Title: Cardiovascular Health and Sleep Disturbances in two Population-based Cohort Studies

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Abstract

Objective: We aimed to investigate the association between cardiovascular health (CVH), as defined by the American Heart Association, and several sleep disturbances.

Methods: Two community-based cohorts, the Paris Prospective Study 3 (PPS3, France, n=6,441) and the CoLaus study (Switzerland, n=2,989) were analyzed. CVH includes 7 metrics which all can be classified as poor, intermediate and ideal. Global CVH score was categorized into poor (0-2 ideal metrics), intermediate (3-4 ideal metrics) and ideal (≥5 ideal metrics). Associations between global CVH and self-reported sleep disturbances [proxy of sleep-disordered breathing (SDB), excessive daytime sleepiness, insomnia symptoms and short/long sleep duration] and SDB severity measured by polysomnography (PSG) were investigated. Adjusted odds ratio (OR)/relative risk ratio (RRR) and 95% confidence intervals (CI) were estimated. Subjects with previous cardiovascular disease were excluded.

Results: Compared to poor CVH, subjects with intermediate and ideal global CVH had lower odds of self-reported SDB in both cohorts (ORs up to 0.55; 95% CI 0.44-0.68 and 0.35; 95% CI 0.22-0.53, respectively) and had lower SDB severity measured by PSG (RRR up to 0.07; 95% CI 0.02-0.20) in CoLaus. Subjects with intermediate and ideal global CVH had lower odds of excessive daytime sleepiness in PPS3 (ORs 0.82; 0.72-0.95 and 0.80; 0.82-1.02, respectively). No consistent associations were found between CVH and sleep duration or insomnia symptoms.

Conclusions: Higher levels of CVH are associated with lower odds of SDB and excessive daytime sleepiness. However, causal interpretation cannot be made and associations might be bidirectional.

Key questions

What is already known about this subject?

- Single cardiovascular risk factors are associated with sleep disturbances.
- Although cardiovascular risk factors usually cluster, their combined effect on sleep disturbances remains unknown.

What does this study add?

- In two population-based cohort studies, higher cardiovascular health - a cluster of modifiable cardiovascular risk factors defined by the American Heart Association – was associated with lower odds of self-reported and objectively measured sleep disordered breathing (odd ratio up to 0.35; 95% confidence interval 0.22-0.53) and excessive daytime sleepiness (odd ratio up to 0.82; 95% confidence interval 0.72-0.95).

How might this impact on clinical practice?

- Given the high prevalence of sleep disordered breathing and excessive daytime sleepiness in the population and their adverse health consequences, promoting higher cardiovascular health to prevent the development of risk factors associated with sleep disordered breathing and excessive daytime sleepiness has the potential for important public health implications.

Introduction

The prevalence of sleep disturbances such as sleep-disordered breathing (SDB, 23% in women and 50% in men),[1] excessive daytime sleepiness (EDS, 20%),[2] insomnia (17%)[3] and short or long sleep durations (35%),[4] is increasing in the population.[3,5] These sleep disturbances have been linked to poor quality of life,[6] increased risk of dementia[7] and cardiovascular disease (CVD), and higher mortality.[8–10] Therefore, identifying modifiable risk factors for sleep disturbances is of public health relevance.

Single cardiovascular risk factors have been associated with several sleep disturbances.[10,11] However, most studies considered single cardiovascular risk factors, although they usually cluster and have an additive effect. The association between clustered cardiovascular risk factors and sleep disturbances remains unclear. Furthermore, most prior studies focused on associations between cardiovascular risk factors and a single sleep disturbance, precluding to help define whether a common or a specific sleep disturbance prevention strategy should be recommended.

The American Heart Association (AHA) has recently re-emphasized the concept of primordial prevention, *i.e.* the prevention of cardiovascular risk factors onset. Hence, the AHA developed the Life's Simple 7, a 7-items tool including four behavioral and three biological metrics to define poor, intermediate and ideal cardiovascular health (CVH).[12] The importance of CVH has been demonstrated by several population-based studies reporting substantial and graded risk reductions in mortality and incident CVD for subjects with intermediate and ideal CVH compared to those with poor CVH.[13–16] Given that sleep disturbances and CVD share some common risk factors, we hypothesized that higher CVH would be related to lower risk of sleep

disturbances. Therefore, using two large contemporary community-based European studies, we quantified the association of CVH with several sleep disturbances.

Methods

Study population

Details are described in the **supplementary methods.**

The Paris Prospective Study 3

The PPS3 (Paris, France) is a prospective observational population-based cohort study on novel determinants of the main phenotypes of CVD.[17] Between 2008 and 2012 10,157 men and women aged 50-75 years were recruited in a preventive medical center. The study-protocol was approved by the Ethics Committee of the Cochin Hospital (Paris, France) and all volunteers signed an informed consent form. 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

This is a Swiss population-based observational prospective study investigating determinants of cardiovascular disease.[18] Between 2003 and 2006, 6,733 subjects (age range 35-75 years) were included from a random sample of the population of Lausanne, Switzerland. The institutional Ethics Committee of the University of Lausanne approved the study (references

16/03 and 33/09) and all participants gave their signed informed consent. The first follow-up of the cohort (median follow-up time 5.4 years) included 5,064 subjects. Subjects underwent a physical examination after an overnight fasting and responded to a questionnaire covering demographic and medical history, health behaviors and sleep quality measures.

Cardiovascular Health

The AHA criteria were used to define the level of each metric and *global CVH* was categorized as poor, intermediate and ideal to reflect 0-2, 3-4 and 5-7 metrics at ideal.[12] Similarly, *behavioral CVH* (smoking, body mass index, diet and physical activity) was categorized as poor, intermediate and ideal to reflect 0-1, 2 and 3-4 behavioral metrics at the ideal level; *biological CVH* (hypertension, total cholesterol and fasting blood glucose) was categorized as poor, intermediate and ideal to reflect to 0-1, 2 and 3 metrics at the ideal level (**supplementary methods** and **supplementary table 1**).[12]

In sensitivity analysis (see below), *global* CVH was examined as a continuous variable considering i) the number of metrics at ideal level (from 0 to 7) and ii) a global cardiovascular health score, calculated by assigning 0 point for each metric at poor level, 1 point for metric at intermediate level and 2 points for metric at ideal level (ranging from 0 to 14).[12]

Sleep quality measures

Sleep-disordered breathing

In both cohorts, a proxy including the main risk factors for SDB was used to measure SDB.[19] Participants reporting to snore at least 1-2 times per week (in CoLaus) or to snore

regularly or often (in PPS3) and being male and/or being at least 55 years old and/or having a BMI ≥30 kg/m^2 and/or having hypertension and/or having EDS were considered to have SDB (**supplementary table 2**).

In CoLaus, a subset of the study population underwent polysomnography.[1] SDB was objectively measured, calculated as the average number of apnea/hypopnea per hours of sleep (apnea-hypopnea index, AHI), and categorized as normal (AHI 0-4), mild (AHI 5-14), moderate (AHI 15-29) and severe (AHI ≥30) according to the American Academy of Sleep Medicine.[20]

Excessive daytime sleepiness

Excessive daytime sleepiness (EDS) was assessed using the Epworth Sleepiness Scale (ESS) in both cohorts.[21] EDS was defined by an ESS ≥11.[21]

Sleep duration

In both cohorts, sleep duration was extracted from the Pittsburgh Sleep Quality Index.[22] Subjects reported their average hours of sleep per night during the last month. Sleep duration was categorized into short (≤6 hours/night), normal (6-9 hours/night), and long (≥9 hours/night).

Insomnia symptoms

Insomnia symptoms were measured using questions from the Pittsburgh Sleep Quality Index. Insomnia symptoms were considered present (yes/no) when subjects reported difficulties initiating sleep and difficulties maintaining sleep or early morning awakening 3-4 times per week.

Confounders

In PPS3, depression score was assessed using the 13-item Questionnaire of Depression second version, Abridged.[23] Depressive status (yes/no) was defined by a score ≥7. In CoLaus, depressive status was measured with the validated 20-item Center for Epidemiologic Studies – Depression Scale questionnaire, and depressive status was considered for a score ≥17 for men and 23 for women.[24] Education level was categorized as low (no graduation in PPS3, mandatory education or apprenticeship in CoLaus), intermediate (high school diploma) and high (university diploma). We categorized alcohol consumption as never/less than daily, 1-2 glasses per day and ≥3 glasses per day. A medical doctor checked the use of medications during a face-to-face interview in PPS3. In CoLaus, subjects self-reported the use of prescribed and over the counter medications.

Exclusion criteria

Participants were excluded from the analyses if they had i) previous history of CVD; ii) missing data on more than one CVH metric; iii) missing data on any sleep variables or iv) missing data on any covariates.

Statistical analyses

Statistical analyses were performed using R version 3.3.3 for PPS3 (www.r-project.org) and STATA 15.1 for CoLaus (Stata Corp, College Station, TX, USA).

Single cohort analyses

The association between global CVH (main exposure) and binary sleep disturbances (outcomes), *i.e.* proxy for SDB, EDS and insomnia symptoms, were examined by logistic regressions for each cohort and prevalence ratios [to be considered as an odds-ratio (OR)] were obtained. The association between CVH and SDB measured by PSG (four categories) and sleep duration (three categories, with 6-9 hours/night as the reference) was quantified by multinomial logistic regressions and relative risk ratios (RRR) were estimated. Regression models adjusted for age, sex, education, living alone status, depression, use of sleep medications and alcohol consumption. Further, the same analyses were performed using behavioral and biological CVH as independent variables (secondary exposure).

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Pooled data cohort analyses

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Mixed effects regressions models with random effects for the cohort were used. Logistic mixed models were used for binary outcomes (proxy for SDB, EDS and insomnia symptoms), whereas linear mixed models were used for sleep duration considered here as a continuous outcome (the normality distribution of the model's residuals was graphically checked). Pooled data analyses were adjusted for the same covariates as for the single cohort analysis. As for the single cohort analysis, global CVH but also behavioral and biological CVH were examined.

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Sensitivity analyses

First, subjects with missing data on any CVH metrics were excluded. Second, the adapted CVH metric diet was measured by all available metrics in each cohort (additionally including sodium in PPS3 and fiber in CoLaus) and time since smoking cessation was taken into account

for the smoking status in PPS3. Third, the association between CVH and each sleep disturbance was further mutually adjusted for the other three sleep disturbances. Fourth, CVH was measured as a continuous variable considering either the number of metrics at the ideal level (0 to 7) or the cardiovascular health score as defined above (ranging from 0 to 14). Next, to limit collinearity, BMI and hypertension were excluded from the definition of CVH and sex was not adjusted for, when estimating its related odds for a proxy for SDB (containing BMI, hypertension and sex in its definition). In this sensitivity analysis, poor, intermediate and ideal CVH corresponded to 0-2, 3, 4-5 metrics at ideal level. Last, we assessed the relationship between global CVH and sleep duration measured by polysomnography in CoLaus.

Results

Study population

From 8,583 participants in PPS3 who answered the sleep questionnaires and from the 5,064 subjects participating in follow-up 1 in CoLaus, respectively 6,441 and 2,989 participants were free of previous CVD and had full data (**figure 1**). Out of the 2,989 subjects in CoLaus, 1,404 had PSG data. The characteristics of excluded and included participants are compared in **supplementary table 3**.

Prevalence of sleep disturbances and bivariate association with CVH

As presented in **table 1**, ideal CVH was present in 9.5% (PPS3) and 11.2% (CoLaus) of the participants.In both cohorts, participants with ideal CVH were more frequently women, had a higher educational level, were more frequently living alone and drank less alcohol. Proxy for

SDB was present in 33% (PPS3) and 20% (CoLaus) of the participants, and decreased with an increasing level of global CVH in both cohorts (p-value<0.001). In CoLaus, prevalence of moderate/severe SDB measured by PSG was 35% and decreased with an increasing level of global CVH (p-value<0.001). EDS was present in 17% (PPS3) and 11% (CoLaus) of the participants, and decreased with increasing level of global CVH in PPS3 (p-value=0.02) but not in CoLaus (p-value=0.41). Insomnia symptoms were present in 14.4% (PPS3) and 7% (CoLaus) of the participants, and decreased with increasing level of global CVH in CoLaus (p-value=0.07) but not in PPS3 (p-value=0.18). There were 25% and 8% of the participants sleeping 6 hours or less per night in PPS3 and CoLaus respectively; and 5,1% and 1.3% sleeping 9 hours or more per night in each cohort. There was no clear pattern between the distribution of short/long sleep duration and global CVH level.

Association of CVH and sleep disturbances: single cohort analysis

CVH and SDB

As presented in **figure 2**, in multivariable logistic regression analysis, the odds for proxy for SDB gradually decreased in subjects with intermediate and ideal levels of global CVH compared to subjects with poor CVH in both cohorts (p-value<0.001 in both cohorts). There was a stronger inverse gradient between higher global CVH and the severity of SDB measured by PSG in a subsample of CoLaus (p-value<0.001, **table 2**).

These inverse associations with either the proxy for SDB (**figure 2**) or SDB measured by PSG in the subsample of CoLaus (**table 2**), were observed for the behavioral and biological CVH.

CVH and EDS

In PPS3, subjects with intermediate and ideal global CVH had lower odds of EDS compared to subjects with poor CVH while no association was found in CoLaus (**figure 2**).

In both cohorts, subjects with intermediate and ideal levels of behavioral CVH had lower odds of EDS, when compared to subjects with poor CVH, although the association with ideal behavioral CVH was borderline significant in CoLaus (p=0.08). Conversely, in both cohorts, subjects with higher biological CVH had higher odds of EDS; however these associations were statistically significant only for subjects with ideal compared to poor biological CVH in CoLaus.

CVH, insomnia symptoms and sleep duration

In both cohorts, no consistent associations were found between CVH and both and insomnia symptoms and sleep duration (**supplementary table 4**).

Pooled analysis

Results of the pooled analysis are reported in **table 3**. The odds for SDB remained significant, being 0.62 (95% CI 0.56 – 0.68) and 0.41 (95% CI 0.33 – 0.49) for intermediate and ideal global CVH when compared to poor global CVH, respectively. The odds for EDS became significant, being 0.87 (95% CI 0.77 – 0.99) and 0.80 (95% CI 0.65 – 0.98) for intermediate and ideal global CVH, respectively. As for the single cohort analysis, there was no significant association between intermediate and ideal global CVH and insomnia or sleep duration.

Sensitivity analyses

Effect size and direction of the association between global CVH and sleep disturbances were consistent with those obtained in main analyses in both cohorts (**supplementary table 5 and supplementary figure 1**).

Discussion

In two large European population-based studies, higher global, behavioral and biological CVH were consistently associated with lower odds of SDB, and higher behavioral CVH was related to lower odds of EDS compared to subjects with poor CVH. In addition, there was some evidence for an association between higher levels of CVH and lower odds for short/long sleep duration. Conversely, CVH was not related to insomnia symptoms.

The distribution of ideal CVH was in the same range in PPS3 (9.5%) and CoLaus (11.2%). In addition, the distribution of socio-demographic characteristics across the levels of CVH was exactly the same in both cohorts. However, there was some difference in the distribution of sleep disturbances between the two studies, in particular regarding the proxy for SDB or short and long sleep duration, although sleep disturbances definitions have been harmonized as much as possible. Notwithstanding these differences, associations between CVH and sleep disturbances were consistent in PPS3 and CoLaus, reinforcing the robustness of the findings.

CVH and SDB

Although several cross-sectional studies have related single cardiovascular risk factors with SDB,[1,25] none investigated the combined association of cardiovascular risk factors as measured by CVH and SDB. In both PPS3 and CoLaus, the combination of several risk factors at intermediate or ideal compared to poor levels was associated with a reduced likelihood of having the proxy for SDB (up to 45% and 65% respectively). The gradual relationships between CVH and SDB were even stronger when the severity of SDB was objectively evaluated using PSG in CoLaus. Thus, the proxy for SDB is a rather conservative measure for SDB and accordingly, it underestimated the prevalence of SDB in CoLaus by 15% when compared to SDB measured by PSG. Finally, these evidences were found for both the behavioral and biological CVH. All these aspects emphasize the validity of the reported association between CVH and SDB. In addition, SDB has been shown to be a contributor to the onset of some of the CVH metrics such as diabetes, dyslipidemia, hypertension,[10] and obesity.[26] It is therefore likely that the association between CVH and SDB is bidirectional.

CVH and EDS

Only one small (n=635) population-based study in rural Ecuador explored the potential relationship between global CVH and EDS and did not find any significant association.[11] Conversely, in our study, using a much larger sample size, two independent European cohorts and additionally considering the behavioral and the biological components of CVH, higher behavioral CVH in both cohorts were significantly associated with lower odds of EDS. This result is in line with previous studies that associated the presence of single cardiovascular risk factors belonging to behavioral CVH (*i.e.* obesity) with EDS.[27] However, the association

between ideal biological CVH and higher prevalence of EDS in both cohorts was unexpected although not confirmed in the pooled analysis, and additional studies are required to clarify this finding.

CVH and insomnia symptoms

The lack of consistent association between CVH and insomnia symptoms in each study is in line with previous studies reporting no significant relationship between single behavioral cardiovascular risk factors – such as obesity, physical activity or smoking – and insomnia symptoms.[28] The present study further suggests the absence of additive effect of seven cardiovascular risk factors on insomnia symptoms.

CVH and sleep duration

There was little evidence for an association between CVH and sleep duration. The relationship was neither gradual nor consistent between the two cohorts, and sensitivity analyses with objectively measured sleep duration did not indicate an association either.

Implications

The lower odds of SDB and EDS associated with CVH carry important public health implications owing to the burden of sleep disturbances in the population and the wide range of sleep-related health consequences.[6–10] Importantly, the lower odds for both SDB and EDS were primarily driven by modifiable behavioral CVH that do not require pharmacological interventions. The results of our sensitivity analysis on CVH score suggest that gaining one additional metric at ideal level is already associated with significant reduced odds of SDB and, to

a lesser extent, EDS. Hence, this approach might be more achievable than promoting to the population the attainment of an ideal global CVH to help preventing the onset of SDB and EDS.

Study limitations

First, as a cross-sectional analysis, causal interpretation cannot be made and associations might be bidirectional. Second, both cohorts are based on voluntary participation resulting in a possible overrepresentation of health aware subjects. Third, sleep disturbances, some cardiovascular risk factors and covariates were self-reported and thus prone to recall, misclassification and reporting bias. Fourth, the 7-item tool used to assess CVH assigns the same weights to each of the metric and further studies are required to refine the tool. Fifth, there were a few participants (n<30) by CVH group in some analyses of sleep disturbances, which may have contributed to the lack of statistical significance and wide confidence intervals. Sixth, declustering the Life's Simple 7 into behavioral and biological CVH is likely to lower the statistical power of these sub-analyses explaining why both subscales were considered as secondary exposures.

Conclusions

Higher levels of CVH were associated with lower odds of SDB and EDS. In addition to benefit on mortality and cardiovascular disease risk, the current study suggests that higher CVH may have secondary benefit on highly prevalent sleep disturbances. Longitudinal and intervention studies are needed to support the promotion of CVH to prevent the development of risk factors associated with SDB and EDS.

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Statements

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Figure legends

Figure 1: Selection procedure, Paris Prospective Study 3 (France) and CoLaus (Switzerland).

Note: numbers are for Paris Prospective Study 3/CoLaus.

Abbreviations: CVD: cardiovascular disease; CVH: cardiovascular health.

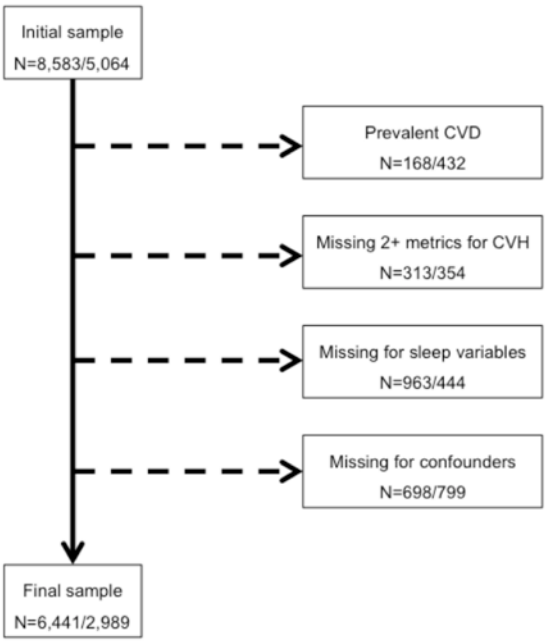

Figure 2: Association of global, behavioral and biological cardiovascular health with sleep disordered breathing and excessive daytime sleepiness, Paris Prospective Study 3 (France) and CoLaus (Switzerland).

Note: multivariable analysis conducted using logistic regression; results are expressed as odds ratio and 95% confidence interval.

Abbreviations: CVH: cardiovascular health, OR: odds ratio, CI: confidence interval.

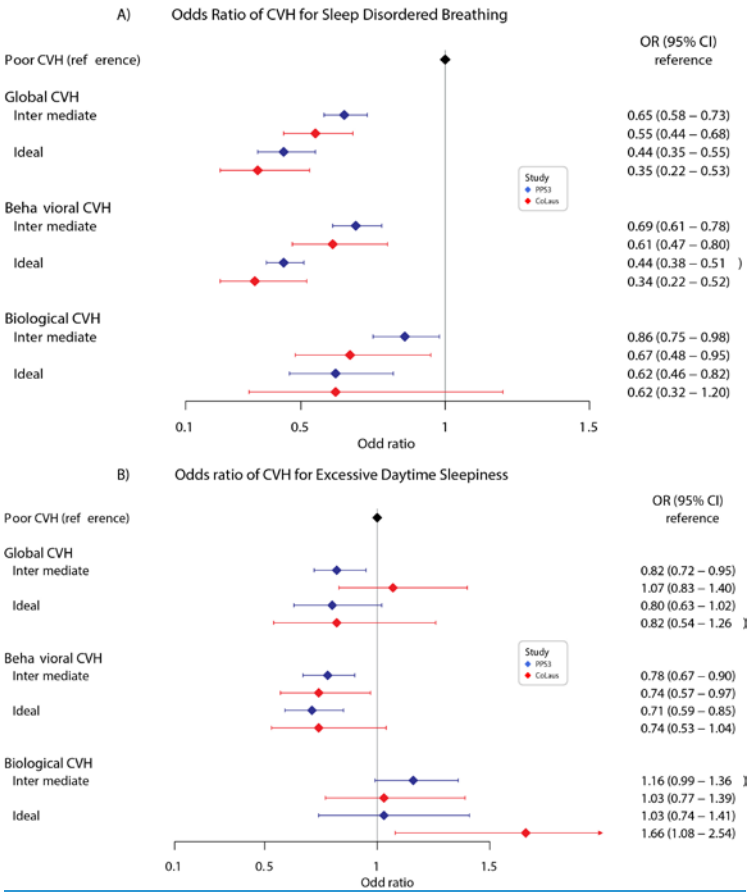

Table 1: Characteristics of the study participants according to cardiovascular health status, Paris Prospective Study 3 (France, n=6,441) and CoLaus (Switzerland, n=2,989).

	Cardiovascular health			
	Poor	Intermediate	Ideal	p-value
PPS3	**N=3,007 (46.7)**	**N=2,820 (43.8)**	**N=614 (9.5)**	
Sleep complaints				
Sleep disordered breathing (proxy)	1,206 (40.1)	780 (27.7)	117 (19.1)	<0.001
Excessive daytime sleepiness	547 (18.2)	440 (15.6)	94 (15.3)	0.02
Insomnia symptoms	411 (13.7)	422 (15.0)	99 (16.1)	0.18
Sleep duration (hours per night)				0.27
≤6	845 (28.1)	773 (27.4)	162 (26.4)	
6-9	1,990 (66.2)	1,917 (68.0)	422 (68.2)	
≥9	172 (6.7)	130 (4.6)	30 (4.9)	
General characteristics				
Male gender	2,244 (74.6)	1,600 (56.7)	271 (44.1)	<0.001
Age (years)	59.3 ± 6.02	59.3 ± 6.21	59.2 ± 6.13	0.84
Education level				0.01
Low	851 (28.3)	704 (25.0)	152 (24.8)	
Intermediate	566 (18.8)	517 (18.3)	103 (16.8)	
High	1,590 (52.9)	1,599 (56.7)	359 (58.4)	
Living alone	598 (19.9)	672 (23.8)	158 (25.7)	<0.001
Alcohol (drinks per day)				<0.001
Never	469 (8.2)	314 (11.1)	98 (16.0)	
1-2	2,229 (74.1)	2,246 (79.6)	485 (79.0)	
≥3	532 (17.7)	260 (19.2)	31 (5.1)	

Depressive status	232 (7.7)	211 (7.5)	40 (6.5)	0.59
Sleep medications	275 (9.1)	296 (10.5)	64 (10.4)	0.20
CoLaus	**N=1,383 (46.3)**	**N=1,272 (42.5)**	**N=334 (11.2)**	
Sleep complaints				
Sleep disordered breathing (proxy)	392 (28.3)	176 (13.8)	27 (8.1)	<0.001
Severity of OSA (from PSG data)				
No	94 (14.7)	225 (37.4)	97 (58.8)	<0.001
Mild	230 (36.1)	227 (37.8)	45 (27.3)	
Moderate	171 (26.8)	96 (16)	19 (11.5)	
Severe	143 (22.4)	53 (8.8)	4 (2.4)	
Excessive daytime sleepiness	142 (10.3)	150 (11.8)	34 (10.2)	0.41
Insomnia symptoms	110 (8.0)	80 (6.3)	16 (4.8)	0.07
Sleep duration (hours per night)				0.08
≤6	124 (9.0)	97 (7.6)	18 (5.4)	
6-9	1,236 (89.4)	1,163 (91.4)	313 (93.7)	
≥9	23 (1.7)	12 (0.9)	3 (0.9)	
General characteristics				
Male gender	881 (63.7)	502 (39.5)	104 (31.1)	<0.001
Age (years)	59.0 ± 9.8	55.0 ± 9.7	50.8 ± 8.3	<0.001
Education				<0.001
Low	744 (53.8)	538 (42.3)	128 (38.3)	
Intermediate	363 (26.2)	380 (29.9)	82 (24.6)	
High	276 (20.0)	354 (27.8)	124 (37.1)	
Living alone	515 (37.2)	576 (45.3)	139 (41.6)	<0.001
Alcohol (drinks per day)				<0.001

Never	226 (16.3)	290 (22.8)	100 (29.9)	
1-2	1,107 (80.0)	964 (75.8)	233 (69.8)	
≥3	50 (3.6)	18 (1.4)	1 (0.3)	
Depressive status	175 (12.7)	158 (12.4)	34 (10.2)	0.46
Sleep medications	186 (13.5)	140 (11.0)	36 (10.8)	0.11

Note: numbers are N (%) or mean ± standard deviation. P-values are from Pearson chi-square or ANOVA where appropriate and refer to the global comparison across the 3 groups.

Abbreviations: OSA: obstructive sleep apnea; PSG: polysomnography.

Table 2: Results of multinomial logistic regression between severity of sleep disordered breathing as measured by polysomnography and global, behavioral and biological cardiovascular health in CoLaus (Switzerland, N=1,404).

	Severity of SDB (no = ref)		
	Mild	Moderate	Severe
	RRR (95% CI)	RRR (95% CI)	RRR (95% CI)
Global CVH			
Poor	1	1	1
Intermediate	0.52 (0.38 - 0.72)	0.37 (0.25 - 0.53)	0.29 (0.19 - 0.46)
Ideal	0.27 (0.17 - 0.42)	0.20 (0.11 - 0.36)	0.07 (0.02 - 0.20)
Behavioral CVH			
Poor	1	1	1
Intermediate	0.59 (0.42 - 0.81)	0.43 (0.29 - 0.62)	0.38 (0.25 - 0.58)
Ideal	0.39 (0.27 - 0.57)	0.22 (0.14 - 0.37)	0.17 (0.09 - 0.31)
Biological CVH			
Poor	1	1	1
Intermediate	0.64 (0.46 - 0.87)	0.51 (0.34 - 0.77)	0.33 (0.19 - 0.57)
Ideal	0.27 (0.15 - 0.49)	0.30 (0.14 - 0.65)	0.13 (0.03 - 0.58)

Abbreviations: SDB: sleep-disordered breathing; RRR: relative risk ratio; ref: reference category. *Note*: Models were adjusted for age, sex, education, living alone status, depression, use of sleep medications and alcohol consumption.

Table 3: Results of mixed effect regressions for the pooled analysis.

	SDB	EDS	Insomnia	Sleep duration
	OR (95% CI)	OR (95% CI)	OR (95% CI)	Regression coefficient (95% CI)
Global CVH				
Poor	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Intermediate	0.62 (0.56 – 0.68)	0.87 (0.77 – 0.99)	0.89 (0.77 – 1.02)	-0.02 (-0.03 – 0.06)
Ideal	0.41 (0.33 – 0.49)	0.80 (0.65 – 0.98)	0.84 (0.67 – 1.06)	0.08 (-0.01 – 0.16)
Behavioral CVH				
Poor	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Intermediate	0.66 (0.59 – 0.73)	0.76 (0.67 – 0.87)	1.01 (0.87 – 1.18)	-0.003 (-0.05 – 0.05)
Ideal	0.41 (0.36 – 0.47)	0.72 (0.61 – 0.85)	0.93 (0.78 – 1.11)	0.06 (0.001 – 0.13)
Biological CVH				
Poor	1 (reference)	1 (reference)	1 (reference)	1 (reference)
Intermediate	0.82 (0.72 – 0.92)	1.13 (0.98 – 1.30)	0.99 (0.84 – 1.16)	0.03 (-0.02 – 0.09)
Ideal	0.62 (0.48 – 0.80)	1.21 (0.93 – 1.56)	0.64 (0.44 – 0.92)	-0.03 (-0.14 – 0.08)

Abbreviations: CVH: cardiovascular health; SDB: sleep disordered breathing; EDS: excessive daytime sleepiness; OR: odd ratio; CI: confidence interval.

Note: odds ratios and regression coefficient were estimated by logistic and linear mixed effect regressions adjusted for age, sex, education, living alone status, depression, use of sleep medications and alcohol consumption.