

Supplementary material

Supplementary Methods: Cohorts Studies

The Paris Prospective Study 3

The design and main objectives of the PPS3 have been published previously.¹ Briefly, it is an ongoing prospective observational cohort study on novel markers for the main phenotypes of cardiovascular disease in mostly healthy subjects. The study complies with the Declaration of Helsinki and the study-protocol was approved by the Ethics Committee of the Cochin Hospital (Paris, France). All volunteers were recruited after signing an informed consent form. Between June 2008 and June 2012, 10,157 men and women aged 50-75 years were recruited at a large preventive medical center, the Centre d'Investigations Préventives et Cliniques (IPC), in Paris (France). The IPC is a preventive medical center that offers a free medical examination every five years to all working and retired employees and their families. It is one of the largest medical centers of this kind in France, having carried out approximately 20,000 – 25,000 health examinations per year since 1970 for people living in the Paris area covering 11 million inhabitants (Paris and suburbs). The standard health check-up included a complete clinical examination including measurement of height, weight and blood pressure, coupled with standard biological tests after an overnight fast. A self-administered questionnaire provided information related to sleep habits, lifestyle (tobacco and alcohol consumption, physical activity, diet), personal and family medical history and current health status.

The CoLaus Study

The CoLaus study is a Swiss population-based observational prospective study investigating determinants of cardiovascular disease. A random sample of the population of Lausanne, Switzerland, was drawn and 6,733 subjects (age range 35-75 years) were recruited between 2003 and 2006. During the first follow-up of the cohort (median follow-up time 5.4 years), all subjects that responded (N=5,064) underwent a physical examination in the morning after an overnight fasting and responded to an extensive questionnaire covering demographic and medical history, health behaviors and sleep quality measures. A detailed description of the design, goals and methodology of the CoLaus Study has been published previously.² The institutional Ethics Committee of the University of Lausanne, which afterwards became the Ethics Commission of Canton Vaud approved the baseline CoLaus study (reference 16/03); the approval was renewed for the first follow-up (reference 33/09). The study was performed in agreement with the Helsinki declaration and its former amendments, and in accordance with the applicable Swiss legislation. All participants gave their signed informed consent before entering the study.

Supplementary Methods: Ideal Cardiovascular Health Metrics.

Body weight and height were measured using a calibrated scale and a vertical stadiometer, respectively (Seca®, Hamburg, Germany). **Body mass index** (BMI) was calculated and categorized according to the AHA criteria.³ Ideal BMI corresponded to a value lower than 25 kg/m². As time since **smoking** cessation was not available in CoLaus, to obtain harmonized definition in both cohorts, smoking status was adapted from the AHA criteria in both cohorts,

and an ideal smoking status was assigned to subjects who never smoked. **Physical activity** was assessed through questions on the frequency of daily walking, sports activities, and recreational activities in PPS3 and information on physical activity in CoLaus stemmed from the physical activity frequency questionnaire (PAFQ). This questionnaire has been validated in the population of Geneva and assesses the type and duration of 70 kinds of (non-) professional activities and sports during the previous week.⁴ In both cohorts, we summed up the duration of all walking items including slow cycling and we considered fast/uphill walking as vigorous activity and summed up the frequency of vigorous activity and sports per week. Subjects who reported walking at least one hour every day or who were practicing sports three times or more per week were categorized as having ideal physical activity. To construct the **diet metric**, we adapted the measure from the AHA criteria as sodium intake was not available in CoLaus and information on fiber was not available in PPS3. To harmonize the definition of diet in both cohorts, the metric was constructed from the intake of fruits and vegetables, fish and sugar-sweetened beverages. Subjects reporting to have a high consumption of fruits and vegetables per day (at least 787 g/day in CoLaus, and at least four times a week in PPS3) and fish (at least 198 g/week in CoLaus and at least two times a week in PPS3) as well as low consumption of sugar-sweetened beverages (less than 153 mL/day in CoLaus and never in PPS3) were considered as having an ideal diet. In CoLaus, the dietary intake was assessed using a self-administered, semi-quantitative food frequency questionnaire (FFQ), which has been validated in the Geneva population.^{5,6} In PPS3, dietary intakes were assessed from an adapted version of the self-reported food frequency questionnaire New Alimentary Self Questionnaire which has been validated against a dietetic interview in France.⁷ From a fasting venous blood sample, ideal **total cholesterol** and ideal **fasting plasma glucose** were defined as untreated values <5.18 mmol/L

and <5.55 mmol/L, respectively. Ideal **blood pressure** was defined as an untreated value <120/80 mmHg.

References

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Supplementary table 1: Number of metrics at ideal level for global, behavioral and biological cardiovascular health (CVH).

	Level of cardiovascular health		
	Poor	Intermediate	Ideal
Global CVH	0 – 2	3 – 4	5 – 7
Behavioral CVH	0 – 1	2	3 – 4
Biological CVH	0 – 1	2	3

Supplementary table 2: Distribution of each component of the definition for the proxy for sleep-disordered breathing, in Paris

Prospective Study 3 (PPS3, France) and CoLaus (Switzerland).

	PPS3			CoLaus		
	No-SDB	SDB	p-value	No-SDB	SDB	p-value
Frequency of snoring			<0.001			<0.001
<i>Never*/never†</i>	1,460 (33.7)	0 (0)		1,984 (82.8)	0 (0)	
<i>Rarely*/less than 1 per week†</i>	2,809 (64.7)	0 (0)		356 (14.9)	0 (0)	
<i>Regularly*/1-2 times per week†</i>	39 (0.9)	1,297 (61.7)		28 (1.2)	286 (48.1)	
<i>Often*/3-4 times per week†</i>	30 (0.7)	806 (38.3)		26 (1.1)	309 (51.9)	
Male	2,488 (57.4)	1,627 (77.4)	<0.001	1,254 (46.8)	233 (75.4)	<0.001
Age >55	3,061 (70.6)	1,489 (70.8)	0.87	1,330 (49.6)	184 (59.6)	0.001
BMI >30	267 (6.2)	273 (13.0)	<0.001	345 (12.9)	79 (25.6)	<0.001
Hypertension	1,317 (30.4)	832 (39.6)	<0.001	953 (35.6)	155 (50.2)	<0.001
Excessive daytime sleepiness	597 (13.8)	484 (23.0)	<0.001	265 (9.9)	61 (19.7)	<0.001

* PPS3; † CoLaus. BMI, body mass index; SDB, sleep-disordered breathing

Supplementary table 3: Characteristics of the included and excluded subjects in Paris Prospective Study 3 (PPS3, France) and CoLaus (Switzerland).

	PPS3			CoLaus		
	Included (N=6,441)	Excluded (N=2,142)	p-value	Included (N=2,898)	Excluded (N=2,075)	p-value
Male gender	4,115 (63.9)	947 (44.2)	<0.001	1,487 (49.8)	870 (41.9)	<0.001
Age (years)	59.3 ± 6	61.4 ± 6	<0.001	56.4 ± 10	59.7 ± 11	<0.001
Education level			<0.001			<0.001
<i>Low</i>	1,707 (26.5)	747 (36.5)		1,410 (47.2)	1,264 (61.1)	
<i>Middle</i>	1,186 (18.4)	336 (16.4)		825 (27.6)	481 (23.2)	
<i>High</i>	3,548 (55.1)	965 (47.1)		754 (25.2)	325 (15.7)	
Living alone	1,428 (22.2)	718 (33.5)	<0.001	1,230 (41.1)	925 (45.6)	0.002
Alcohol			0.001			0.009
<i>Never</i>	881 (13.4)	283 (13.5)		616 (20.6)	274 (24.3)	
<i>1-2 drinks/day</i>	4,960 (77.0)	1,560 (74.2)		2,301 (77.1)	817 (72.6)	
<i>≥3 drinks/day</i>	823 (12.8)	258 (12.3)		69 (2.3)	35 (3.1)	
Depressive status	483 (7.5)	224 (10.5)	<0.001	367 (12.3)	234 (18.0)	<0.001
Sleep medications	635 (9.9)	270 (12.6)	<0.001	362 (12.1)	399 (19.23)	<0.001

Supplementary table 4: Results of multivariate regression analyses between cardiovascular health and insomnia symptoms/sleep duration in Paris Prospective Study 3 (PPS3, France, N=6,441) and CoLaus (Switzerland, N=2,989).

	Insomnia symptoms OR (95% CI)	Sleep duration	
		≤6 hours per night RRR (95% CI)	≥9 hours per night RRR (95% CI)
PPS3			
Global CVH			
Poor	1 (ref.)	1 (ref.)	1 (ref.)
Intermediate	0.91 (0.78 – 1.07)	0.93 (0.83 - 1.05)	0.76 (0.60 - 0.97)
Ideal	0.90 (0.69 – 1.17)	0.88 (0.72 - 1.08)	0.79 (0.52 - 1.19)
Behavioral CVH			
Poor	1 (ref.)	1 (ref.)	1 (ref.)
Intermediate	0.99 (0.83-1.17)	0.95 (0.84 - 1.08)	0.82 (0.64 - 1.07)
Ideal	0.94 (0.77-1.14)	0.87 (0.75 - 1.01)	0.81 (0.60 - 1.09)
Biological CVH			
Poor	1 (ref.)	1 (ref.)	1 (ref.)
Intermediate	1.03 (0.86-1.23)	1.01 (0.88 - 1.16)	1.00 (0.75 - 1.33)
Ideal	0.67 (0.44-1.00)	1.02 (0.77 - 1.34)	0.85 (0.44 – 1.63)
CoLaus			
Global CVH			
Poor	1 (ref.)	1 (ref.)	1 (ref.)
Intermediate	0.78 (0.56 - 1.07)	0.89 (0.66 - 1.20)	0.78 (0.37 - 1.63)
Ideal	0.62 (0.35 - 1.10)	0.63 (0.37 - 1.08)	1.05 (0.29 – 3.79)
Behavioral CVH			
Poor	1 (ref.)	1 (ref.)	1 (ref.)
Intermediate	1.00 (0.71 - 1.38)	0.90 (0.67 - 1.21)	0.80 (0.38 - 1.65)
Ideal	0.86 (0.56 - 1.32)	0.75 (0.50 - 1.13)	0.89 (0.34 - 2.34)
Biological CVH			
Poor	1 (ref.)	1 (ref.)	1 (ref.)
Intermediate	0.88 (0.60 – 1.27)	0.62 (0.42 - 0.90)	0.73 (0.27 - 1.97)
Ideal	0.56 (0.25 – 1.26)	0.92 (0.51 - 1.65)	0.77 (0.10 - 6.11)

Abbreviations: OR: odds ratio (from multivariate logistic regression), RRR: relative risk ratio (from multinomial logistic regression), CI: confidence interval, CVH: cardiovascular health.

Supplementary table 5: Results of sensitivity analyses between cardiovascular health and sleep disturbances in the Paris Prospective Study 3 (PPS3, France, N=6,441) and CoLaus (Switzerland, N=2,989).

	Sleep duration				
	SDB OR (95% CI)	EDS OR (95% CI)	Insomnia symptoms OR (95% CI)	≤6 hours per night RRR (95% CI)	≥9 hours per night RRR (95% CI)
With all the 7 metrics available *					
PPS3 - Global CVH					
Poor CVH	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Intermediate	0.60 (0.54 - 0.67)	0.83 (0.72 - 0.95)	0.88 (0.76 - 1.04)	0.92 (0.81 - 1.03)	0.68 (0.54 - 0.86)
Ideal	0.34 (0.19 - 0.55)	1.15 (0.71 - 1.81)	0.83 (0.47 - 1.40)	1.05 (0.69 - 1.60)	1.06 (0.49 - 2.26)
CoLaus – Global CVH					
Poor CVH	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Intermediate	0.54 (0.43 - 0.68)	1.07 (0.82 - 1.42)	0.79 (0.56 - 1.10)	0.84 (0.61 - 1.15)	0.76 (0.31 - 1.83)
Ideal	0.35 (0.22 - 0.54)	0.84 (0.54 - 1.30)	0.63 (0.35 - 1.12)	0.56 (0.32 - 0.98)	1.09 (0.28 - 4.22)
Using all available information on smoking and diet metrics †					
PPS3 - Global CVH					
Poor	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Intermediate	0.61 (0.55 - 0.69)	0.82 (0.72 - 0.95)	0.86 (0.76 - 1.04)	0.93 (0.82 - 1.04)	0.70 (0.55 - 0.88)
Ideal	0.45 (0.38 - 0.57)	0.93 (0.74 - 1.16)	0.96 (0.75 - 1.23)	0.98 (0.81 - 1.19)	0.69 (0.46 - 1.04)
CoLaus – Global CVH					
Poor	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Intermediate	0.54 (0.43 - 0.66)	1.04 (0.80 - 1.35)	0.73 (0.53 - 1.00)	0.87 (0.64 - 1.17)	0.45 (0.20 - 1.03)
Ideal	0.35 (0.23 - 0.55)	0.79 (0.51 - 1.00)	0.65 (0.37 - 1.16)	0.62 (0.36 - 1.09)	0.95 (0.27 - 3.42)

Simultaneous adjustment for the 4 sleep disturbances^{††}

PPS3 - Global CVH

Poor	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Intermediate	0.66 (0.59 - 0.74)	0.88 (0.76 - 1.02)	0.91 (0.77 - 1.08)	0.98 (0.86 - 1.11)	0.77 (0.60 - 0.99)
Ideal	0.45 (0.36 - 0.55)	0.91 (0.71 - 1.16)	0.92 (0.70 - 1.21)	0.92 (0.74 - 1.15)	0.81 (0.53 - 1.23)

CoLaus – Global CVH

Poor	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
Intermediate	0.54 (0.44 - 0.67)	1.15 (0.88 - 1.51)	0.81 (0.58 - 1.12)	0.95 (0.69 - 1.29)	0.82 (0.39 - 1.74)
Ideal	0.35 (0.23 - 0.55)	0.91 (0.60 - 1.40)	0.68 (0.38 - 1.23)	0.71 (0.41 - 1.24)	1.14 (0.32 - 4.14)

After excluding BMI and hypertension from the definition of CVH, without adjustment on sex

PPS3 - Global CVH

Poor	1 (ref)	-	-	-	-
Intermediate	0.78 (0.69 – 0.90)	-	-	-	-
Ideal	0.45 (0.34 – 0.58)	-	-	-	-

CoLaus – Global CVH

Poor	1 (ref)	-	-	-	-
Intermediate	0.68 (0.52 – 0.89)	-	-	-	-
Ideal	0.49 (0.28 – 0.86)	-	-	-	-

Sleep duration measured by polysomnography in CoLaus (N=1,404)

CoLaus – Global CVH

Poor		1 (ref.)	1 (ref.)
Intermediate		0.94 (0.71 – 1.24)	1.55 (0.60 – 4.00)
Ideal		0.71 (0.44 – 1.14)	1.65 (0.46 – 5.91)

Abbreviations: OR: odds ratio (from multivariate logistic regression), RRR: relative risk ratio (from multinomial logistic regression), CI: confidence interval, CVH: cardiovascular health, BMI: body mass index.

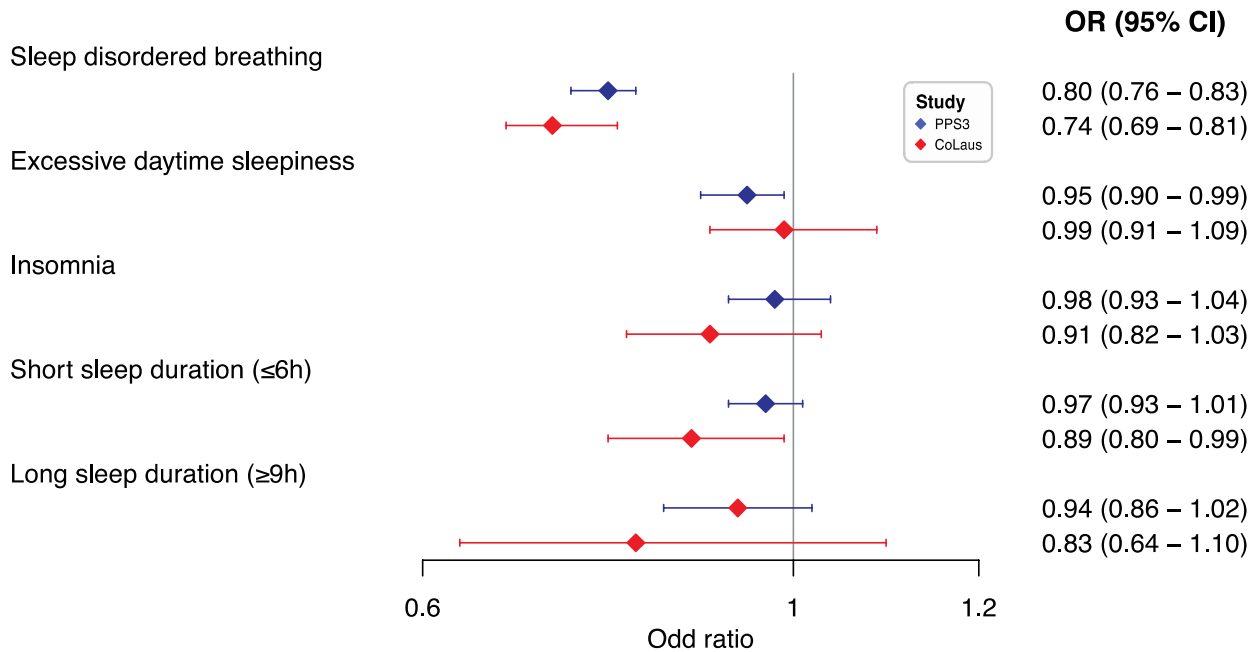
* subjects with any missing CVH metric excluded.

† CVH constructed with all available information in each cohort (i.e. adding the consumption of sodium in PPS3 and fiber in CoLaus for the diet metric, and taking into account time since smoking cessation in PPS3 for the smoking metric).

†† analyses were simultaneously adjusted for the 4 sleep disturbances.

Supplementary figure 1: Forest plot: odds ratios of sleep disturbances for global cardiovascular health measured as a continuous variables A) per additional metric at the ideal level (from 0 to 7) and B) per 1 point increase in the score of cardiovascular health (from 0 to 14).

A) Odds ratio for global CVH score (0 to 7) and sleep complaints



B) Odds ratio for global CVH score (0 to 14) and sleep complaints

