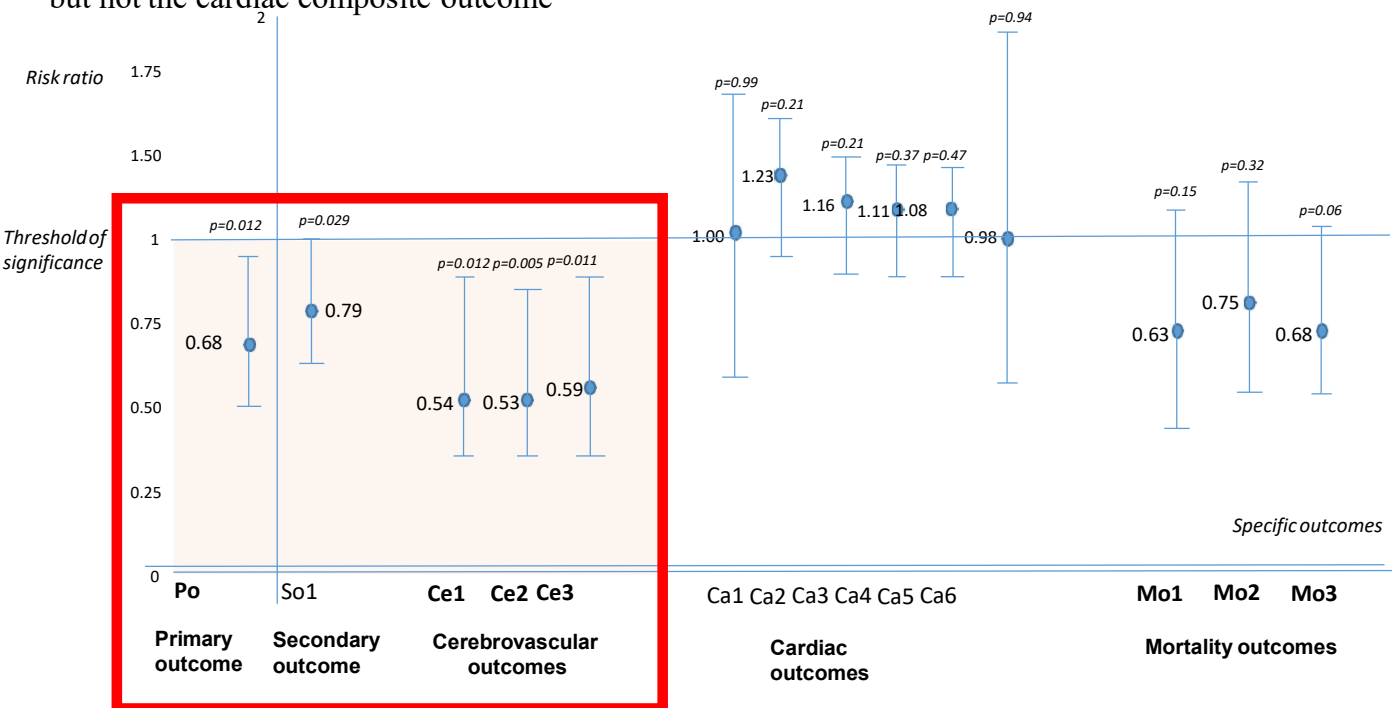
Shahrokh Javaheri; Miguel Angel Martinez-Garcia; Francisco Campos-Rodriguez; Alfonso Muriel; Yüksel Peker

improved the **primary composite outcome RR 0.68** [95% CI, 0.50 to 0.92]; $P=0.01$, and RD -0.05 [95% CI, -0.09 to -0.003], $P=0.001$

CPAP use also improved cerebrovascular composite outcome RR 0.59

[95% CI, 0.39 to 0.89]; $P=0.01$, and RD -0.05 [95% CI -0.04 to 0.01], $P=0.001$; $I^2:0\%$; $p=0.55$),

but not the cardiac composite outcome



Sleep SMART

5 eligible trials with 943 CPAP users
and 1141 controls CPAP

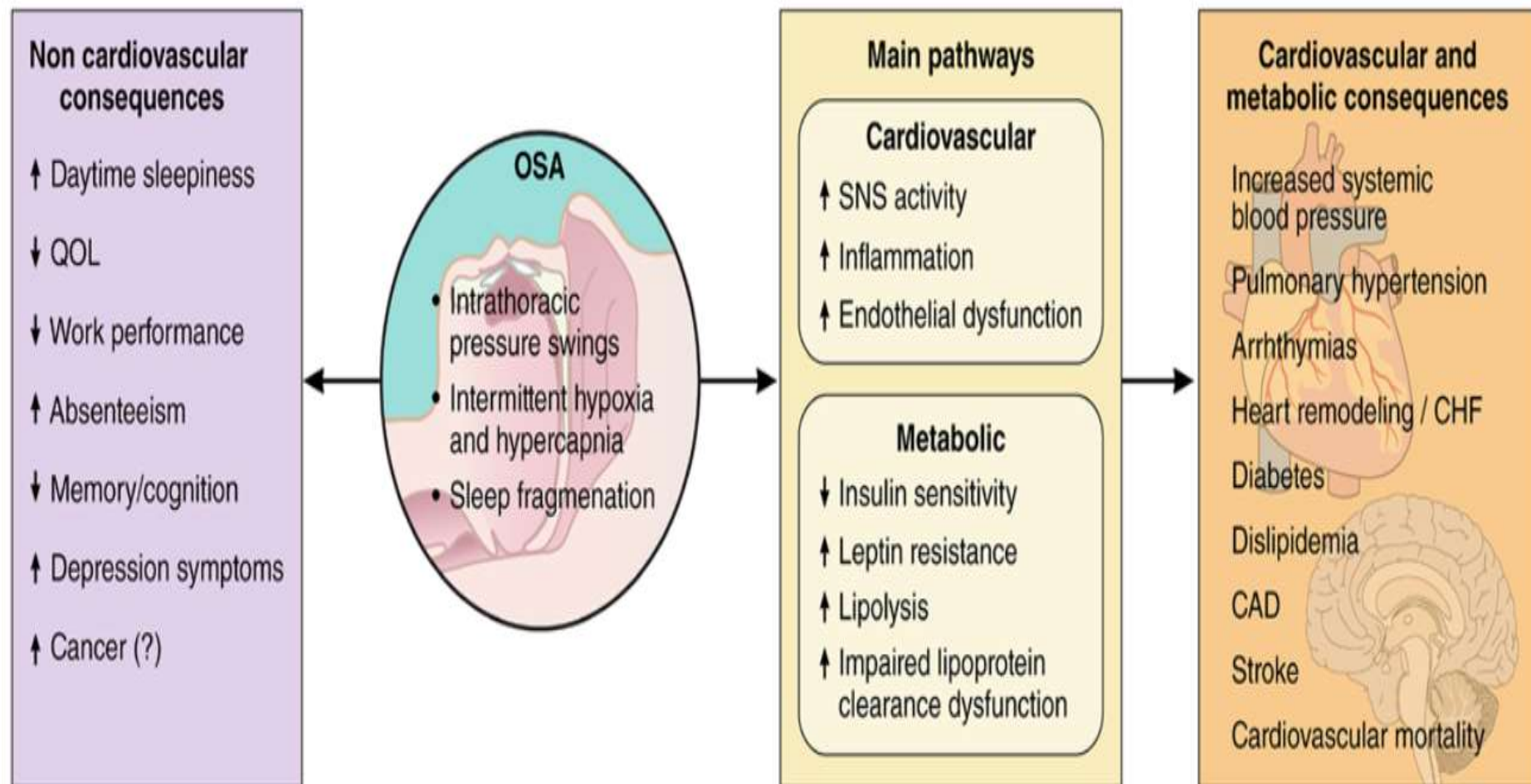
at least 4 hours/night,
compared with no CPAP

Am j resp crtic care med 2020

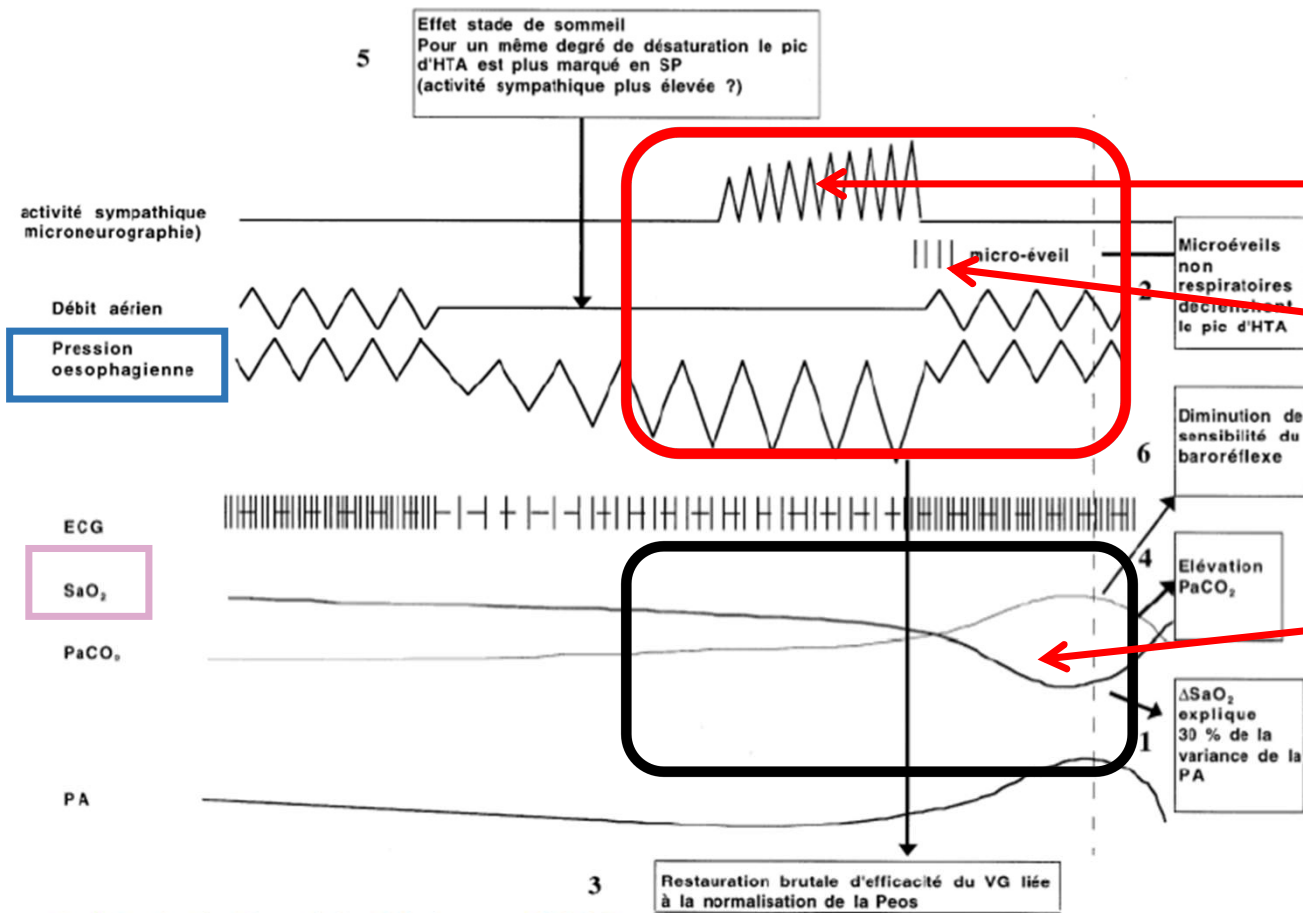
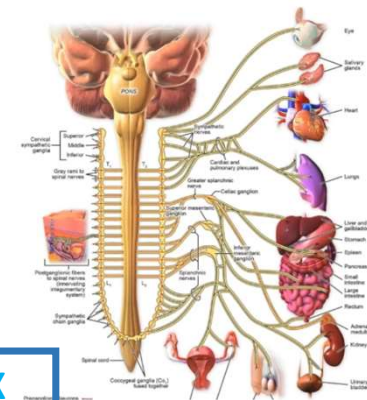
PHYSIOPATHOLOGIE

**INFLUENCE DU SNA
FONCTION ENDOTHELIALE,
SENSIBILITE A L INSULINE ,HVG ,IVG**

SAOS et SNA



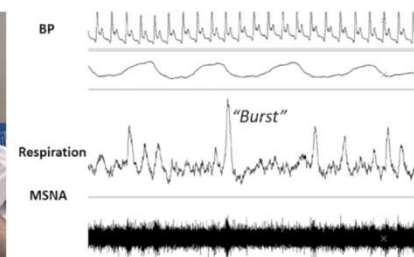
OUTILS DE DETECTION ET SNA



NOUVEAUX
OUTILS

POLYSOMNOGRAPHIE

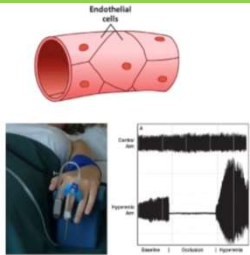
POLYGRAPHIE



POPULATION < 30 ANS SURPOIDS

Sympathetic activation is associated to Sub Clinical Organ Damage

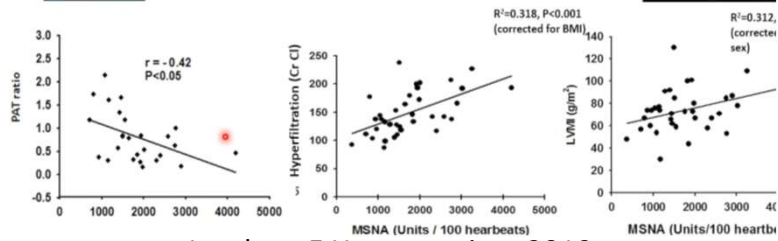
Endothelial Function



Renal Function

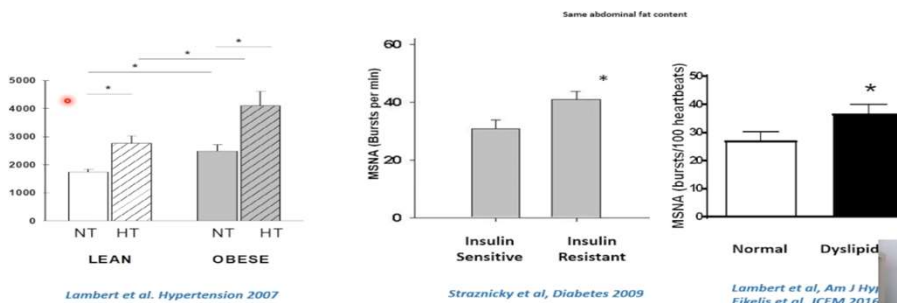


Cardiac Function



Lambert E Hypertension. 2010

Muscle SNA is influenced by the presence of elevated blood pressure, insulin sensitivity and dyslipidemia

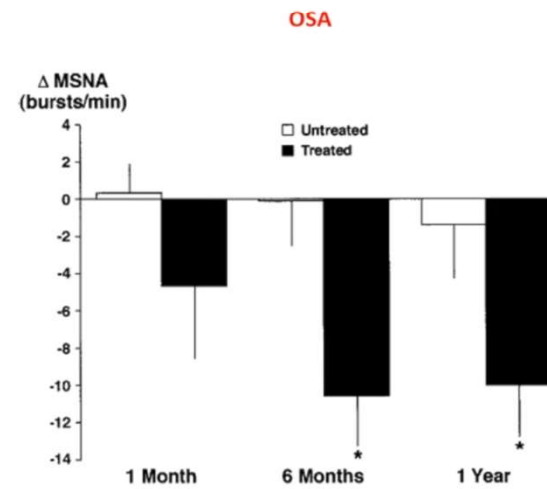


Lambert et al. Hypertension 2007

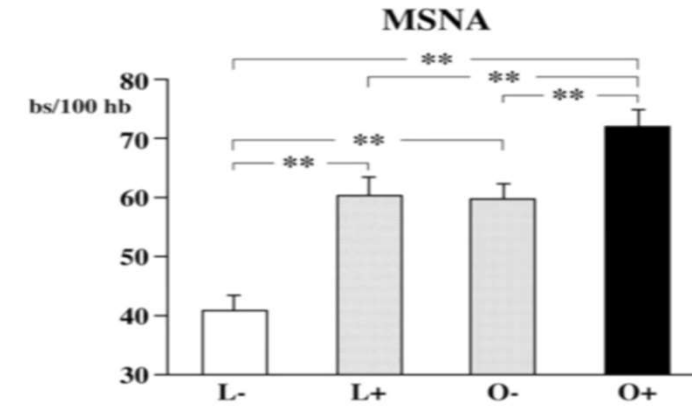
Straznicki et al. Diabetes 2009

Lambert et al. Am J Hypertens 2016

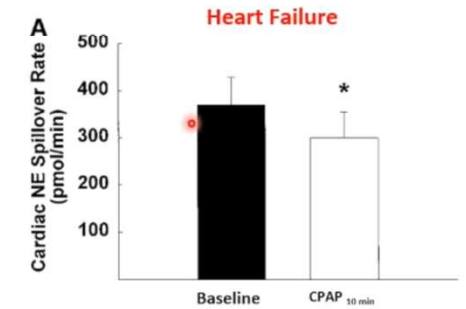
Influence of CPAP on SNS ac



Narkiewicz et al. Circulation 1999



Hypertension 2005;46:321-325



Kaye et al. Circulation 2001

TABLE 2. ENDPOINT OUTCOME MEASURES

	Control Group (n = 21)	CPAP Group (n = 19)	p Value*
LVEF, %			
Baseline	33.6 ± 2.6	37.6 ± 2.5	
3 mo	35.1 ± 3.1	42.6 ± 0.3	
Δ	1.5 ± 1.4	5.0 ± 1.0 [†]	0.04
UNE, nmol/mmol creatinine			
Baseline	21.3 ± 1.9	23.5 ± 4.8	
3 mo	22.9 ± 3.9	13.7 ± 2.5	
Δ	1.6 ± 3.7	-9.9 ± 3.6 [†]	0.036

Mansfield et al. Am J Respir Crit Care Med, 2004



DE LA NECESSITE D'UNE PRISE EN CHARGE PRECOCE

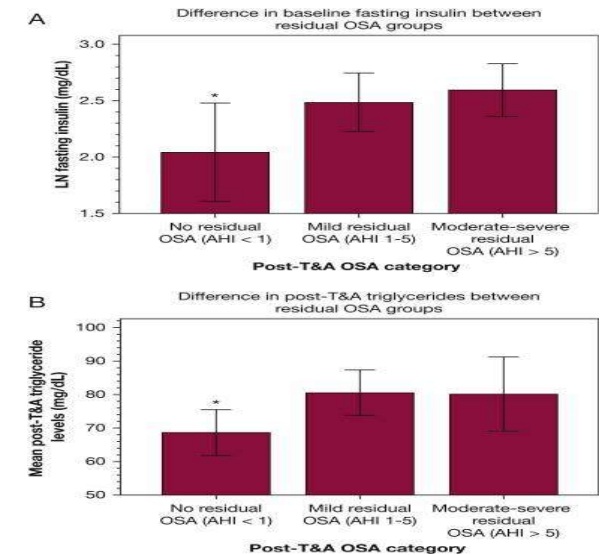
IMPACT OSA ENFANT GLYCEMIE HOMA IR HDL

- Fasting plasma insulin (FPI, $14.4 \pm 9.4 \rightarrow 12.6 \pm 9.7 \mu\text{IU/mL}$, $P = .008$),
- homeostasis model assessment-IR ($3.05 \pm 2.13 \rightarrow 2.62 \pm 2.22$, $P = .005$), and
- high-density lipoprotein (HDL) ($51.0 \pm 12.9 \rightarrow 56.5 \pm 14.4 \text{ mg/dL}$, $P = .007$)

improved despite increased BMI z score ($1.43 \pm 0.78 \rightarrow 1.52 \pm 0.62$, $P = .001$)

OSA in < 25% of all children and only 10% of obese children

**SENSIBILITE A L INSULINE
corrélée à l IAH résiduel post AA**



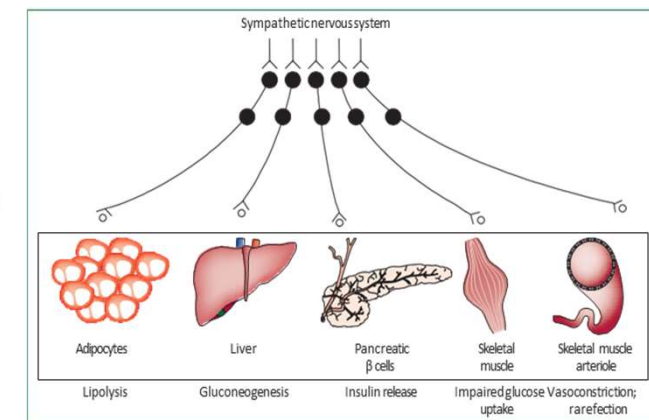
Metabolic syndrome: a sympathetic disease?

Markus Schlaich, Nora Straznicky, Elisabeth Lambert, Gavin Lambert

Metabolic syndrome is associated with adverse health outcomes and is a growing problem worldwide. Although efforts to harmonise the definition of metabolic syndrome have helped to better understand the prevalence and the adverse outcomes associated with the disorder on a global scale, the mechanisms underpinning the metabolic



Lancet Diabetes Endocrinol 2014
Published Online
April 2, 2014



Koren D, Gozal D. *Eur Respir J*. 2016;

Marinez-Ceron EAm J Respir Crit Care Med 2016

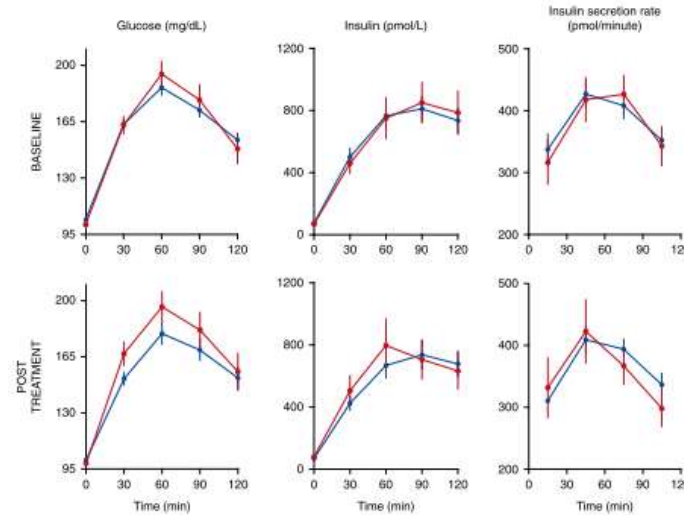
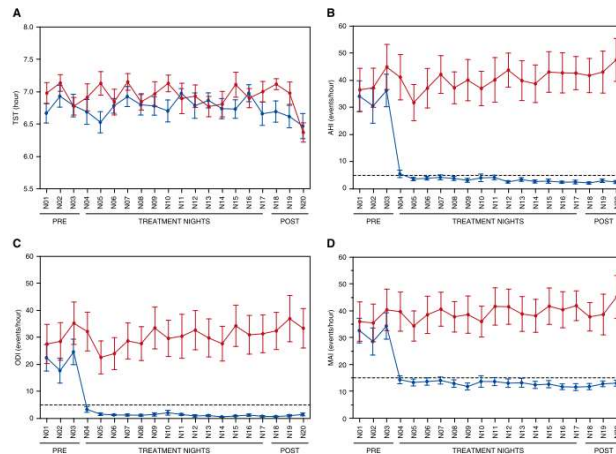
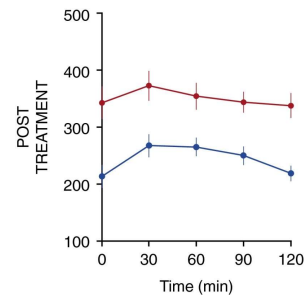
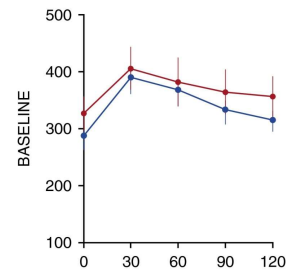
ORIGINAL ARTICLE

Eight Hours of Nightly Continuous Positive Airway Pressure Treatment of Obstructive Sleep Apnea Improves Glucose Metabolism in Patients with Prediabetes A Randomized Controlled Trial

Sushmita Pamidi¹, Kristen Wroblewski², Magdalena Stepień³, Khalid Sharif-Sidi³, Jennifer Kilkus³, Harry Whitmore³, and Esra Tasali³

¹Respiratory Division, Department of Medicine, McGill University, Montreal, Quebec, Canada; and ²Department of Public Health Sciences and ³Department of Medicine, University of Chicago, Chicago, Illinois

area under the curve for glucose during 2-hour oral glucose tolerance testing



Odi iah rera residuals

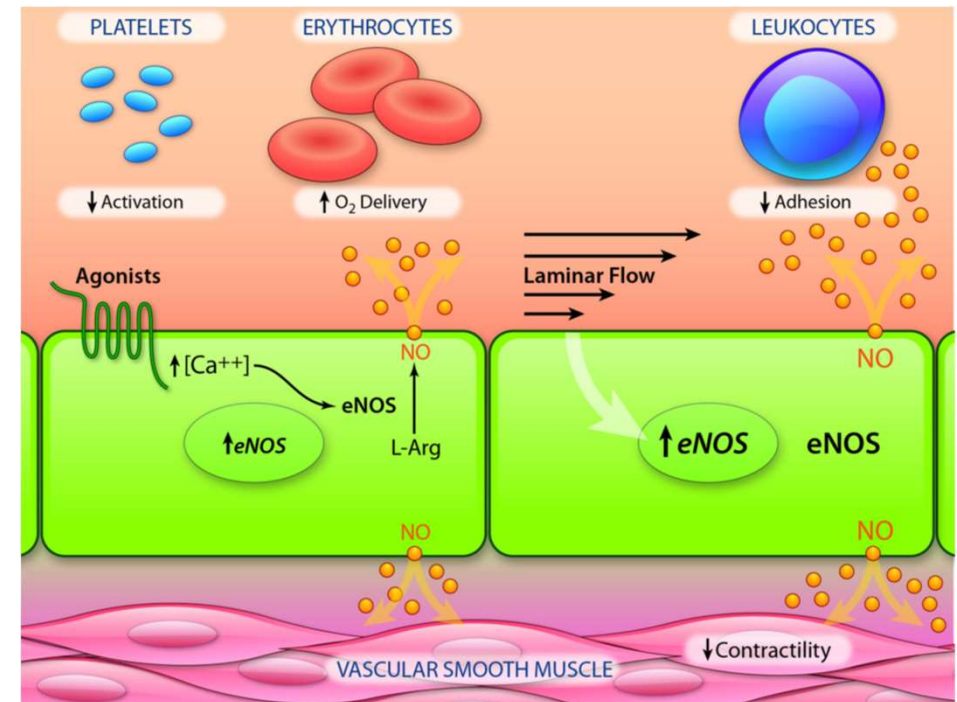
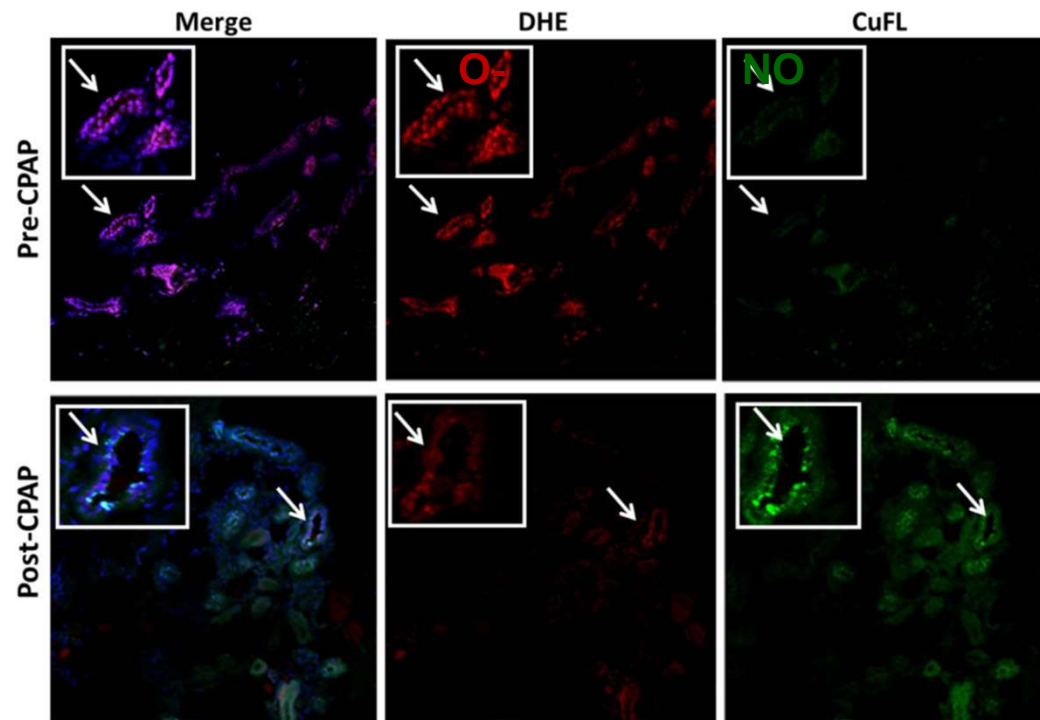
2 semaines
8h PPC / nuit pré-diabète
n = 26 or oral placebo n = 13

// noradrenaline

- ❑ The overall glucose response was reduced ($-1,276.9[\text{mg/dl}] \cdot \text{min}$ [95% CI, $-2,392.4$ to -161.5]; $P = 0.03$)
- ❑ insulin sensitivity was improved ($: 0.77 [\text{mU/L}](^{-1}) \cdot \text{min}(-1)$ [95% CI, 0.03 - 1.52]; $P = 0.04$)
- ❑ norepinephrine levels and 24-hour blood pressure were reduced

ENDOTHELIAL NITRIC OXIDE SYNTHASE UNCOUPLING: A NOVEL PATHWAY IN OSA INDUCED VASCULAR ENDOTHELIAL DYSFUNCTION

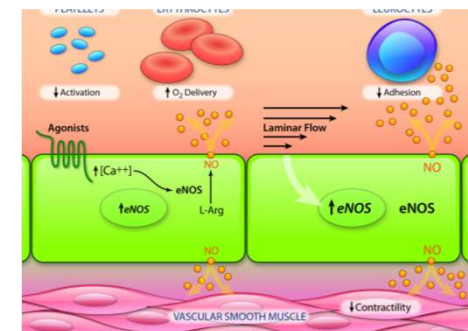
Saradhadevi Varadharaj, Ohio State University, Columbus, OH



FONCTION ENDOTHELIALE ET SAOS CHEZ L ENFANT

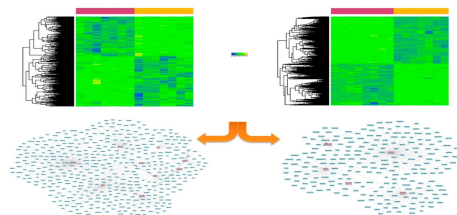
SENSIBILITE A L INSULINE

Circulating Plasma Extracellular Microvesicle MicroRNA Cargo and Endothelial Dysfunction in **Children** with Obstructive Sleep Apnea



ENDOTHELIAL FUNCTION IN CHILDREN WITH OSA

EFFECTS OF ADENOTONSILLECTOMY



expression of exosomal miRNA-630

- reduced in children with ED
- normalized after therapy

Plasma exosomes

- obese children
 - or nonobese children with OSA from endothelial cell
- RECAPITULATED ED**
- in naive human endothelial cells and also
 - *in vivo* when injected into mice

CHILDHOOD OSA IS AN INDEPENDENT DETERMINANT OF BLOOD PRESSURE IN ADULTHOOD

longitudinal follow-up study

TROS A 10 ANS HTA A 20 OR = 2.06

[Kate Ching-Ching Chan](#) THORAX 2020

47 HYPERTENSIVE PATIENTS (66.2%) BECAME NONHYPERTENSIVE AFTER SURGERY.

Characteristic	AT (n = 32)			Non-AT (n = 31)		
	Baseline	Reassessment	P Value ^a	Baseline	Reassessment	P Value ^a
Age, y	9.9 ± 2.6	10.7 ± 2.6	< .001	10.6 ± 3.1	11.3 ± 2.9	< .001
FMD %	7.7 ± 1.5	8.5 ± 1.2	< .001	8.5 ± 1	8.1 ± 0.9	.71

KATE C, CHEST JANUARY 2015

A khalyfa American Journal of Respiratory and Critical Care 2016 cho-hsueh lee Jama 2018

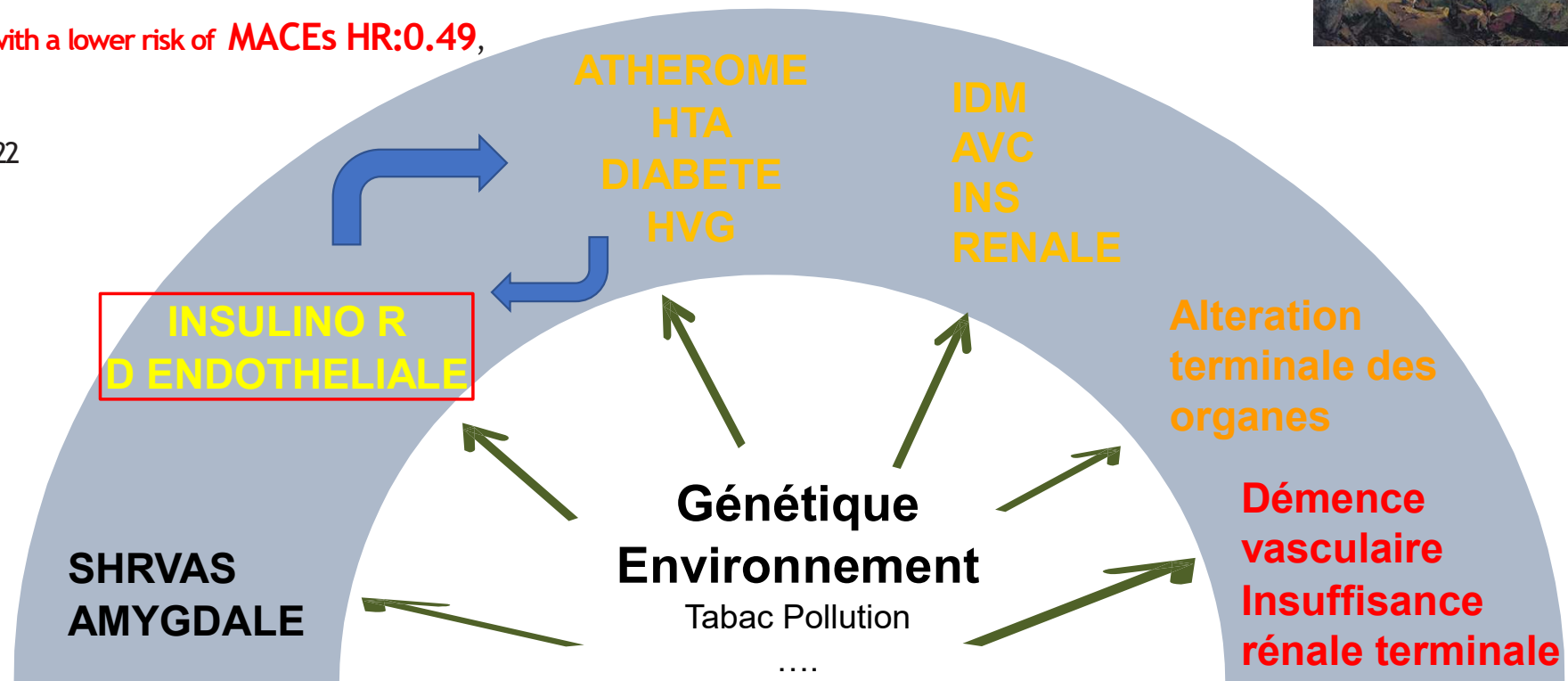
CARDIOVASCULAR DISEASE FROM CRADLE TO GRAVE



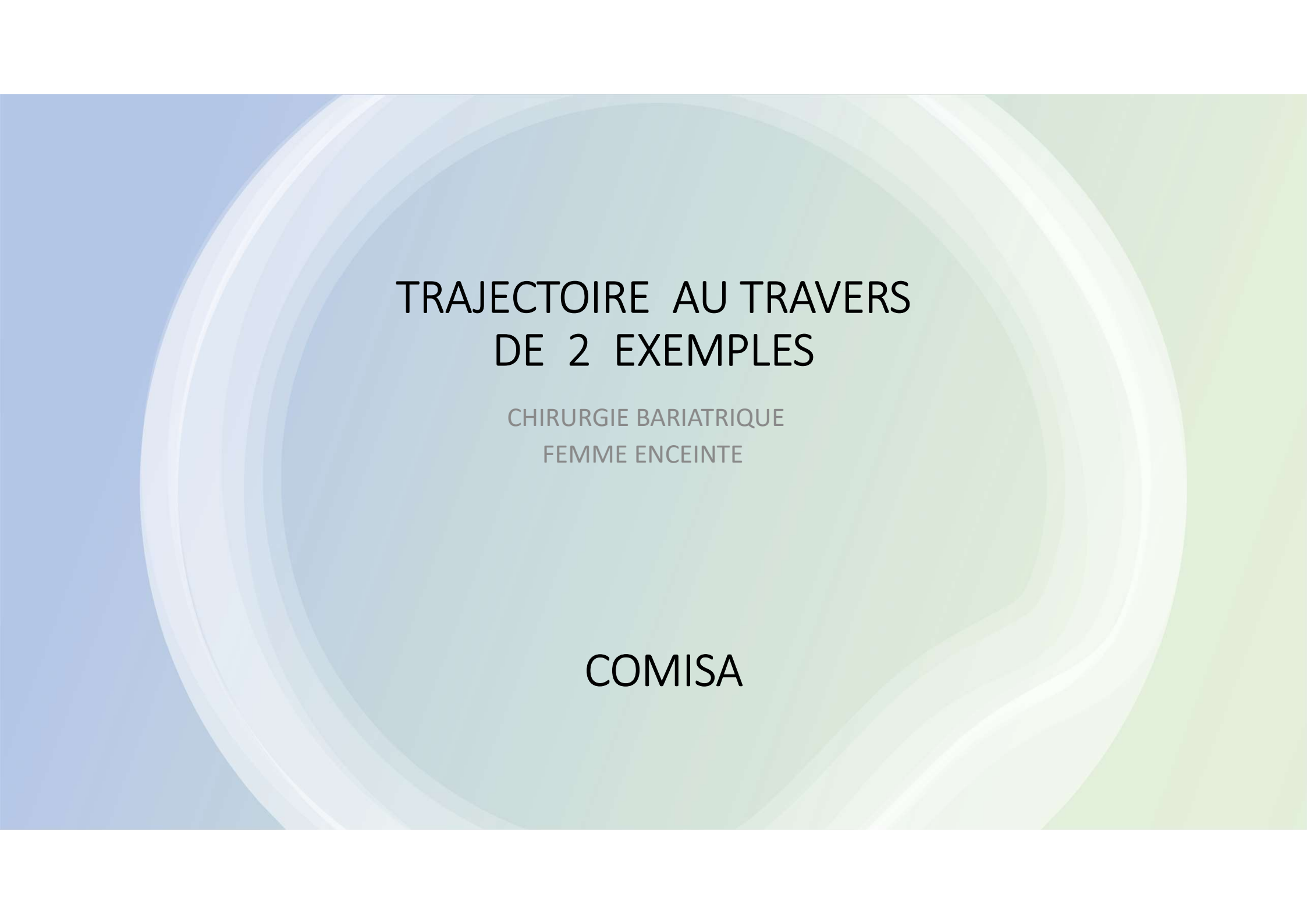
younger, **more obese**, had more severe OSA (higher AHI and TST90) and more cardiovascular risks, in whom **regular CPAP** was associated with a lower risk of **MACEs HR:0.49**, 95% CI 0.25 to 0.95)

EIM (**AHI $\geq$ 50**) (WMD = 0.073, 95% CI = 0.022 to 0.124, Z = 2.80, p = 0.005)

Pei-Hang Xu, BMJ 2022



After a certain amount of training in pediatrics, I concluded that there is no difference between pediatric medicine and adult medicine. Everything starts during childhood, and **what we see in adults is the result of what happened during childhood.**
C Guilleminault

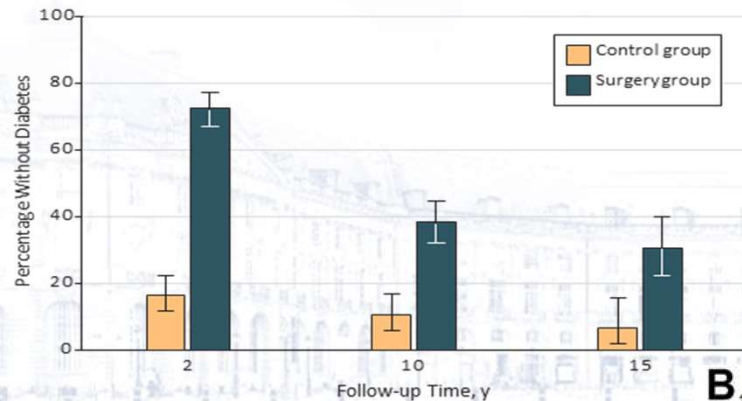


TRAJECTOIRE AU TRAVERS DE 2 EXEMPLES

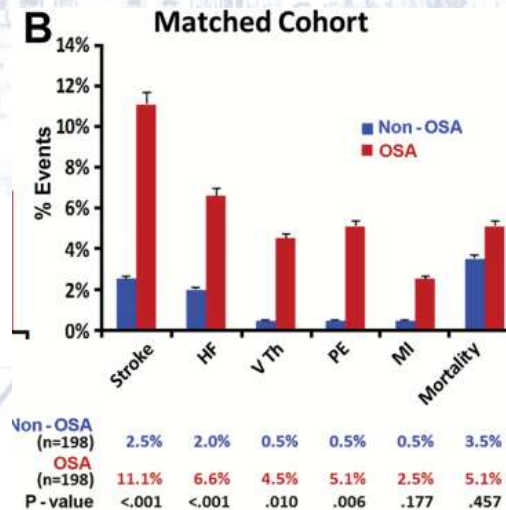
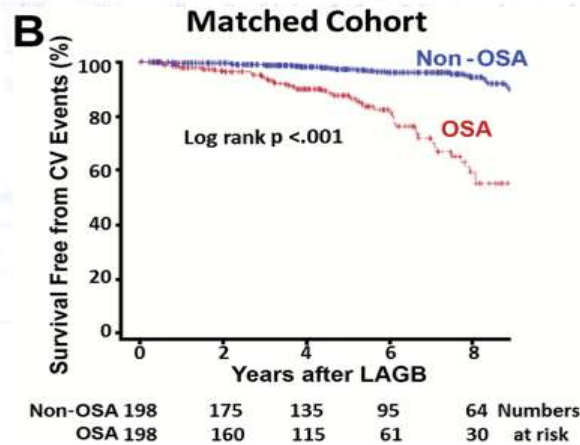
CHIRURGIE BARIATRIQUE
FEMME ENCEINTE

COMISA

SOMMEIL ET VISION CARDIO MÉTABOLIQUE DE LA CHIRURGIE BARIATRIQUE



type 2 diabetes remitted in 66 of 88 patients (75%) at 2 years, in 54 of 87 patients (62%) at 6 years, and in 43 of 84 patients (51%) at 12 years (BYPASS)



OSA HR: 6.92, 95% CI: 3.39–14.13, $p < 0.001$ remained an independent predictor of CV events after multivariate analysis

830 PATIENTS
LAPARO SLEEVE OU BYP
27 % OSA - 27 KG

sos study Lars Sjöström JAMA 2014

Ted D. Adams N Engl J Med. 2017

Dalmar sleepj 2018

CONGRÈS ANNUEL
DE LA SOCIÉTÉ FRANÇAISE ET FRANCOPHONE
DE CHIRURGIE DE L'OBÉSITÉ
ET DES MALADIES MÉTABOLIQUES



Bordeaux
2021

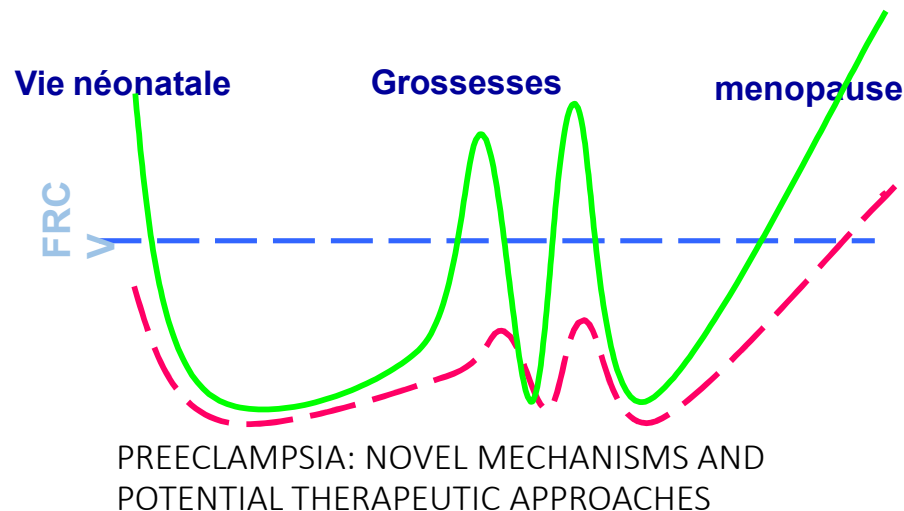
PREGNANCY OFFERS AN OPPORTUNITY TO IDENTIFY WOMEN AT-RISK OF FUTURE CVD

Zaher Armaly 2018 frontier in neurology

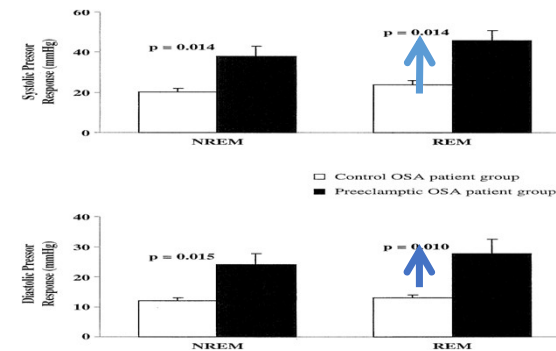
“ Les mères présentent une prédisposition génétique de pathologie cardiovasculaire en consequence ,la prééclampsie correspond plus a un stress-test qu'à une pathologie autonome “



HTA GRAVIDIQUE	OR 1.8
PREECLAMPSIE	2.19
DIABETE GESTATIONNEL	1.60
PRETERME	1.75



VULNERABILITE SNA ET ENDOTHELIALE



18

11

Edwards Am J hypert. 2001

Sattar N . BMJ 2002;

- Cluster analysis:
- - To detect patterns of association in symptoms
- - No assumptions or a priori hypotheses

SAOS ET PHENOTYPE



THE DIFFERENT CLINICAL FACES OF OBSTRUCTIVE SLEEP APNOEA: A CLUSTER ANALYSIS

- Cluster 1: **DISTURBED SLEEP GROUP (32.7%)**
- Cluster 2: **MINIMALLY SYMPTOMATIC GROUP (24.7%)**
- Cluster 3: **EXCESSIVELY SLEEPY GROUP (42.6%)**

INSOMNIE ET SAOS LE COMISA

39–58% OSA + Ins
Ins + OSA



Co-Morbid Insomnia and Sleep Apnea (COMISA): Prevalence, Consequences, Methodological Considerations, and Recent Randomized Controlled Trials

Alexander Sweetman brain science 2019

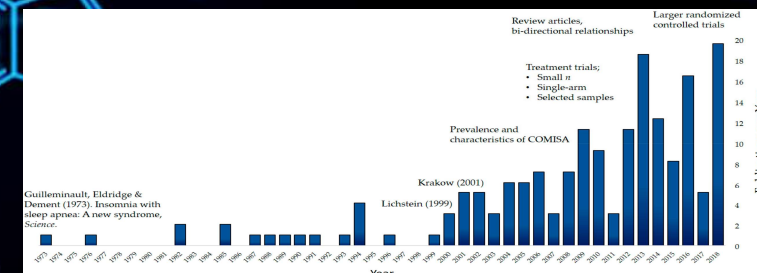


Figure 1. History of research in co-morbid insomnia and sleep apnea, including Guilleminault and colleague's 1973 article, and a lack of widespread research attention until two articles by Lichstein and colleagues (1999) and Krakow and colleagues (2001).

SYMPTOMATOLOGIE

FRAGMENTATION
SNA



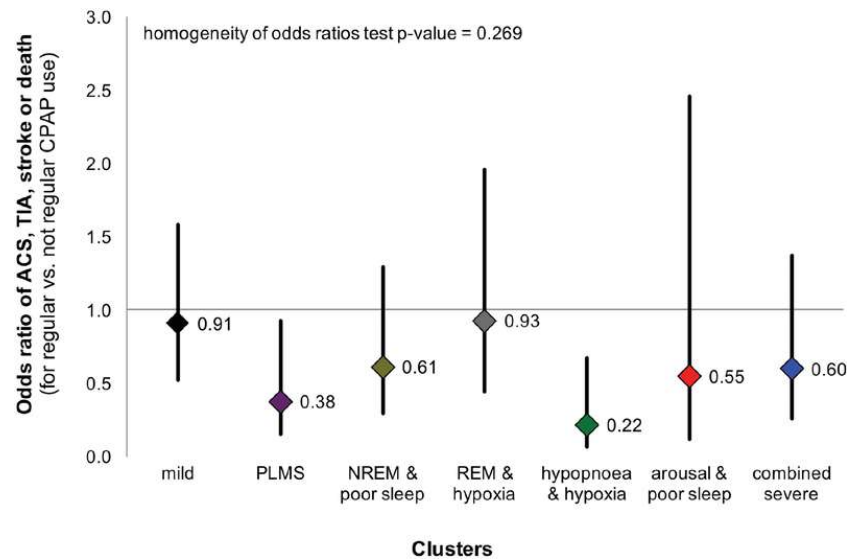
COMISA and incident hypertension in our fully adjusted models ([OR], 2.09; 95% [CI], 1.45–3.00) compared with SDB alone (OR, 1.55; 95% CI, 1.14–2.09)

11,623 Hispanic/Latino participants in the Hispanic Community Health Study/Study of Latinos (visit 1, 2008–2011; visit 2, 2014–2017
IAH 5 WHIIRC 9

SDB was associated with

- 1.54 higher adjusted odds of INCIDENT HYPERTENSION (95% [CI], 1.18-2.00)
- 1.33 higher odds of INCIDENT DIABETES (95% CI, 1.05-1.67) compared with no SDB.

Insomnia was associated with incident hypertension (odds ratio, 1.37; 95% CI, 1.11-1.69)



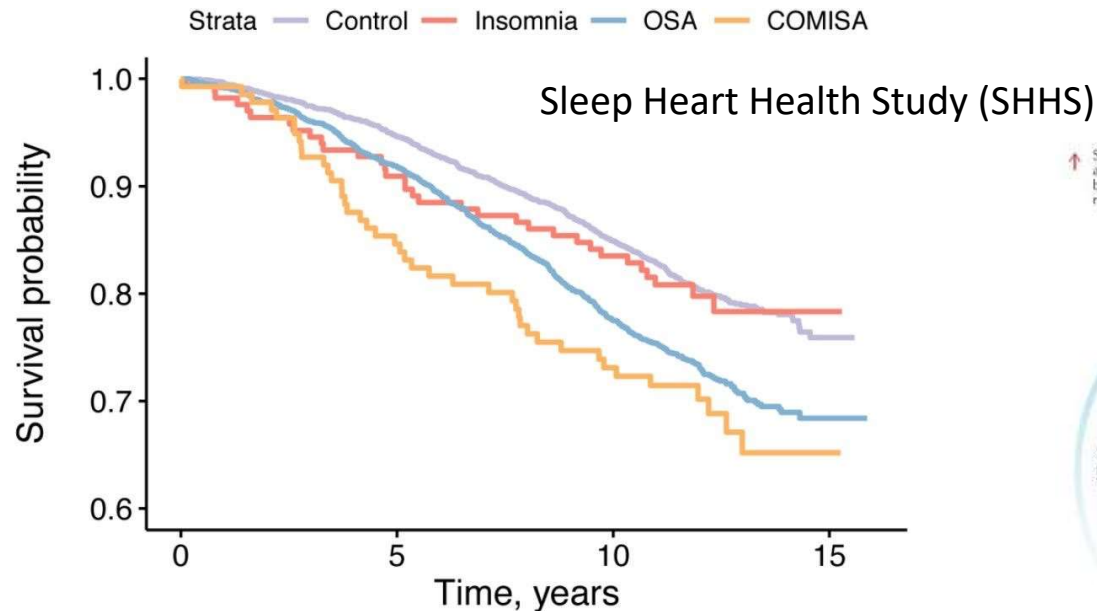
ZINCHUK THORAX 2018

Table E3. Effect estimates from survey logistic regression models for the association between comorbid SDB and insomnia and 6-year incident hypertension (N=6965) / diabetes (N=8023), HCHS/SOL (2008–2017)

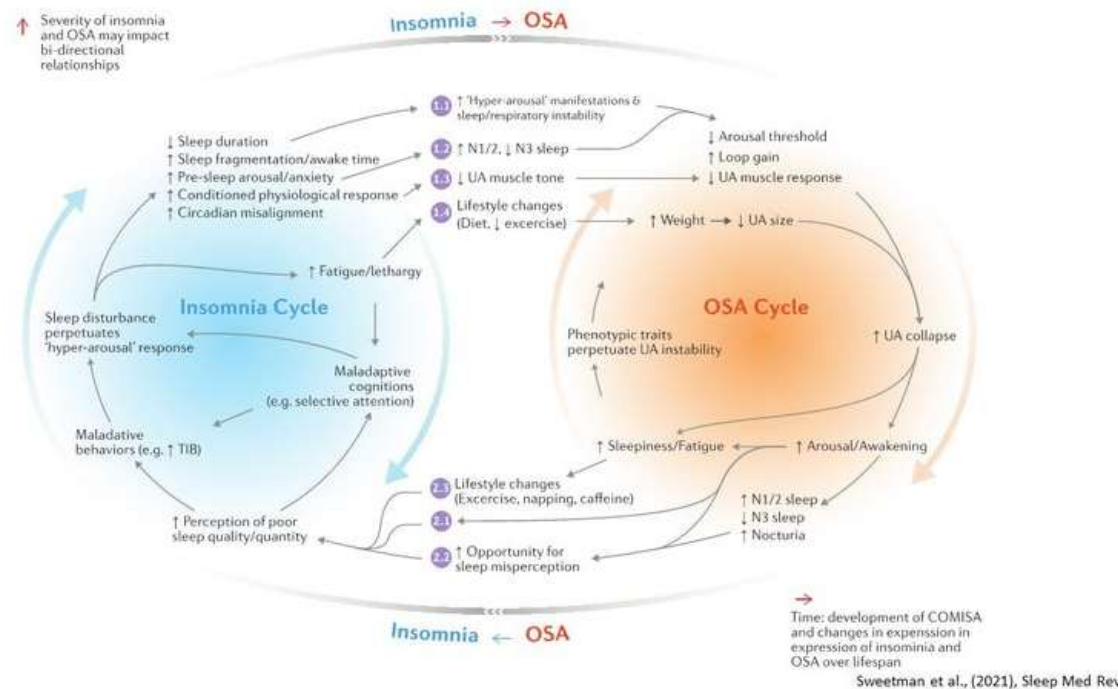
	Model 1		Model 2		Model 3	
	OR	[95% CI]	OR	[95% CI]	OR	[95% CI]
Hypertension						
Comorbid SDB and insomnia						
Neither SDB nor insomnia (ref)						
SDB	3.37 ***	[2.62, 4.34]	1.94 ***	[1.46, 2.57]	1.55 **	[1.14, 2.09]
Insomnia	1.82 ***	[1.43, 2.31]	1.43 **	[1.09, 1.88]	1.37 *	[1.04, 1.81]
SDB & insomnia	5.23 ***	[3.87, 7.07]	2.73 ***	[1.94, 3.85]	2.09 ***	[1.45, 3.00]
Diabetes						
Comorbid SDB and insomnia						
Neither SDB nor insomnia (ref)						
SDB	3.35 ***	[2.64, 4.26]	2.30 ***	[1.76, 2.99]	1.46 **	[1.10, 1.93]
Insomnia	1.58 **	[1.19, 2.12]	1.36 *	[1.00, 1.86]	1.25	[0.91, 1.72]
SDB & insomnia	3.83 ***	[2.81, 5.21]	2.36 ***	[1.71, 3.26]	1.41 *	[1.00, 1.99]

COMISA RISQUE MAJEUR

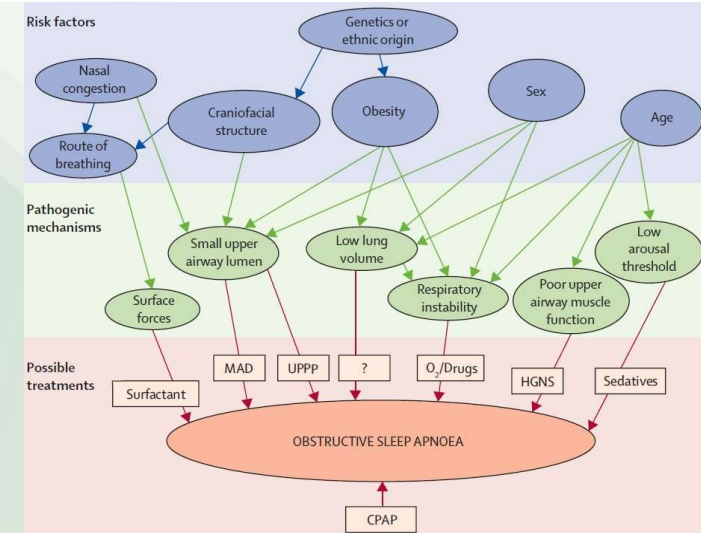
5236 2221 (42%) had OSA-alone, and 137 (3%) had COMISA



- **COMISA** was associated with a **47% (HR, 95% CI; 1.47 (1.06, 2.07)) increased risk of mortality**
- Insomnia-alone and OSA-alone were associated with higher risk of hypertension but not cardiovascular disease



INTERET DU TTT MULTIMODAL et PERSONNALISE



1 ENREGISTREMENT PRECOCE

2 KINE OROLINGUAL ORTHOPHONIE

3  SOH pneumo , KINE, ORL stimulation XII, orthodontiste, TCC

4 SPORT RHD

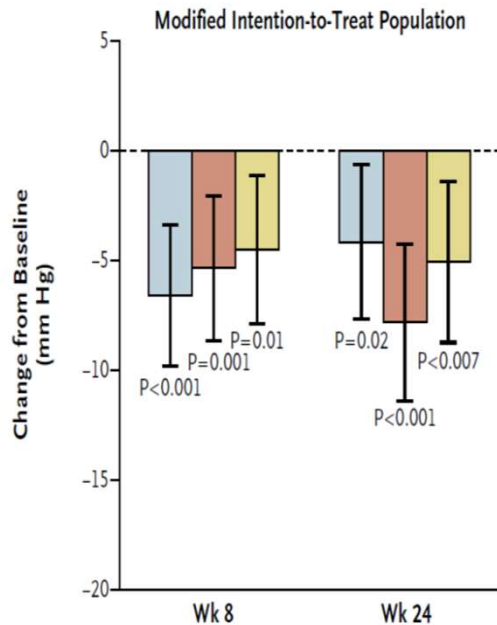


ORL
 PNEUMOLOGUE
 CARDIOLOGUE
 GENERALISTE
 ENDOCRINOLOGUE
 KINE OROLINGUALE
 ORTHODONTISTE
 PSYCHIATRE
 OSTEOPATHE
 COACH SPORTIF
 THERAPIE COMPORTEMENTALE
 CHIR MAXILOFACIALE
 CHIRURGIEN BARIATRIQUE
 DENTISTE

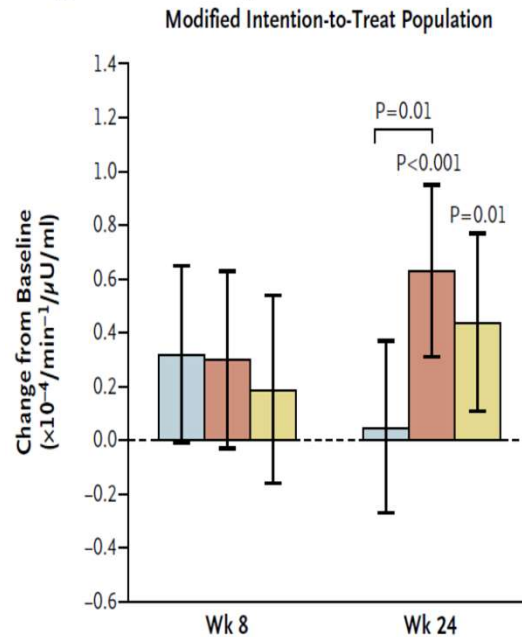
CPAP, WEIGHT LOSS, OR BOTH FOR OBSTRUCTIVE SLEEP APNEA

SYNERGIE HTA HOMA POIDS CRP

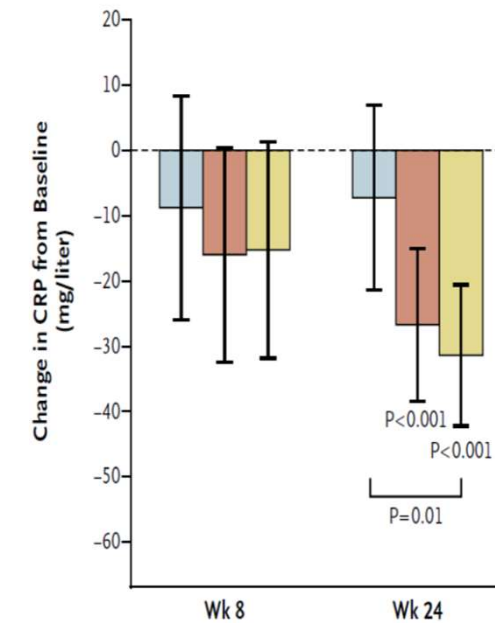
Change in Systolic Blood Pressure



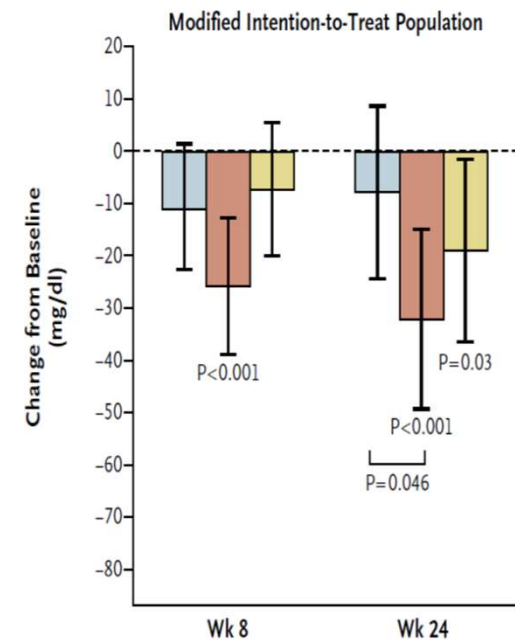
Change in Insulin Sensitivity Index



A Modified Intention-to-Treat Population



Change in Serum Triglyceride Levels



■ CPAP alone ■ Weight loss+CPAP ■ Weight loss alone

Chirinos JA

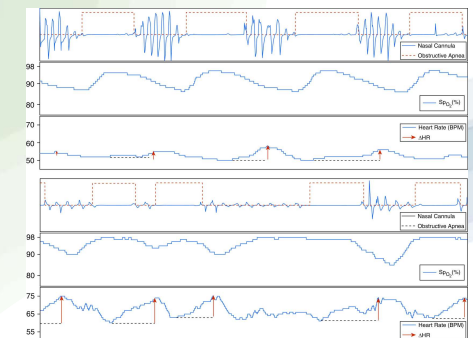
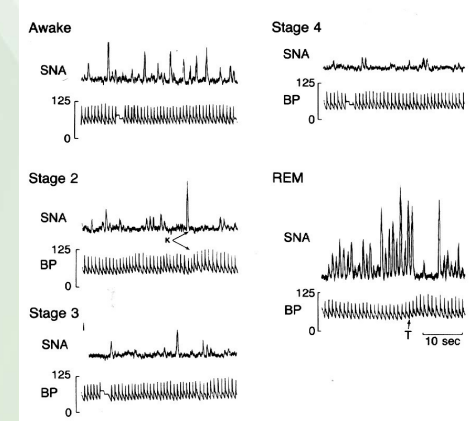
N Engl J Med 2014;370:2265-75

PPC

1 ACTEUR DE SA PRISE EN CHARGE / TRAJECTOIRE

2 ACCEPTABILITE ET OBSERVANCE REM (annonce ,TCC , sport ..

3 PRESSION ADAPTEE / SNA (EFFORT RESP)



“Our study suggests that there is, in fact, a subgroup of non-sleepy patients with OSA for whom CPAP could provide a reduction in risk—those with a higher pulse rate response to their respiratory events,” said Azarbarzin

Somers nejm 1993

Mini Symposium Cardiovascular Benefit of CPAP Is Modified by the Sleep Apnea Related Pulse Rate Response in Coronary Artery Disease Patients with Nonsleepy OSA: Findings from the RICCADSA Randomized Controlled Trial

A. Azarbarzin 1, A. Zinchuk 2, D. Wellman 1, L. Taranto Montemurro 1, D. Vena 1, L. Gell1, L. Messineo 1, D. White 1, D. J. Gottlieb 1, S. S. Redline 1, Y. Peker3

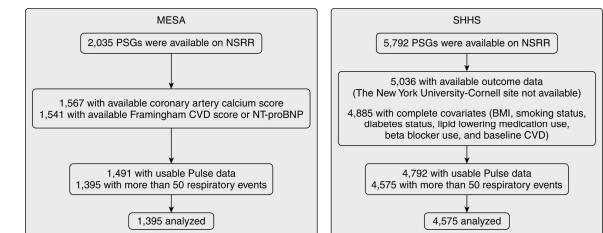
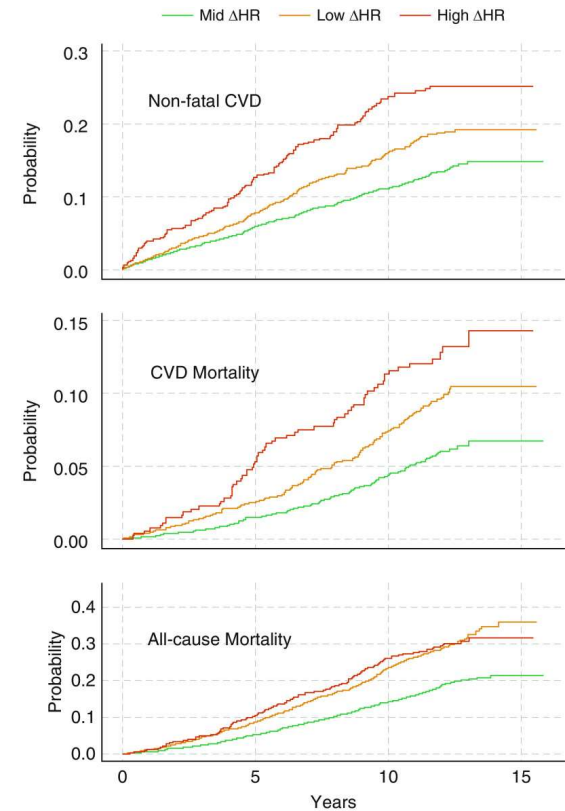
- **Δ HR WERE AT INCREASED RISK OF NONFATAL OR FATAL CVD AND ALL-CAUSE MORTALITY** (nonfatal adjusted hazard ratio [95% confidence interval (CI)], 1.60 [1.28-2.00]; fatal adjusted hazard ratio [95% CI], 1.68 [1.22-2.30]; all-cause adjusted hazard ratio [95% CI], 1.29 [1.07-1.55]).
 - The risk associated with a high Δ HR was particularly high in those with a substantial hypoxic burden (nonfatal, 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 **nonsleepy individuals**
- azarbazin mesa sleep heart study**

❑ at elevated Δ HR (10.8 BPM, +1SD) **treatment HR was 0.39** [0.15-0.98]

❑ in contrast to no significant effect at normal Δ HR (7.1 BPM)

NORMALIZED Δ HR MEASURES WERE STRONGER DETERMINANTS OF TREATMENT-RELATED RISK REDUCTION, arousal intensity, and event duration. “Treatment benefit is associated with greater normalized Δ HR (responsiveness) rather than just event severity

- AZARBAZIN AM J CRIT CARE 2021



MERCI