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Abstract

Background Although sleep characteristics have been linked to cardiovascular disease and cardiovascular risk factors, the association between sleep characteristics measured by polysomnography and cardiovascular health (CVH) remains unknown.

Methods and Results In a population-based sample (n=1826), sleep characteristics were assessed by both sleep questionnaires and polysomnography. Global, behavioral and biological CVH were defined according to the American Heart Association. Multinomial logistic regressions were performed to estimate relative risk ratios (RRR) and 95% confidence intervals (CI). Strong dose-response associations were found between all oxygen saturation-related variables [oxygen desaturation index, mean oxygen saturation and percentage of total sleep time spent under 90% oxygen saturation] and obstructive sleep apnea [severity categories and apnea/hypopnea index (AHI)] with global, behavioral and biological CVH. Mean oxygen saturation had the strongest positive association [RRR 1.31 (CI 1.22-1.41); 1.78 (CI 1.55-2.04) for intermediate resp. ideal CVH] and oxygen desaturation index the strongest negative association [RRR 0.71 (CI 0.65-0.78); 0.45 (CI 0.34-0.58) for intermediate resp. ideal CVH] with global CVH, and these associations were also the most robust in sensitivity analyses. The impact of sleep architecture and sleep fragmentation were less consistent.

Conclusions Mean oxygen saturation, oxygen desaturation index and AHI were associated with CVH. Conversely, most variables related to sleep architecture and sleep fragmentation were not consistently related to CVH. Sleep-disordered breathing and the associated oxygen (de-)saturation were stronger associated to CVH than sleep fragmentation.

Keywords cardiovascular health; sleep characteristics; polysomnography; mean oxygen saturation; oxygen desaturation index

Clinical Perspective

What is new?

- This study highlights that higher oxygen saturation is associated with better cardiovascular health.
- Respiratory disturbances during sleep and the associated oxygen (de-)saturation are stronger determinants of cardiovascular health than sleep architecture or fragmentation.

What are the clinical implications?

- As respiratory disturbances during sleep are highly prevalent in the general population and were found to be associated with worse cardiovascular health, clinicians should be educated to expedite diagnosis and treatment
- Our results suggest that treatment of obstructive sleep apnea might improve cardiovascular health, since the associated oxygen desaturation was consistently associated with cardiovascular health.

Introduction

Cardiovascular disease is the leading cause of mortality worldwide[1]. Although a sizable fraction of cardiovascular disease events could be prevented by simple measures[2], still preventive measures towards cardiovascular disease are insufficiently implemented[3]. Recently, the American Heart Association has re-emphasized the need for primordial prevention, i.e. the prevention of cardiovascular risk factors, to promote cardiovascular health (CVH)[4]. Indeed, several population-based cohort studies have demonstrated the importance of the CVH concept, as they found substantial risk reductions in cardiovascular disease incidence and mortality for subjects with ideal CVH compared to those with poor CVH[5,6]. The American Heart Association defined four behavioral [smoking status, body mass index (BMI), physical activity, diet] and three biological [fasting blood glucose, total cholesterol, blood pressure] cardiovascular risk factors to assess CVH[4]. Thus, behavioral CVH is modifiable by lifestyle changes whereas a change in biological CVH usually requires pharmacological interventions.

Sleep-related disorders such as obstructive sleep apnea, excessive daytime sleepiness and insufficient sleep are highly prevalent in the population[7–9], and have been associated with cardiovascular disease[7]. In a recent review, several sleep characteristics including obstructive sleep apnea, excessive daytime sleepiness and insufficient sleep, were linked with cardiovascular risk factors such as obesity, sedentary lifestyle, poor diet, diabetes and high blood pressure[7]. Although some sleep characteristics measured by polysomnography (PSG) have previously been associated with cardiovascular disease[10] and with some cardiovascular risk factors[7,11,12], no study has ever assessed the effect of sleep characteristics measured by PSG on CVH.

Hence, we aimed to investigate the association between various sleep characteristics measured by questionnaire and by PSG and CVH. We hypothesized that subjects with optimal sleep characteristics were more likely to have ideal CVH compared to persons with poor sleep characteristics or sleep disorders such as obstructive sleep apnea or excessive daytime sleepiness.

Methods

Due to the sensitivity of the data and the lack of consent for online posting, individual data cannot be made accessible. Only metadata will be made available in digital repositories. Metadata requests can also be performed via the study website www.colaus-psycolaus.ch

Population sampling

HypnoLaus is a population-based sleep cohort study conducted in Lausanne, Switzerland. The HypnoLaus study was performed between September 1, 2009 and June 30, 2013 and participants were recruited among the CoLaus/PsyCoLaus study[13]. This observational prospective study was conducted to assess the prevalence and determinants of cardiovascular risk factors and cardiovascular disease, and to identify new determinants of these risk factors. Participants of the CoLaus/PsyCoLaus were identified from a random sample of all adults aged 35-75 years living in the city of Lausanne, Switzerland (117,161 habitants), and the initial cohort included 6,733 participants (52.5% women)[13].

For the HypnoLaus study, the first consecutive 3,043 participants of the first follow-up of the CoLaus/PsyCoLaus study were invited to have a full PSG at home. Of these, 2,168 (71%) accepted the invitation; 60 (3%) had technical problems and were invited to undergo a second PSG; six participants declined and 54 participants agreed [8]. Therefore, 2,162 complete PSG recordings were obtained in the HypnoLaus cohort and included in this study. The ethics committee of the University of Lausanne approved the CoLaus/HypnoLaus study. The study complies with the Declaration of Helsinki and written informed consent was obtained from all participants.

Clinical data collection

Participants from CoLaus/HypnoLaus study were invited to attend the outpatient clinic at the University Hospital of Lausanne (CHUV, Lausanne, Switzerland) in the morning after an overnight fasting for questionnaire completion, clinical assessment and blood samples collection. Body weight and height were measured using a calibrated scale and a vertical stadiometer, respectively (Seca®, Hamburg, Germany). Systolic and diastolic blood pressure were evaluated in triplicate on the left arm at 5-min intervals with the participant seated and resting for at least 10 min using a calibrated

automated oscillometric sphygmomanometer (Omron® HEM-907, Matsusaka, Japan)[14]. Overnight fasting blood samples were taken from the antecubital vein of each participant. Glucose, and total cholesterol were quantified by colorimetric assays as previously described[13]. These assays were performed within 2 hours on fresh blood samples by the CHUV Clinical Laboratory (Lausanne, Switzerland).

Cardiovascular health

Global CVH was based on, and adapted from the seven metrics defined by the American Heart Association[4]: four behavioral (smoking, BMI, diet, physical activity) and three biological (fasting blood glucose, total cholesterol, blood pressure). Global CVH was measured according to the number of metrics at ideal level and categorized into poor (0-2), intermediate (3-4) and ideal (5-7) – irrespective of whether subjects had one missing CVH metric. Poor, intermediate and ideal behavioral CVH were defined as having 0-1, 2 and 3-4 behavioral metrics at ideal level respectively 0-1, 2 and 3 biological metrics at ideal level for biological CVH. The definition of the CVH metrics is described in **supplementary file 1** and the thresholds and categorization of the CVH metrics are summarized in **supplementary table 1**.

Polysomnography

The detailed description of the PSG procedure was described previously[8]. The following PSG measures were used in the analyses: total sleep time: time spent asleep in minutes from sleep onset to morning awakening categorized as <6h, 6-8h & >8h; stage 1 and 2, slow wave sleep and rapid eye movement: measured as percentage of total sleep time; sleep efficiency: percentage of total time in bed spent asleep; arousal index: number of arousals measured by EEG per hour of total sleep time divided by 5; autonomic arousal index: number of autonomic arousals measured by pulse wave amplitude drops (of at least >30% of baseline PWA) per hour of total sleep time (**supplementary figure 1)**. PWA drops were obtained from finger photoplethysmography and reflect peripheral vasoconstriction[15]; autonomic arousal duration: mean duration of autonomic arousals in seconds (**supplementary figure 1**); periodic limb movement index during sleep: number of periodic limb

movements divided per hours of sleep; apnea/hypopnea index (AHI): number of apneas/hypopneas per hour of sleep; severity of obstructive sleep apnea: no (AHI<5/h), mild (5≤AHI<15 events per hour of sleep), moderate (15≤AHI<30 events per hour of sleep), and severe (AHI≥30 events per hour of sleep); oxygen desaturation index: number of ≥3% oxygen saturation drops per hour of sleep; mean oxygen saturation: mean oxygen saturation during sleep; time spent under 90% oxygen saturation: percentage of total sleep time spent under a 90% oxygen saturation threshold.

Subjective sleep characteristics

Subjective sleep duration was self-reported and categorized as <6h, 6-8h and >8h. Excessive daytime sleepiness stemmed from the Epworth sleepiness scale[16]. Excessive daytime sleepiness was considered as present with sum score ≥11.

Exclusion criteria

Participants were excluded from the analyses if they 1) had previous history of cardiovascular disease; 2) lacked information for more than one CVH metric; 3) lacked information on sleep characteristics or 4) lacked information for covariates.

Statistical analyses

All statistical analyses were performed using STATA 15.1 (Stata-Corp, College Station, TX, USA). To characterize the study population and to present the prevalence of sleep characteristics according to their CVH continuous variables were summarized as means ± standard deviation, and categorical variables as the number of subjects with column percentages. Pearson chi-square (for categorical variables) or ANOVA (for continuous variables) were used to evaluate differences in sleep characteristics between the global CVH categories. As the proportional odds assumption for ordinal regressions was violated, we performed multinomial logistic regressions to assess the effect of sleep characteristics on global, behavioral and biological CVH and to estimate relative risk ratios (RRR). We adjusted for age, sex, education and living alone status and removed the covariates depression, use

of sleeping pills and alcohol consumption from the final analyses, as Akaike's Information Criterion/Bayesian Information Criterion and likelihood ratio test indicated best model fit.

In order to check for the robustness of the results, we performed several sensitivity analyses: First, we operationalized CVH as a continuous variable with the number of metrics at ideal level (0-7) and the sum of metrics at poor, intermediate or ideal level (score ranging from 0 to 14) (**supplementary table 1**). Second, we re-constructed behavioral CVH without BMI and re-ran the analyses with and without adjustment for BMI. Third, we adjusted for depression, sleeping pills and alcohol consumption (**supplementary file 2**). Fourth, we performed multinomial regression including all sleep characteristics as explanatory variables for global CVH. Statistical significance was considered for a two-sided test with $p<0.05$.

Results

Study population and characteristics

Of the initial 2162 subjects undergoing PSG, 336 (15.5%) were excluded due to previous self-reported history of cardiovascular disease (n=180), missing information for more than one CVH metric (n=104) and missing information on sleep characteristics (n=23) and covariates (n=1) resulting in a sample size of 1826 (84.5%, **figure 1**). Excluded subjects were older, with lower educational level, had more often depressive status and consumed more sleeping pills and less alcohol than included ones (**supplementary table 2**).

Figure 1 Flowchart of study population.

Table 1 summarizes the characteristics of the study sample according to the global CVH status. Almost half of subjects had poor (46.2%) or intermediate (42.4%) global CVH, and only 11.5% of subjects had ideal global CVH. Subjects with poor global CVH were more frequently male, were older, had lower education and were living less frequently alone than subjects with intermediate or ideal global CVH. Subjects with poor global CVH had shorter total sleep time, spent higher percentage of total sleep time on stage 1 and 2 and lower percentage in slow wave sleep and rapid eye

movement than subjects with intermediate or ideal global CVH. They also had poorer sleep efficiency, higher arousal index, lower autonomic arousal index, longer autonomic arousal duration and higher periodic limb movement index than subjects with intermediate or ideal global CVH. Further, subjects with poor global CVH had higher AHI, higher oxygen desaturation index, lower mean oxygen saturation, and spent more time under 90% oxygen saturation compared to subjects with intermediate and ideal global CVH. Subjects with poor global CVH were more likely to report short (<6h) and long (>8h) sleep duration than subjects with intermediate and ideal global CVH. No statistically significant differences for excessive daytime sleepiness were found between global CVH levels.

Table 1: Characteristics of the subjects, according to global cardiovascular health levels, HypnoLaus study, Lausanne, 2009-2013 (N=1826).

Sleep architecture and cardiovascular health

Subjects with higher percentage of Stage 1 were less likely and those with higher percentage of slow wave sleep were more likely to have intermediate global CVH compared to poor CVH (**table 2**). Similar associations were found for behavioral CVH but not for biological CVH (**table 3**). Sleep efficiency was only associated with behavioral CVH. Subjects with higher arousal index were less likely to have intermediate and ideal global CVH relative to poor CVH. Similar associations were found for behavioral and biological CVH. Autonomic arousal index was not significantly related to global CVH but subjects with higher autonomic arousal index were more likely to have intermediate and ideal behavioral CVH, and conversely less likely to have intermediate biological CVH compared to poor CVH. Subjects with longer autonomic arousals were more likely to have intermediate global CVH compared to poor CVH. Finally, no associations were found between total sleep time, stage 2, rapid eye movement, and periodic limb movement index with global, behavioral or biological CVH.

Obstructive sleep apnea severity and cardiovascular health

Subjects with higher AHI were less likely to have intermediate and ideal global, behavioral and biological CVH as compared to poor CVH (**tables 2 & 3**). The associations were strongest with global CVH, followed by biological and behavioral CVH. Subjects with more severe obstructive sleep apnea were less likely to have intermediate and even less likely to have ideal global CVH than subjects with no obstructive sleep apnea (**figure 2**).

Figure 2 Association of obstructive sleep apnea severity with global cardiovascular health, HypnoLaus study, Lausanne, 2009-2013 (N=1826)

Oxygen saturation related variables and cardiovascular health

Subjects with higher oxygen desaturation index and higher time spent under 90% oxygen saturation were less likely to have intermediate and ideal global CVH compared to poor CVH (**table 2**). These associations were also significant for behavioral and biological CVH, except for time spent under 90% oxygen saturation and biological CVH (**table 3**). The associations were strongest with global CVH, followed by biological and behavioral CVH. Moreover, subjects with higher oxygen saturation were more likely to have better global, behavioral and biological CVH.

Subjective sleep characteristics and cardiovascular health

Subjects reporting short sleep duration were more likely to have poor global CVH, and less likely to have intermediate and ideal CVH, when compared to subjects reporting ideal sleep duration (6-8h) (**table 2**). Subjects reporting long sleep duration were also less likely to have ideal global CVH compared to those reporting ideal sleep duration. Similar results were found for behavioral but not for biological CVH (**table 3**). No relationship between excessive daytime sleepiness and CVH was found.

Table 2: Multivariable analysis of the associations between sleep characteristics and global cardiovascular health for each variable separately, adjusted for age, sex, education and marital status. HypnoLaus study, Lausanne, 2009-2013 (N=1826).

Table 3: Multivariable analyses of the associations between sleep characteristics and behavioral and biological cardiovascular health for each variable separately, adjusted for age, sex, education and marital status. HypnoLaus study, Lausanne, 2009-2013 (N=1826).

Sensitivity analyses

In the first sensitivity analysis, sleep characteristics that were significantly associated with CVH in the main analyses retained their associations with global CVH scores (0-7 or 0-14) (**supplementary table 3**). Additionally, autonomic arousal index and periodic limb movement index were significantly associated with global CVH (0-14). The standardized beta coefficients revealed strongest effects for mean oxygen saturation followed by oxygen desaturation index and AHI.

In the sensitivity analysis using behavioral CVH without BMI, only the association between oxygen desaturation index and intermediate/ideal behavioral CVH (without adjustment for BMI) remained significant, and both mean oxygen saturation and time spent under 90% oxygen saturation retained their association with ideal behavioral CVH (with and without adjustment for BMI). Additionally, both subjective and PSG-assessed short sleep duration were associated with a lower relative risk of having ideal behavioral CVH (**supplementary table 4**).

In the sensitivity analysis adjusting for depression, sleeping pills and alcohol consumption, the sleep characteristics that were significantly associated with CVH in the main analyses retained their significance – except that the association between stage 1, slow wave sleep and subjective sleep duration were no longer associated with global CVH (**supplementary table 5**). Conversely, periodic limb movement index was significantly associated with intermediate CVH.

When including all sleep characteristics as explanatory variables for CVH, mean oxygen saturation was significantly associated with intermediate and ideal CVH. The association between oxygen desaturation index and ideal CVH as well as autonomic arousal duration and intermediate CVH remained significant. Periodic limb movement index was additionally associated with intermediate CVH (**supplementary table 5**).

Finally, when performing sex-stratified analyses and included age squared as a covariate, the results remain stable (results not shown).

Discussion

To our knowledge, this is the first population-based study investigating the association between objective PSG-derived and subjective sleep characteristics, and CVH. We found that all variables related to respiratory disturbances – especially those associated with oxygen (de-)saturation – were strongly associated with global, behavioral and biological CVH.

Sleep-disordered breathing and oxygen (de-)saturation

We found strong dose-response relationships between sleep-disordered breathing (SDB) and associated oxygen saturation variables with CVH. Subjects with more severe obstructive sleep apnea (and higher AHI) were less likely to have high levels of global, behavioral and biological CVH. Interestingly, the association between AHI and CVH became non-significant after adjusting for variables related to oxygen saturation. Obstructive sleep apnea is associated with increased sympathetic activity[17] and is characterized by intermittent hypoxia. Hypoxemia has been linked to endothelial dysfunction[18], arterial stiffness[19] and oxidative stress[7,20,21], which are possible underlying mechanisms of how obstructive sleep apnea affects the cardio- and cerebro-vascular system. Our findings that mean oxygen saturation, oxygen desaturation index and time spent under 90% oxygen saturation were gradually and consistently associated with global, behavioral and biological CVH are

in line with previous studies linking these oxygen saturation-related variables with glucose intolerance, hypertension, increased cholesterol and obesity[12,22,23]. Moreover, sensitivity analyses revealed that mean oxygen saturation and oxygen desaturation index had the strongest and most robust effects on CVH. Hence, mean oxygen saturation and oxygen desaturation index probably explained the association between other sleep characteristics (stage 1, slow wave sleep, arousal index, AHI) and CVH.

Sleep architecture

Although stage 1 and slow wave sleep were associated with global and behavioral CVH, these associations were not robust when performing sensitivity analyses. As obese persons suffer more often from obstructive sleep apnea and consequently have more awakenings during the night, they shift more frequently from slow wave sleep and rapid eye movement to light sleep (i.e. stages 1&2). This suggests that obstructive sleep apnea may be responsible for these results.

Arousal index measured by EEG was consistently and inversely related to global, biological and behavioral CVH. The increased sympathetic activity resulting of arousals (and also of hypoxia) can lead to vasoconstriction and has been linked to hypertension, diabetes and dyslipidemia[17] – all of which are components of CVH.

Pulse wave amplitude drops associated with autonomic arousals probably reflect vessel's contractility[15]. Previous studies reported inverse associations between pulse wave amplitude drops index and CV risk in SDB patients[24] and in obstructive sleep apnea patients treated with CPAP[25]. Our finding that autonomic arousal index was positively related to biological CVH and autonomic arousal duration inversely related to global CVH suggests that frequent and quickly reversible vasoconstrictions are related to increased CVH levels. However, the association between autonomic arousal index and behavioral CVH was unstable, and this hypothesis still needs to be further investigated by prospective studies. Surprisingly, autonomic arousal duration was not negatively associated with ideal CVH. A possible hypothesis is residual confounding, as favorable health

behaviors tend to cluster in subjects with ideal CVH[26]. These unmeasured health behaviors could affect autonomic arousal duration.

Although periodic limb movement index was not associated with global, behavioral and biological CVH, periodic limb movement index had significant effects on global CVH, when additional variables (depression, sleeping pills, alcohol consumption and other sleep characteristics) were included in the model suggesting interactions with these additional variables. Our unstable findings regarding stage 1, slow wave sleep and arousal measures and the lack of a relationship between total sleep time, stage 2 and rapid eye movement with CVH are in line with a previous study that found no association between sleep architecture and cardiovascular risk factors[11]. As most variables related to sleep architecture were not consistently related to CVH, we conclude that sleep structure and sleep fragmentation have minor effects on CVH.

Implications

Sleep disorders are highly prevalent in the population[7–9] and have adverse effects on cardiovascular disease [7,10]. Hence, both clinicians and the public in general should be educated about sleep disorders, to expedite diagnosis and treatment[27]. Treatment of obstructive sleep apnea might be a mean to improve CVH, as variables associated with oxygen saturation were consistently associated with global, behavioral and biological CVH. This is of great public health relevance, since the modification of the highly prevalent cardiovascular risk factors forming biological CVH otherwise require pharmacological interventions. However, the effect of obstructive sleep apnea treatment on cardiovascular disease has not been established[21] and prospective randomized studies should fill this gap.

Limitations

We acknowledge several limitations. First, as HypnoLaus is a monocentric study focusing on middle-aged and elderly subjects, the external validity might be limited to similar aged populations.

Second, we had to adapt the smoking and diet metrics as defined by the American Heart Association due to limited information (see supplementary file 1 for more detail). However, such adaptions have previously been used, and yielded consistent results compared to the original American Heart Association CVH score[28]. Third, although PSG is the gold standard for sleep studies, the recording of a single night cannot account for night-to-night variability. In order to limit this so-called "first-night effect", PSG was performed at home and 20 randomly selected participants underwent a second PSG at home to determine short-term variability. Only, the % of TST spent in REM differed between the two nights (21.4 ± 6.7 versus 24 ± 5%, P = 0.04). Finally, due to the cross-sectional design, causal inferences can only be drawn with caution and future longitudinal studies are needed to confirm the observed effects. Further, longitudinal studies should also assess whether the associations between sleep characteristics and CVH are bidirectional, since effects of cardiovascular risk factors such as diabetes, dyslipidemia, hypertension or obesity on sleep have been established[7,29].

In conclusion, higher oxygen saturation was associated with better CVH while having a higher oxygen desaturation index and AHI were associated with worse CVH. Our results suggest that respiratory disturbances during sleep and their associated oxygen (de-)saturation, are stronger determinants of CVH than sleep architecture or sleep fragmentation.

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Disclosures: none

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Figures

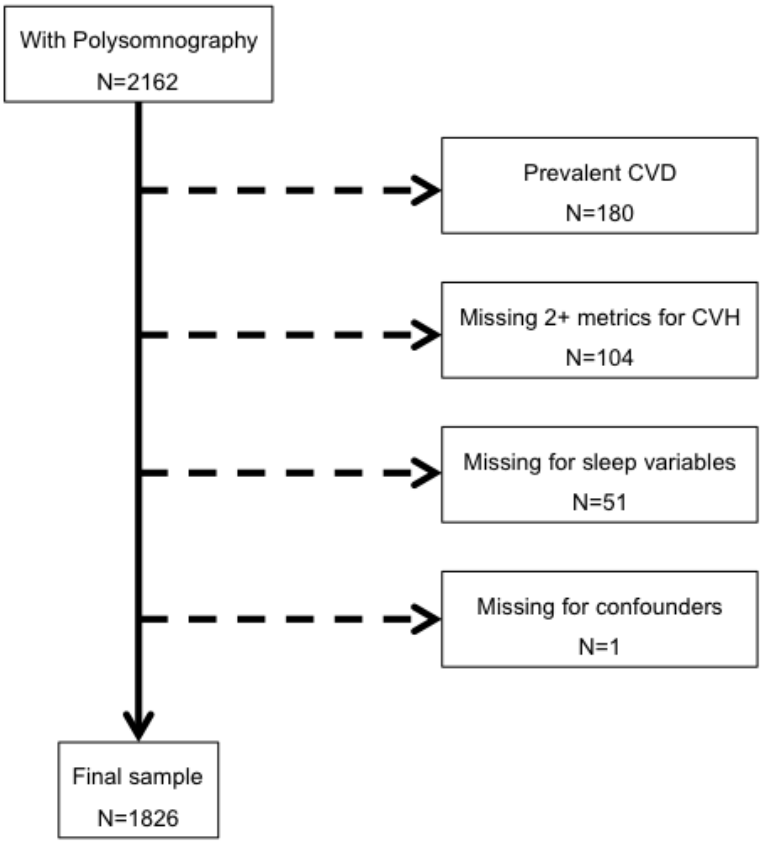

Figure 1 Flowchart of study population

CVD: cardiovascular disease

CVH: cardiovascular health

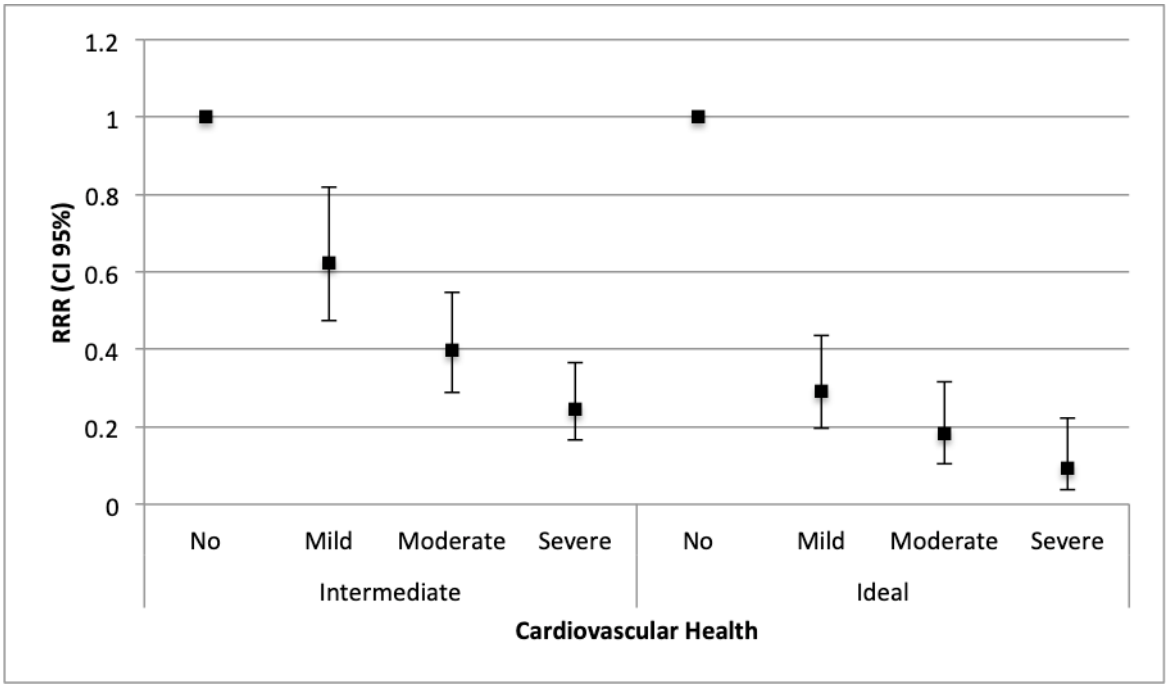

Figure 2 Association of obstructive sleep apnea severity with global cardiovascular health, HypnoLaus study, Lausanne, 2009-2013 (N=1826)

RRR: relative risk ratio

Table 1: Characteristics of the subjects, according to cardiovascular health levels, HypnoLaus study, Lausanne, 2009-2013 (N=1826).

	Cardiovascular health			P-value
	Poor (N=842)	**Intermediate (N=775)**	**Ideal (N=209)**	
General characteristics				
Men	524 (62.2)	289 (37.3)	67 (32.1)	<0.001
Age ±	59.3 (10.0)	55.2 (9.7)	50.5 (8.1)	<0.001
Education				<0.001
High	142 (16.9)	206 (26.6)	68 (32.5)	
Middle	222 (26.4)	232 (29.9)	59 (28.2)	
Low	478 (56.8)	337 (43.5)	82 (39.2)	
Living alone status	299 (35.5)	352 (45.4)	95 (45.5)	<0.001
Alcohol consumption				<0.001
Never/rare	128 (17.2)	164 (25.1)	45 (26.8)	
1-2 drinks per day	595 (80.1)	483 (74.0)	122 (72.6)	
3+ drinks per day	20 (2.7)	6 (0.9)	1 (0.6)	
Sleeping pills	121 (14.4)	108 (13.9)	32 (15.3)	0.877
Depression	121 (15.4)	95 (13.1)	26 (13.1)	0.395
PSG sleep characteristics				
Total sleep time				0.001
<6h	241 (28.6)	176 (22.7)	31 (14.8)	
6-8h	503 (59.7)	494 (63.7)	149 (71.3)	
>8h	98 (11.6)	105 (13.6)	29 (13.9)	
Stage 1 (% of TST)	13.1±7.6	10.7±6.2	9.8±4.2	<0.001
Stage 2 (% of TST)	46.7±10.3	45.5±9.8	45.0±8.0	0.005
Slow wave sleep (% of TST)	18.7±8.5	21.1±8.0	21.8±7.8	<0.001
Rapid eye movement (% of TST)	21.5±6.1	22.7±5.5	23.3±5.7	<0.001
Sleep efficiency (%)	83.8±10.5	86.3±10.0	88.1±8.5	<0.001
Arousal index	23.5±11.9	19.0±9.0	16.6±7.3	<0.001
Autonomic arousal index	63.0 (23.6)	66.1 (23.1)	71.7 (23.1)	<0.001

Autonomic arousal duration	14.6 (3.3)	13.8 (2.8)	13.6 (2.7)	<0.001
Periodic limb movement index	16.2±25.1	10.5±19.1	7.8±14.2	<0.001
Apnea/hypopnea index	20.2±18.5	10.9±11.6	6.7±7.9	<0.001
Obstructive sleep apnea severity				<0.001
No (AHI<5/h)	135 (16.0)	282 (36.4)	127 (60.8)	
Mild (5≤AHI<15)	289 (34.3)	311 (40.1)	56 (26.8)	
Moderate (15≤AHI<30)	232 (27.6)	128 (16.5)	20 (9.6)	
Severe (AHI≥30)	186 (22.1)	54 (7.0)	6 (2.9)	
Oxygen desaturation index	1.5±1.8	0.6±1.0	0.3±0.6	<0.001
Mean oxygen saturation (SpO_2)	93.5±1.8	94.6±1.6	95.4±1.2	<0.001
SpO_2<90±	6.1 (14.6)	2.0 (8.7)	0.4 (2.2)	<0.001
Subjective sleep characteristics				
Subj. sleep duration[1]				0.002
<6h	89 (10.7)	58 (7.6)	12 (5.7)	
6-8h	666 (79.9)	645 (84.0)	190 (90.9)	
>8h	79 (9.5)	65 (8.5)	7 (3.4)	
Excessive daytime sleepiness[2]	106 (13.2)	106 (14.2)	26 (12.9)	0.817

1 N (%) or ± mean (SD). P-values from Pearson chi2 or ANOVA when appropriate. [1] N=1811 [2] N=1750

2 PSG, polysomnography; TST; total sleep time; AHI, apnea-hypopnea index; SpO_2<90, Percentage of total sleep

3 time spent under a 90% oxygen saturation threshold

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Table 2: Multivariable analysis of the associations between sleep characteristics and global cardiovascular health for each variable separately, adjusted for age, sex, education and marital status. HypnoLaus study, Lausanne, 2009-2013 (N=1826).

	Cardiovascular health (poor=ref.)			
	Intermediate		Ideal	
	RRR (95% CI)	p-value	RRR (95% CI)	p-value
PSG sleep characteristics				
Total sleep time				
6-8h (ref.)	1		1	
<6h	1.05 (0.82-1.35)	0.701	0.74 (0.48-1.16)	0.189
>8h	0.96 (0.69-1.32)	0.790	0.83 (0.51-1.34)	0.442
Stage 1 (% of TST)	**0.98 (0.96-1.00)**	**0.026**	0.97 (0.94-1.00)	0.068
Stage 2 (% of TST)	1.00 (0.99-1.01)	0.477	1.00 (0.98-1.02)	0.924
Slow wave sleep (% of TST)	**1.02 (1.00-1.03)**	**0.021**	1.02 (1.00-1.04)	0.129
Rapid eye movement (% of TST)	1.00 (0.99-1.02)	0.599	1.00 (0.97-1.03)	0.871
Sleep efficiency	1.00 (0.99-1.01)	0.908	1.00 (0.98-1.02)	0.834
Arousal index[§]	**0.91 (0.86-0.96)**	**<0.001**	**0.82 (0.74-0.91)**	**<0.001**
Autonomic arousal index[§]	1.00 (0.97-1.02)	0.764	1.02 (0.98-1.06)	0.296
Autonomic arousal duration	**0.96 (0.92-0.99)**	**0.017**	0.98 (0.92-1.05)	0.633
Periodic limb movement index	1.00 (0.99-1.00)	0.127	1.00 (0.99-1.01)	0.510
Apnea/hypopnea index[‖]	**0.75 (0.69-0.82)**	**<0.001**	**0.55 (0.44-0.68)**	**<0.001**
Oxygen desaturation index[‖]	**0.71 (0.65-0.78)**	**<0.001**	**0.45 (0.34-0.58)**	**<0.001**
Mean oxygen saturation (SpO_2)	**1.31 (1.22-1.41)**	**<0.001**	**1.78 (1.55-2.04)**	**<0.001**
SpO_2<90	**0.97 (0.96-0.98)**	**<0.001**	**0.85 (0.77-0.94)**	**0.001**
Subjective sleep characteristics				
Sleep duration[1]				
6-8h (ref.)	1		1	
<6h	**0.68 (0.47-0.99)**	**0.044**	**0.48 (0.25-0.94)**	**0.031**
>8h	0.94 (0.65-1.38)	0.767	**0.39 (0.17-0.90)**	**0.028**
Excessive daytime sleepiness[2]	0.97 (0.71-1.33)	0.868	0.71 (0.44-1.17)	0.181

[§]divided by 5; [‖] divided by 10; [1] N=1811; [2] N=1750

RRR, relative risk ratio; PSG, polysomnography; TST, total sleep time; SpO_2<90, Percentage of total sleep time spent under a 90% oxygen saturation threshold

Table 3: Multivariable analysis of the associations between sleep characteristics and behavioral and biological cardiovascular health for each variable separately, adjusted for age, sex, education and marital status. HypnoLaus study, Lausanne, 2009-2013 (N=1826).

	Behavioral cardiovascular health (poor=ref.)				**Biological cardiovascular health (poor=ref.)**			
	Intermediate		**Ideal**		**Intermediate**		**Ideal**	
	RRR	**p-value**	**RRR**	**p-value**	**RRR**	**p-value**	**RRR**	**p-value**
PSG sleep characteristics								
Total sleep time								
6-8h (ref.)	1		1		1		1	
<6h	0.89 (0.69-1.13)	0.338	0.73 (0.51-1.03)	0.069	0.95 (0.70-1.28)	0.725	1.47 (0.89-2.43)	0.137
>8h	0.78 (0.57-1.08)	0.134	0.76 (0.50-1.14)	0.187	1.15 (0.82-1.61)	0.426	1.13 (0.64 2.01)	0.671
Stage 1 (% of TST)	**0.98 (0.97-1.00)**	**0.046**	**0.96 (0.94-0.98)**	**0.002**	1.00 (0.98-1.02)	0.854	0.98 (0.94-1.02)	0.312
Stage 2 (% of TST)	1.00 (0.99-1.01)	0.941	1.01 (0.99-1.02)	0.286	0.99 (0.98-1.00)	0.220	0.99 (0.97-1.02)	0.640
Slow wave sleep (% of TST)	**1.01 (1.00-1.03)**	**0.029**	1.01 (1.00-1.03)	0.097	1.01 (0.99-1.02)	0.294	1.01 (0.99-1.04)	0.327
Rapid eye movement (% of TST)	0.99 (0.98-1.01)	0.580	0.99 (0.97-1.02)	0.562	1.01 (0.99-1.03)	0.458	1.01 (0.97-1.05)	0.752
Sleep efficiency	**0.99 (0.98–1.00)**	**0.049**	1.00 (0.99-1.02)	0.660	1.01 (1.00-1.03)	0.082	0.98 (0.96-1.00)	0.119
Arousal index[§]	**0.94 (0.90-0.99)**	**0.025**	**0.88 (0.82-0.95)**	**0.001**	**0.91 (0.85-0.97)**	**0.005**	**0.82 (0.71-0.94)**	**0.004**
Autonomic arousal index[§]	**1.03 (1.01-1.06)**	**0.010**	**1.04 (1.00-1.07)**	**0.026**	**0.97 (0.95-1.00)**	**0.044**	1.03 (0.98-1.08)	0.298
Autonomic arousal duration	0.97 (0.94-1.00)	0.069	0.98 (0.94-1.03)	0.458	0.98 (0.93-1.02)	0.254	0.96 (0.88-1.05)	0.353
Periodic limb movement index	1.00 (0.99-1.00)	0.223	1.00 (0.99-1.00)	0.429	1.00 (0.99-1.00)	0.398	0.99 (0.98-1.01)	0.405
Apnea/hypopnea index[‖]	**0.84 (0.78-0.91)**	**<0.001**	**0.66 (0.57-0.76)**	**<0.001**	**0.80 (0.71-0.89)**	**<0.001**	**0.57 (0.41-0.79)**	**0.001**
Oxygen desaturation index[‖]	**0.82 (0.76-0.89)**	**<0.001**	**0.59 (0.50-0.69)**	**<0.001**	**0.76 (0.67-0.86)**	**<0.001**	**0.52 (0.37-0.75)**	**<0.001**

Mean oxygen saturation (SpO_2)	**1.19 (1.11-1.27)**	**<0.001**	**1.71 (1.53-1.91)**	**<0.001**	**1.18 (1.09-1.28)**	**<0.001**	**1.37 (1.17-1.61)**	**<0.001**
SpO_2<90*	**0.99 (0.98-1.00)**	**0.012**	**0.88 (0.83-0.93)**	**<0.001**	0.98 (0.97-1.00)	0.052	0.91 (0.82-1.01)	0.080
Subjective sleep characteristics								
Sleep duration[1]								
6-8h (ref.)	1		1		1		1	
<6h	**0.60 (0.41-0.87)**	**0.007**	0.66 (0.40-1.08)	0.095	0.69 (0.44-1.06)	0.090	0.73 (0.34-1.54)	0.408
>8h	0.93 (0.65-1.34)	0.697	**0.45 (0.24-0.83)**	**0.010**	0.79 (0.50-1.25)	0.313	0.39 (0.13-1.11)	0.078
Excessive daytime sleepiness[2]	0.76 (0.56-1.04)	0.084	0.77 (0.51-1.16)	0.210	1.03 (0.74-1.45)	0.849	1.07 (0.62-1.84)	0.802

1 [§]divided by 5; [‖] divided by 10; [1] N=1811 [2] N=1750

2 RRR; relative risk ratio; PSG, polysomnography; TST, total sleep time; SpO_2<90, Percentage of total sleep time spent under a 90% oxygen saturation threshold

Supplemental material

Supplementary file 1: Cardiovascular health metrics in CoLaus/HypnoLaus.

Supplementary table 1: CVH metrics as defined by American Heart Association and as used in CoLaus/HypnoLaus.

Supplementary figure 1: Measurement of pulse wave amplitude drops of at least >30% of baseline pulse wave amplitude

Supplementary file 2: Covariates.

Supplementary table 2: Characteristics of the included and excluded subjects.

Supplementary table 3: Results of sensitivity analyses for multivariate linear regression: effect of sleep characteristics on CVH measured as continuous variable ranging from 0-7 and 0-14.

Supplementary table 4: Results of sensitivity analyses for multinomial logistic regressions: Effects of sleep characteristics on behavioral CVH constructed without BMI 1) and no adjustment 2) with adjustment for BMI.

Supplementary table 5: Results of sensitivity analyses for multinomial logistic regressions: Effect of sleep characteristics on global CVH with adjustment for 1) depression, sleeping pills and alcohol 2) all sleep characteristics.