



Article scientifique

Article

2019

Published version

Open Access

This is the published version of the publication, made available in accordance with the publisher's policy.

Social inequalities in sleep-disordered breathing: Evidence from the CoLaus|HypnoLaus study

Petrovic, Dusan; Haba-Rubio, José; Carmeli, Cristian; Vollenweider, Peter; Heinzer, Raphael;
Stringhini, Silvia

How to cite

PETROVIC, Dusan et al. Social inequalities in sleep-disordered breathing: Evidence from the CoLaus|HypnoLaus study. In: Journal of sleep research, 2019, vol. 28, n° 5, p. e12799. doi: 10.1111/jsr.12799

This publication URL: <https://archive-ouverte.unige.ch/unige:155963>

Publication DOI: [10.1111/jsr.12799](https://doi.org/10.1111/jsr.12799)

REGULAR RESEARCH PAPER



Social inequalities in sleep-disordered breathing: Evidence from the CoLaus|HypnoLaus study

Dusan Petrovic¹ | José Haba-Rubio² | Cristian Carmeli¹ | Peter Vollenweider³ | Raphaël Heinzer^{2,*} | Silvia Stringhini^{1,*}

¹Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Lausanne, Switzerland

²Center for Investigation and Research in Sleep, Lausanne University Hospital, Lausanne, Switzerland

³Department of Medicine, Internal Medicine, Lausanne University Hospital, Lausanne, Switzerland

Correspondence

Silvia Stringhini, Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Lausanne, Switzerland. Email: silvia.stringhini@chuv.ch

Funding Information

This work is supported by the Lifepath project, which is funded by the European Commission (Horizon 2020 grant 633666), the Swiss State Secretariat for Education, Research and Innovation (SERI), the Swiss National Science Foundation, the Medical Research Council and the Portuguese Foundation for Science. The CoLaus|HypnoLaus study was and is supported by research grants from GlaxoSmithKline, the Faculty of Biology and Medicine of the University of Lausanne, and the Swiss National Science foundation (Grants 3200B0-105993, 3200B0-118308, 33CSO-122661, 33CSO-139468 and 33CSO-148401). The funders had no role in study design, data collection and analysis, decision to publish or preparation of the manuscript.

Abstract

Sleep-disordered breathing is a common condition, related to a higher cardiometabolic and neurocognitive risk. The main risk factors for sleep-disordered breathing include obesity, craniofacial characteristics, male sex and age. However, some studies have suggested that adverse socioeconomic circumstances and lifestyle-related behaviours such as smoking and alcohol use, may also be risk factors for sleep-disordered breathing. Here, we investigate the associations between socioeconomic status and sleep-disordered breathing, as measured by sleep apnea–hypopnea and oxygen desaturation indexes. Furthermore, we assess whether these associations are explained by lifestyle-related factors (smoking, sedentary behaviour, alcohol use and body mass index [BMI]). We used data from the CoLaus|HypnoLaus study, a population-based study including 2162 participants from Lausanne (Switzerland). Socioeconomic status was measured through occupation and education. Sleep-disordered breathing was assessed through polysomnography and measured using the apnea–hypopnea index (AHI: number of apnea/hypopnea events/hr: $\geq 15/\geq 30$ events), and the $\geq 3\%$ oxygen desaturation index (ODI: number of oxygen desaturation events/hr: $\geq 15/\geq 30$ events). Lower occupation and education were associated with higher AHI and ODI (occupation: AHI₃₀, odds ratio (OR) = 1.88, 95% confidence interval (CI) [1.07; 3.31]; ODI₃₀, OR = 2.29, 95% CI [1.19; 4.39]; education: AHI₃₀, OR = 1.21, 95% CI [0.85; 1.72]; ODI₃₀, OR = 1.26, 95% CI [0.83; 1.91]). BMI was associated with socioeconomic status and AHI/ODI, and contributed to the socioeconomic gradient in SDB, with mediation estimates ranging between 43% and 78%. In this Swiss population-based study, we found that low socioeconomic status is a risk factor for sleep-disordered breathing, and that these associations are partly explained by BMI. These findings provide a better understanding of the mechanisms underlying social differences in sleep-disordered breathing and may help implement policies for identifying high-risk profiles for this disorder.

KEYWORDS

BMI, mediation, obstructive sleep apnea, oxygen desaturation, sleep-disordered breathing, socioeconomic status

*Senior authors.

1 | INTRODUCTION

Sleep-disordered breathing (SDB) affects a large number of individuals and has detrimental effects on human health (Epstein et al., 2009; Heinzer et al., 2015). SDB is characterised by recurrent collapses of the upper airway during sleep, resulting in total (apnea) or partial (hypopnea) cessations of airflow and leading to gas exchange derangements and repetitive arousals from sleep (Punjabi, 2008). Although the immediate effects of SDB include fatigue, daytime sleepiness and impaired work performance, in the long term this disorder has been related to an increased incidence of several chronic diseases, such as hypertension, fatal and non-fatal cardiovascular events, type 2 diabetes and neurocognitive impairment (Li, Sundquist, & Sundquist, 2008; Marti-Soler et al., 2016; Punjabi, 2008; Tufik, Santos-Silva, Taddei, & Bittencourt, 2010).

Risk factors for SDB include obesity, neck circumference, craniofacial characteristics, male sex and age, whereas adverse health behaviours such as smoking and heavy drinking have also been suspected to play a role in the pathophysiology of SDB (Li et al., 2008; Scharf, Seiden, DeMore, & Carter-Pokras, 2004; Tarasiuk et al., 2006; Tufik et al., 2010; Ulfberg, Carter, Talback, & Edling, 1997; Young, Skatrud, & Peppard, 2004). Furthermore, some studies have suggested that socioeconomic status (SES) could be involved in the occurrence and severity of SDB (Li et al., 2008; Tufik et al., 2010). However, the associations between SES and SDB have seldom been investigated, and these studies have yielded inconsistent results. A Brazilian study reported that unemployed women or those with a low income had a greater chance of OSA, whereas the opposite was observed in men, with those with higher income being more at risk of OSA (Tufik et al., 2010). Another Swedish study observed a higher risk of OSA among lower-educated men and those occupying certain manual jobs, whereas no meaningful associations were observed in women (Li et al., 2008). In addition, the mechanisms underlying socioeconomic differences in SDB are unknown.

In this study, we investigate the association between SES, as measured by occupational position and educational level, and SDB, as measured by apnea–hypopnea and oxygen desaturation indexes, in the Swiss population-based CoLaus|HypnoLaus cohort. We also examine the role of lifestyle-related factors, namely smoking, alcohol intake, sedentary behaviour and BMI, as potential contributors to the socioeconomic gradient in SDB. We hypothesise that there is an inverse gradient between socioeconomic status and SDB, and that this association is explained by the lifestyle-related factors indicated above.

2 | MATERIALS AND METHODS

2.1 | Study population

Data were drawn from the CoLaus|HypnoLaus study, a cross-sectional study investigating sleep characteristics in a general population sample of the city of Lausanne, Switzerland. The CoLaus|HypnoLaus study is embedded within the CoLaus prospective cohort ($n = 5,064$)

and comprises a random sample of CoLaus participants who agreed to undergo a level 2 polysomnogram (PSG) recording at home ($n = 2,162$) (Berry et al., 2012; Stringhini et al., 2015). The included participants attended a medical appointment, which comprised an anthropometric examination, as well as blood and urine collection following an overnight fast. Information on demographic data, socioeconomic and marital status, health-related behaviours, personal and family history of disease, cardiovascular risk factors and treatment was collected through a questionnaire. The CoLaus|HypnoLaus study was approved by the Institutional Ethics Committee of the University of Lausanne (Firmann et al., 2008; Stringhini et al., 2015).

2.2 | Measures

2.2.1 | Socioeconomic status (SES)

Socioeconomic status was assessed through two standard indicators used in epidemiologic research, occupational position and educational level, which capture multiple dimensions of SES. Occupational position represents one's position in the occupational hierarchy and is strongly related to income, level of responsibility in the job, attained education, retirement benefits and professional exposures (Galobardes, Shaw, Lawlor, Lynch, & Smith, 2006; Stringhini et al., 2011). Occupational position was self-reported and grouped into three categories: “high” (managers: liberal professions, directors and professors), “middle” (lower level executives: teachers, qualified technicians and nurses) and “low” (low qualified non-manuals and manual: sales-assistants, clerks and manual workers). Participants who were not currently working were assigned their past occupational position. Participants who had never worked (students and housewives) were not included in the analysis. Education is another standard marker of SES, which is acquired in early life and reflects an individual's intellectual resources, as well as future employment and income (Galobardes et al., 2006). The highest level of attained education was self-reported and further classified into three categories: “high” (university education), “middle” (higher secondary education) and “low” (lower secondary education or lower).

2.2.2 | Sleep-disordered breathing

During a visit to the Center for Investigation and Research in Sleep (Lausanne University Hospital, Switzerland), certified technicians equipped the participants with a PSG recorder (Titanium, Embla® Flaga, Reykjavik, Iceland). The recorder was set between 17:00 and 20:00 hours before the participants returned home. All sleep recordings took place in the patients' home environment and included a total of 18 channels: six for electroencephalography (F3/M2, F4/M1, C3/M2, C4/M1, O1/M2 and O2/M1), two for electrooculography, three for surface electromyography (one submental region and two anterior tibialis muscle), and one for electrocardiogram, nasal pressure, thoracic and abdominal belts, body position, oxygen saturation and pulse rate, in accordance with the set-up recommended by the American Association of Sleep Medicine (AASM) (Berry et al., 2012).

All PSG recordings were manually scored by two trained sleep technicians using Somnologica software (Version 5.1.1 by Embla® Flaga) and reviewed by an expert sleep physician. Random quality checks were performed by a second sleep physician. Sleep stages and arousals were scored according to the AASM recommendations from 2012 (Berry et al., 2012; Stringhini et al., 2015).

We defined apnea as a drop of at least 90% of airflow from baseline lasting 10 s or longer, whereas hypopnea was defined as $\geq 30\%$ drop of airflow lasting at least 10 s with either an arousal or $\geq 3\%$ oxygen saturation drop, following the 2.4 AASM criteria 1A (Berry et al., 2012; Heinzer et al., 2015). In the present analyses, we used the apnea–hypopnea index (AHI) and the $\geq 3\%$ oxygen desaturation index (ODI) as outcome variables. The AHI represents the number of apneas and hypopneas per hour of sleep, including both obstructive and central events (Heinzer et al., 2015; Punjabi, 2008). AHI was dichotomised into ≥ 15 events/hr versus less (AHI15), and into ≥ 30 events/hr versus less (AHI30), following the definition of moderate and severe SDB in the ICSDIII manual (American Academy of Sleep Medicine, 2014). The ODI represents the number of desaturation events per hour of sleep, which are defined as $\geq 3\%$ decrease in oxygen saturation (SpO_2) (Heinzer et al., 2015). The ODI was also dichotomised into ≥ 15 events/hr versus less (ODI15) and ≥ 30 events/hr versus less (ODI30), following the definition of moderate and severe SDB in the ICSDIII manual (American Academy of Sleep Medicine, 2014).

2.2.3 | Other factors

Socio-demographic covariates included in the present analyses were age, sex, marital status (married or cohabiting/living alone) and place of birth (Switzerland/other). Lifestyle-related factors included smoking, alcohol intake, sedentary behaviour and BMI, and were assessed through questionnaire and medical examination. Smoking status was categorised as current and non-current smokers, the latter category including former smokers. Alcohol intake was assessed using questions on the number of alcoholic drinks usually consumed within a week, then categorised as hazardous intake (>3 daily alcoholic drinks for men; >2 daily alcoholic drinks for women) versus non-hazardous intake. Sedentary behaviour was defined as lower tertile versus higher tertiles of total weekly energy expenditure in kcal/week, based on a validated physical activity frequency questionnaire, which establishes the amount of energy spent according to standard activities or groups of activities (Bernstein et al., 1998). Body mass index (BMI) was defined as weight in kg divided by the square of height in metres.

2.3 | Statistical analyses

The associations between SES indicators, lifestyle-related factors and AHI/ODI were analysed using linear and logistic regression models. First, the association between SES and AHI/ODI was analysed, by adjusting for age, sex, birth place and marital status, and without including lifestyle-related factors. Second, the associations between

SES and lifestyle-related factors were tested using two regression models: a model adjusted for age, sex, birth place and marital status, and a model additionally adjusted for all lifestyle-related factors simultaneously. Third, the associations between lifestyle-related factors and AHI/ODI were also assessed using the least and the fully adjusted regression models. Finally, the lifestyle-related factors that were simultaneously associated with SES indicators and AHI/ODI were then tested as mediators of the association between SES and AHI/ODI. The associations between SES and AHI/ODI, and the mediating effect of selected lifestyle-related factors, were assessed by applying the counterfactual mediation method (Valeri & VanderWeele, 2013). This method is based on the computation of natural direct effects (NDE [odds ratio]: effect of exposure on outcome via pathways that do not involve the mediator), natural indirect effects (NIE [odds ratio]: effect of exposure on the outcome operating through the mediator), the marginal total effect (MTE = NDE + NIE: total effect of the exposure on the outcome), and the proportion of the association between the exposure and the outcome that is mediated by the mediator of interest (proportion mediated, PM). When compared with other mediation approaches, the counterfactual method is valid in the presence of interaction between the exposure and the mediator, which is not the case for other commonly used methods for assessing mediation, such as the “difference method” (Jiang & VanderWeele, 2015; Valeri & VanderWeele, 2013; VanderWeele & Vansteelandt, 2010). Confidence intervals for MTE, NDE, NIE and PM parameters were computed by applying the bootstrap procedure (10,000 simulations). All statistical analyses were conducted using Stata software v.14 (Stata Corp, College Station, TX, USA). Statistical significances were set at $p < 0.05$.

3 | RESULTS

In the CoLaus|HypnoLaus study, information on occupational position was only available for participants who were employed at the time of study. Thus, of the 2162 participants who underwent the PSG recording, 850 participants were excluded from analyses using occupational position. Two participants were excluded from analyses because of missing information on education. Compared with the included participants, those excluded were more frequently women (57% versus 43%, $p < 0.05$), were older (mean age 65 versus 52 years, $p < 0.05$), were more frequently Swiss born (72% versus 58%, $p < 0.05$), had a lower education (17% versus 25% in the high education group, $p < 0.05$), had a higher mean BMI (27 versus 26 kg/m^2 , $p < 0.05$), were less frequently smokers (15% versus 21%, $p < 0.05$), were more sedentary (46% versus 24%, $p < 0.05$) and had more apnea–hypopnea events per hour of sleep (mean AHI 19 versus 14/hr, $p < 0.05$), as well as more oxygen desaturation events (mean ODI 18 versus 13/hr, $p < 0.05$), than included participants.

3.1 | Sample characteristics

The general characteristics of the sample by sex are displayed in Table 1. A higher proportion of men than women were living with a

partner, had a higher occupational position, achieved higher education, had a higher BMI, were at higher risk of hazardous alcohol intake and experienced more apnea–hypopnea and oxygen desaturation events per hour of sleep (all $p < 0.05$).

3.2 | Association between SES indicators and AHI/ODI

The results for the association between occupational position and education, and AHI/ODI are presented in Table 2. Generally, there was an inverse socioeconomic gradient in AHI/ODI, with lower occupational position being associated with an increased risk of AHI30 and ODI30 (AHI30, OR = 1.79, 95% CI [1.05; 2.03]; ODI30, OR = 2.07, 95% CI [1.14; 3.73]). Weaker associations were observed between education and AHI/ODI, the only meaningful association being observed for ODI15 (OR = 1.50, 95% CI [1.17; 1.93]).

3.3 | Selection of lifestyle-related factors as potential mediators

3.3.1 | Association between SES indicators and lifestyle-related factors

The results for the socioeconomic gradient in lifestyle-related factors are displayed in Table 3. Both occupational position and education were strongly associated with BMI, with low SES individuals being at a higher risk of an increased BMI (occupational position (lowest versus highest): BMI, $\beta_{M1} = 1.59$, 95% confidence interval [0.94; 2.24]; education (lowest vs. highest): BMI, $\beta_{M1} = 1.77$, 95% CI [1.31; 2.23]). Alternatively, there were few, inconsistent, associations between both SES indicators and the remaining lifestyle-related factors, with high occupational position being associated with an increased risk of hazardous alcohol intake in the least and the fully adjusted models, whereas low educational level was associated with a higher risk of smoking.

3.3.2 | Association between lifestyle-related factors and AHI/ODI

The associations between lifestyle-related factors and AHI/ODI are shown in Table 4. BMI was consistently associated with all AHI and ODI, with stronger associations for ODI than AHI (BMI, AHI15: $\beta_{M1} = 1.16$, 95% CI [1.13; 1.19]; BMI, AHI30: $\beta_{M1} = 1.16$, 95% CI [1.13; 1.20]; BMI, ODI15: $\beta_{M1} = 1.21$, 95% CI [1.18; 1.24]; BMI, ODI30: $\beta_{M1} = 1.21$, 95% CI [1.18; 1.26]), whereas there were inconsistent associations between the remaining lifestyle-related factors and AHI/ODI. Sedentary behaviour was associated with a lower risk of experiencing ≥ 30 ODI events/hr (OR_{M1} = 0.68, 95% CI [0.50; 0.92]), but this association was no longer significant upon adjusting for smoking, hazardous alcohol intake and BMI (OR_{M2} = 0.92, 95% CI [0.66; 1.27]). Hazardous alcohol intake was associated with an increased risk of having ≥ 30 AHI events/hr (OR_{M1} = 1.56, 95% CI

TABLE 1 General characteristics of included participants (HypnoLaus|CoLaus study)

	Men (n = 1,055)	Women (n = 1,106)	p-value ^{a,b}
Age, mean \pm SD (year)	56.8 (\pm 10.5)	57.6 (\pm 10.6)	0.059
Country of birth, n (%)			
Switzerland	677 (64)	697 (63)	0.578
Other	378 (36)	409 (37)	
Marital status, n (%)			
Living alone	324 (31)	576 (52)	<0.001
Living in a couple	731 (69)	530 (48)	
Occupational position, n (%)			
High	143 (21)	40 (6)	<0.001
Middle	282 (41)	222 (36)	
Low	263 (38)	361 (58)	
Education, n (%)			
High	274 (26)	190 (17)	<0.001
Middle	273 (26)	316 (29)	
Low	507 (48)	600 (54)	
Body mass index (BMI), mean \pm SD (kg/m ²)	26.9 (\pm 4)	25.6 (\pm 4.7)	<0.001
Overweight (BMI > 25), n (%)	716 (68)	534 (48)	<0.001
Health behaviours, n (%)			
Current smoking	200 (19)	204 (18)	0.760
Hazardous alcohol consumption ^c	85 (8)	56 (5)	0.005
Sedentary behaviour	344 (33)	371 (34)	0.643
Apnea–hypopnea index (AHI)			
AHI, continuous score, mean \pm SD (events/hr)	20.4 (\pm 18.2)	10.9 (\pm 12.7)	<0.001
≥ 15 AHI events/hr, n (%)	530 (50)	260 (24)	<0.001
≥ 30 AHI events/hr, n (%)	239 (23)	84 (8)	<0.001
Oxygen desaturation index (ODI)			
ODI, continuous score, mean \pm SD (events/hr)	19.1 (\pm 17)	10.6 (\pm 12)	<0.001
≥ 15 ODI events/hr, n (%)	512 (48)	244 (22)	<0.001
≥ 30 ODI events/hr, n (%)	201 (19)	72 (7)	<0.001

Data are mean \pm SD for continuous variables and n (%) for categorical variables.

^aThe Mann–Whitney U-test was performed between men and women for continuous variables.

^bThe χ^2 contingency test was performed between men and women for categorical variables.

^cHazardous alcohol use was defined as having >3 alcoholic drinks per day for men and >2 alcoholic drinks per day for women.

[1.00; 2.44]; OR_{M2} = 1.64, 95% CI [1.02; 2.64]) and tended to be associated with an increased risk of having ≥ 15 ODI events/hr (OR_{M1} = 1.45, 95% CI [0.99; 2.13]; OR_{M2} = 1.52, 95% CI [1.01; 2.30]).

TABLE 2 Association between socioeconomic status indicators (occupational position, educational attainment) and apnea–hypopnea index/oxygen desaturation index

	M1: OR [95% CI] ^a	p-value ^b	n
Occupational position			
≥15 AHI events/hr	1.31 [0.91; 1.90]	0.149	1,311
≥30 AHI events/hr	1.79 [1.05; 3.03]	0.032	1,311
≥15 ODI events/hr	1.40 [0.96; 2.04]	0.080	1,311
≥30 ODI events/hr	2.07 [1.14; 3.73]	0.016	1,311
Education			
≥15 AHI events/hr	1.20 [0.94; 1.53]	0.147	2,160
≥30 AHI events/hr	1.20 [0.87; 1.65]	0.270	2,160
≥15 ODI events/hr	1.50 [1.17; 1.93]	0.001	2,160
≥30 ODI events/hr	1.31 [0.92; 1.85]	0.132	2,160

OR, odds ratio; SES, socioeconomic status; AHI, apnea–hypopnea index; ODI, oxygen desaturation index.

^aRegression coefficients for the association between SES indicator (predictor, lowest versus highest) and AHI/ODI, adjusted for age, sex, country of birth and marital status.

^bSignificance threshold for the association of SES indicators and AHI/ODI was set at $p < 0.0125$ (0.05/4) because of multiple comparisons.

3.4 | The contribution of BMI to the socioeconomic gradient in AHI/ODI

Figure 1 displays the associations between SES indicators and AHI/ODI, and the mediating effect of BMI, which was the only lifestyle-related factor to be simultaneously associated with SES and AHI/ODI. Individuals with a lower occupational position were more likely to have a higher risk of AHI and ODI events (occupational position: AHI15, MTE (odds ratio) = 1.40, 95% CI [0.89; 2.16]; AHI30, MTE

(odds ratio) = 1.88, 95% CI [1.07; 3.32]; ODI15, MTE = 1.66, 95% CI [1.02; 2.69]; ODI30, MTE = 2.29, 95% CI [1.19; 4.39]). BMI mediated 43% (95% CI [19%; 168%]) and 47% (95% CI [27%; 134%]) of the associations between occupational position and AHI30 and ODI30, respectively. Education was associated with ODI15 (MTE = 1.59, 95% CI [1.14; 2.21]), and BMI explained 78% (95% CI [50%; 236%]) of this association.

3.5 | Stratification of analyses by sex

We performed sensitivity analyses by stratifying all associations by sex. In men, low occupational position tended to be associated with an increased risk of ODI30, but failed to reach the Bonferroni threshold. In women, occupational position tended to be associated with an increased risk of AHI30, whereas education was associated with an increased risk of ODI15 (Supporting Information Table S1). Low occupational position and low educational level were associated with a higher risk of having an increased BMI in men, whereas low educational level was also associated with an increased risk of smoking. In women, low occupational position and low educational level were associated with a lower risk of hazardous alcohol intake and a higher risk of an increased BMI, with stronger associations in women than in men. In both men and women, BMI was associated with an increased risk of AHI/ODI, whereas there were no meaningful associations between smoking, sedentary behaviour and hazardous alcohol intake, and AHI/ODI (Supporting Information Table S2). Low occupational position was associated with a higher risk of ODI30 in men, with a mediating effect of 49% by BMI (Supporting Information Figure S1). In women, low occupational position was strongly associated with a higher risk of having ≥30 AHI events/hr and ≥30 ODI events/hr,

TABLE 3 Association between socioeconomic status indicators (occupational position and education) and lifestyle-related factors (smoking, sedentary behaviour, hazardous alcohol intake and body mass index)

	M1: OR [95% CI] ^a	p-value ^d	M2: OR [95% CI] ^b	p-value ^d	n
Occupational position					
Smoking	1.28 [0.86; 1.91]	0.229	1.44 [0.96; 2.16]	0.082	1,311
Sedentary behaviour	0.86 [0.58; 1.25]	0.420	1.04 [0.70; 1.53]	0.850	1,311
Hazardous alcohol intake	0.53 [0.29; 0.96]	0.036	0.51 [0.28; 0.94]	0.030	1,311
BMI ^c	1.59 [0.94; 2.24]	<0.001	1.56 [0.92; 2.20]	<0.001	1,311
Education					
Smoking	1.55 [1.16; 2.06]	0.003	1.71 [1.28; 2.28]	<0.001	2,160
Sedentary behaviour	0.79 [0.62; 1.01]	0.063	0.95 [0.74; 1.23]	0.713	2,160
Hazardous alcohol intake	0.68 [0.45; 1.03]	0.070	0.62 [0.40; 0.95]	0.028	2,160
BMI ^c	1.77 [1.31; 2.23]	<0.001	1.75 [1.30; 2.20]	<0.001	2,160

OR, odds ratio; CI, confidence interval; BMI, body mass index.

^aRegression coefficients for the association between socioeconomic status (SES) indicator (predictor, lowest versus highest) and lifestyle-related factor, adjusted for age, sex, country of birth and marital status.

^bRegression coefficients for the association between SES indicator (predictor, lowest versus highest) and lifestyle-related factor, adjusted for age, sex, country of birth, marital status and the three remaining lifestyle-related factors.

^cA linear regression model was used for the association between SES indicator and BMI, and logistic regression models for associations using smoking, sedentary behaviour and hazardous alcohol intake.

^dSignificance threshold was set at $p < 0.0125$ (0.05/4) because of multiple comparisons.

TABLE 4 Association between lifestyle-related behaviours and apnea–hypopnea/oxygen desaturation indexes

	M1: OR [95% CI] ^a	p-value ^c	M2: OR [95% CI] ^b	p-value ^c	N
Smoking					
≥15 AHI events/hr	0.98 [0.76; 1.26]	0.859	1.06 [0.81; 1.38]	0.676	2,161
≥30 AHI events/hr	0.75 [0.52; 1.08]	0.120	0.78 [0.54; 1.14]	0.200	2,161
≥15 ODI events/hr	0.93 [0.72; 1.20]	0.552	1.01 [0.76; 1.32]	0.966	2,161
≥30 ODI events/hr	0.81 [0.55; 1.19]	0.283	0.88 [0.59; 1.33]	0.549	2,161
Sedentary behaviour					
≥15 AHI events/hr	0.81 [0.66; 1.01]	0.064	1.03 [0.82; 1.29]	0.825	2,161
≥30 AHI events/hr	0.81 [0.61; 1.08]	0.150	1.03 [0.77; 1.39]	0.832	2,161
≥15 ODI events/hr	0.88 [0.71; 1.09]	0.245	1.18 [0.93; 1.50]	0.164	2,161
≥30 ODI events/hr	0.68 [0.50; 0.92]	0.013	0.92 [0.66; 1.27]	0.597	2,161
Hazardous alcohol intake					
≥15 AHI events/hr	1.29 [0.88; 1.88]	0.194	1.31 [0.88; 1.96]	0.187	2,161
≥30 AHI events/hr	1.56 [1.00; 2.44]	0.049	1.64 [1.02; 2.64]	0.040	2,161
≥15 ODI events/hr	1.45 [0.99; 2.13]	0.054	1.52 [1.01; 2.30]	0.047	2,161
≥30 ODI events/hr	1.45 [0.90; 2.34]	0.129	1.49 [0.88; 2.52]	0.133	2,161
BMI					
≥15 AHI events/hr	1.16 [1.13; 1.19]	<0.001	1.16 [1.13; 1.19]	<0.001	2161
≥30 AHI events/hr	1.16 [1.13; 1.20]	<0.001	1.16 [1.13; 1.20]	<0.001	2161
≥15 ODI events/hr	1.21 [1.18; 1.24]	<0.001	1.22 [1.18; 1.25]	<0.001	2161
≥30 ODI events/hr	1.21 [1.18; 1.26]	<0.001	1.21 [1.17; 1.25]	<0.001	2161

OR, odds ratio; CI, confidence interval; AHI, apnea–hypopnea index; ODI, oxygen desaturation index.

^aLogistic regression (OR) for the association between lifestyle-related factors and AHI/ODI, adjusted for age, sex, country of birth and marital status.

^bLogistic regression (OR) for the association between lifestyle-related factors and AHI/ODI, adjusted for age, sex, country of birth, marital status and the remaining lifestyle-related factors.

^cSignificance threshold was set at $p < 0.0125$ (0.05/4) because of multiple comparisons.

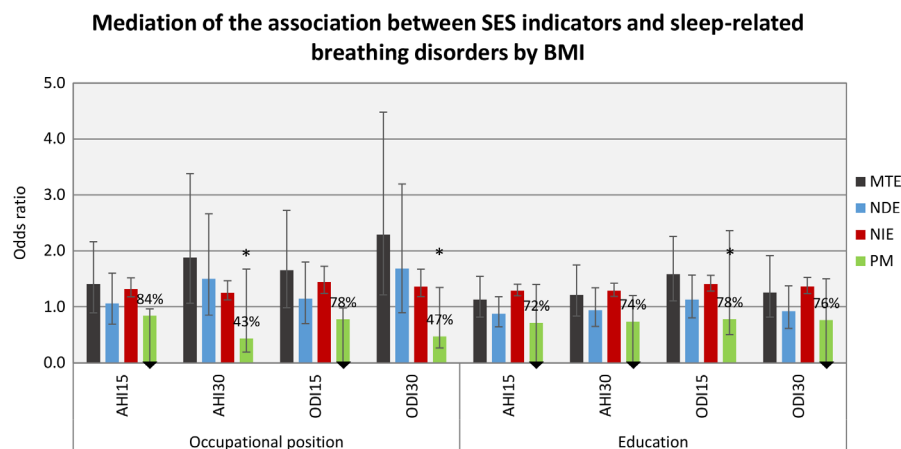


FIGURE 1 Counterfactual mediation by body mass index (BMI) for the association between two socioeconomic status (SES) indicators, and apnea-hypopnea (AHI) and oxygen desaturation index (ODI). MTE, marginal total effect (odds ratio [OR], 95% confidence interval [CI]); NDE, natural direct effect (OR, 95% CI); NIE, natural indirect effect (OR, 95% CI); PM, proportion of the association between SES indicators and AHI and ODI that is mediated by continuous or dichotomised BMI (*significant mediation). Lower and upper arrows indicate that CIs extend beyond the limits of the graph

with a mediating effect of 22% by BMI (AHI30), whereas low educational level was associated with a higher risk of ODI15 (PM by BMI, 76%). Finally, we also assessed the mediating effect by

dichotomised BMI ($<25 \text{ kg/m}^2$, $\geq 25 \text{ kg/m}^2$) to the association between SES and AHI/ODI and found similar results to the mediating effect by continuous BMI (results available from the authors).

4 | DISCUSSION

In this study, we found that individuals with a low occupational position and low educational level were at a higher risk of SDB as measured by AHI and ODI. As BMI was also strongly related to AHI/ODI and SES, a substantial part (43–78%) of the associations between SES indicators and sleep-disordered breathing was explained by the higher BMI of individuals with low SES.

The inverse associations between occupational position and education and AHI/ODI tend to be in line with the existing literature (Li et al., 2008; Spilsbury et al., 2006; Tufik et al., 2010). In a Swedish study investigating the occupational and educational determinants of sleep health, men with low educational level and those occupying specific manual jobs were found to be at an increased risk of hospitalisation for obstructive sleep apnea, whereas no meaningful associations were observed in women (Li et al., 2008). Further, another study conducted in the USA has shown that neighbourhood disadvantage was strongly related to obstructive sleep apnea (Spilsbury et al., 2006). A study conducted in Brazil found that women with low income were at a higher risk of obstructive sleep apnea, but that this association was reversed in men (Tufik et al., 2010). Given the important mediating role of BMI in shaping social differences in sleep-disordered breathing, our results suggest that inconsistencies across studies may be related to the different social patterning of BMI and obesity in different countries (Petrovic et al., 2018; Wilkinson, 1994).

We also observed a strong association between BMI and frequent AHI and ODI events. This association is in line with previous research and is related to the fact that fat deposition on the airway anatomy alters the upper respiratory function and increases the collapsibility of the airway, eventually resulting in cessation of breathing during sleep (Benumof, 2004; Wolk, Shamsuzzaman, & Somers, 2003; Young et al., 2004). Another mechanism linking obesity to SDB may be related to leptin, a hormone that is produced by the adipose tissue, and which was found to play an important role in central respiratory control mechanisms (O'Donnell, Tankersley, Polotsky, Schwartz, & Smith, 2000; Wolk et al., 2003).

Furthermore, we observed that smoking, sedentary behaviour and hazardous alcohol intake were not strongly related to AHI and ODI. The lack of association between adverse lifestyle behaviours and sleep-disordered breathing is inconsistent with former research, which suggested that smoking, physical inactivity and heavy drinking are possible risk factors for obstructive sleep apnea (Hong & Dimsdale, 2003; Punjabi, 2008; Young, Peppard, & Gottlieb, 2002). However, our results may be explained by the lack of statistical power and the small sample size of this study.

Health behaviours and BMI were patterned by SES, the association being particularly strong for BMI, confirming previous research reporting a negative socioeconomic gradient in BMI in high-income countries (Stringhini et al., 2012). This is generally explained by the fact that low SES individuals eat unhealthier diets and are less physically active than their more advantaged counterparts (McLaren, 2007; Pampel, Krueger, & Denney, 2010), as a result of lack of

resources, knowledge and the motivation to follow a healthy lifestyle, and are also more exposed to obesogenic environments (World Health Organization, 2003; Adam & Epel, 2014; Pampel et al., 2016; Stringhini et al., 2010).

As a result of strong associations between SES indicators and BMI, and between BMI and AHI/ODI, BMI explained a large proportion of the association between both SES indicators and sleep apnea and oxygen desaturation. To our knowledge, this is the first study to explore potential underlying mechanisms for the socioeconomic gradient in SDB (sleep apnea and oxygen desaturation) and to demonstrate that an important part of the SES effect on sleep-disordered breathing occurs through BMI.

In sex-stratified analyses, we observed a stronger socioeconomic gradient in sleep-disordered breathing in women. These results are explained by the fact that there was a stronger association between SES and BMI in women when compared with men, and may be related to the epidemiologic transition of chronic diseases and lifestyle-related risk factors, in particular obesity and obstructive sleep apnea (Gaziano, 2010; Stringhini et al., 2012; Wilkinson, 1994). Another explanation may be that low SES women often have to combine the psychosocial strain of unqualified lower-paid jobs with the strain of household responsibilities, resulting in higher stress and obesogenic behaviours, such as overeating and energy-dense diets (Artazcoz, Borrell, Benach, Cortes, & Rohlf, 2004; Petrovic et al., 2016).

Our findings have important research and clinical implications. First, this study provides a comprehensive understanding of the underlying mechanisms of socioeconomic inequalities in sleep-disordered breathing. Further, this study will also help improve clinical practices that aim to identify high-risk SDB profiles, by encouraging health professionals to focus on the socioeconomic background of patients in addition to other risk factors.

4.1 | Strengths and limitations

Our study has several strengths. To our knowledge, this is the first study to assess the socioeconomic gradient in obstructive sleep apnea and oxygen desaturation, objectively measured by polysomnography, and to explore the potential underlying mechanisms of this association. Another strength is the richness of the sociodemographic, lifestyle, physiological and health-related data of this population-based study. Our study also has some limitations. First, this study is based on cross-sectional data, which does not allow determination of the causal direction of associations, which can be a particular issue for the associations between BMI and sleep-disordered breathing. Second, the proportion-mediated parameter (PM) that was used to compute mediation was initially developed for rare outcomes and may thus not be valid for lower thresholds of AHI and ODI (i.e. <15 events/hr versus ≥15 events/hr), which have prevalence estimates that are higher than more severe indexes (i.e. <30 events/hr versus ≥30 events/hr) in the studied population. Finally, the participation rate of this study was relatively low and the objective measurements of sleep were performed in less than half of participants who were enrolled in the first follow-up,

which implies that this study may not be representative of the general population.

4.2 | Conclusion and perspectives

In conclusion, this Swiss population-based study suggests that BMI is a potential mechanism explaining the inverse association between SES and sleep-disordered breathing. Additional longitudinal analyses should be conducted to examine the causal direction between SES, BMI, sleep apnea and oxygen desaturation. Moreover, further research should assess the role of other potential mediators of the socioeconomic gradient in sleep health, such as job characteristics, exposure to industrial pollutants, psychosocial factors and house allergens.

ETHICS STATEMENT

The institutional Ethics Committee of the Faculty of Medicine of the University of Lausanne approved the CoLaus|HypnoLaus study. All participants signed a written informed consent after having received a detailed description of study objectives.

ACKNOWLEDGEMENTS

The authors would like to express their gratitude to Professor Gérard Waeber for critically revising and helping to improve this manuscript, and Professor Mehdi Tafti for his contribution to the CoLaus|HypnoLaus study.

AUTHOR CONTRIBUTIONS

SS, RH, JHR, DP and CC designed the study. RH, JHR and PV actively contributed to data acquisition. DP, SS, CC, RH and JHR analysed the data. DP, SS, CC, RH, JHR and PV critically revised the manuscript.

CONFLICT OF INTEREST

None to declare.

ORCID

Dusan Petrovic  <https://orcid.org/0000-0003-3684-4582>

José Haba-Rubio  <https://orcid.org/0000-0001-7466-6436>

Cristian Carmeli  <https://orcid.org/0000-0002-1463-4587>

Peter Vollenweider  <https://orcid.org/0000-0002-0765-896X>

Raphaël Heinzer  <https://orcid.org/0000-0002-3215-7788>

Silvia Stringhini  <https://orcid.org/0000-0002-4387-8943>

REFERENCES

Adam, T. C., & Epel, E. S. (2007). Stress, eating and the reward system. *Physiology & Behavior*, 91, 449–458. <https://doi.org/10.1016/j.physbeh.2007.04.011>

American Academy of Sleep Medicine. (2014). *International classification of sleep disorders—third edition (ICSD-3)*. Darien, IL: American Academy of Sleep Medicine.

Artazcoz, L., Borrell, C., Benach, J., Cortes, I., & Rohlf, I. (2004). Women, family demands and health: The importance of employment status and socio-economic position. *Social Science & Medicine*, 59, 263–274. <https://doi.org/10.1016/j.socscimed.2003.10.029>

Benumof, J. L. (2004). Obesity, sleep apnea, the airway and anesthesia. *Current Opinion in Anaesthesiology*, 17, 21–30. <https://doi.org/10.1097/00001503-200402000-00005>

Bernstein, M., Slutski, D., Kumanyika, S., Sparti, A., Schutz, Y., & Morabia, A. (1998). Data-based approach for developing a physical activity frequency questionnaire. *American Journal of Epidemiology*, 147, 147–154. <https://doi.org/10.1093/oxfordjournals.aje.a009427>

Berry, R. B., Budhiraja, R., Gottlieb, D. J., Gozal, D., Iber, C., Kapur, V. K., ... Quan, S. F. (2012). Rules for scoring respiratory events in sleep: Update of the 2007 AASM manual for the scoring of sleep and associated events: Deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. *Journal of Clinical Sleep Medicine: JCSM: Official Publication of the American Academy of Sleep Medicine*, 8, 597.

Epstein, L. J., Kristo, D., Strollo, P. J., Friedman, N., Malhotra, A., Patil, S. P., ... Weaver, E. M. (2009). Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *Journal of Clinical Sleep Medicine*, 5, 263–276.

Firmann, M., Mayor, V., Vidal, P. M., Bochud, M., Pécoud, A., Hayoz, D., ... Yuan, X. (2008). The CoLaus study: A population-based study to investigate the epidemiology and genetic determinants of cardiovascular risk factors and metabolic syndrome. *BMC Cardiovascular Disorders*, 8, 6. <https://doi.org/10.1186/1471-2261-8-6>

Galobardes, B., Shaw, M., Lawlor, D. A., Lynch, J. W., & Smith, G. D. (2006). Indicators of socioeconomic position (part 1). *Journal of Epidemiology & Community Health*, 60, 7–12. <https://doi.org/10.1136/jecph.2004.023531>

Gaziano, J. M. (2010). Fifth phase of the epidemiologic transition: The age of obesity and inactivity. *JAMA*, 303, 275–276. <https://doi.org/10.1001/jama.2009.2025>

Heinzer, R., Vat, S., Marques-Vidal, P., Marti-Soler, H., Andries, D., Tobback, N., ... Waeber, G. (2015). Prevalence of sleep-disordered breathing in the general population: The HypnoLaus study. *The Lancet Respiratory Medicine*, 3, 310–318. [https://doi.org/10.1016/s2213-2600\(15\)00043-0](https://doi.org/10.1016/s2213-2600(15)00043-0)

Hong, S., & Dimsdale, J. E. (2003). Physical activity and perception of energy and fatigue in obstructive sleep apnea. *Medicine and Science in Sports and Exercise*, 35, 1088–1092. <https://doi.org/10.1249/01.mss.0000074566.94791.24>

Jiang, Z., & VanderWeele, T. J. (2015). When is the difference method conservative for assessing mediation? *American Journal of Epidemiology*, 182, 105–108. <https://doi.org/10.1093/aje/kwv059>

Li, X., Sundquist, K., & Sundquist, J. (2008). Socioeconomic status and occupation as risk factors for obstructive sleep apnea in Sweden: A population-based study. *Sleep Medicine*, 9, 129–136. <https://doi.org/10.1016/j.sleep.2007.02.003>

Marti-Soler, H., Hirotsu, C., Marques-Vidal, P., Vollenweider, P., Waeber, G., Preisig, M., ... Tufik, S. (2016). The NoSAS score for screening of sleep-disordered breathing: A derivation and validation study. *The Lancet Respiratory Medicine*, 4, 742–748. [https://doi.org/10.1016/s2213-2600\(16\)30075-3](https://doi.org/10.1016/s2213-2600(16)30075-3)

McLaren, L. (2007). Socioeconomic status and obesity. *Epidemiologic Reviews*, 29, 29–48. <https://doi.org/10.1093/epirev/mxm001>

O'Donnell, C. P., Tankersley, C. G., Polotsky, V. P., Schwartz, A. R., & Smith, P. L. (2000). Leptin, obesity, and respiratory function. *Respiration Physiology*, 119, 163–170. [https://doi.org/10.1016/s0034-5687\(99\)00111-5](https://doi.org/10.1016/s0034-5687(99)00111-5)

- Pampel, F. C., Krueger, P. M., & Denney, J. T. (2010). Socioeconomic disparities in health behaviors. *Annual Review of Sociology*, 36, 349–370. <https://doi.org/10.1146/annurev.soc.012809.102529>
- Petrovic, D., de Mestral, C., Bochud, M., Bartley, M., Kivimäki, M., Vineis, P., ... Stringhini, S. (2018). The contribution of health behaviors to socioeconomic inequalities in health: A systematic review. *Preventive Medicine*, 113, 15–31. <https://doi.org/10.1016/j.ypmed.2018.05.003>
- Petrovic, D., Pivin, E., Ponte, B., Dhayat, N., Pruijm, M., Ehret, G., ... Pechère-Bertschi, A. (2016). Sociodemographic, behavioral and genetic determinants of allostatic load in a Swiss population-based study. *Psychoneuroendocrinology*, 67, 76–85. <https://doi.org/10.1016/j.psyneuen.2016.02.003>
- Punjabi, N. M. (2008). The epidemiology of adult obstructive sleep apnea. *Proceedings of the American Thoracic Society*, 5, 136–143. <https://doi.org/10.1513/pats.200709-155mg>
- Scharf, S. M., Seiden, L., DeMore, J., & Carter-Pokras, O. (2004). Racial differences in clinical presentation of patients with sleep-disordered breathing. *Sleep and Breathing*, 8, 173–183. <https://doi.org/10.1055/s-2004-860894>
- Spilisbury, J. C., Storer-Isser, A., Kirchner, H. L., Nelson, L., Rosen, C. L., Drotar, D., & Redline, S. (2006). Neighborhood disadvantage as a risk factor for pediatric obstructive sleep apnea. *The Journal of Pediatrics*, 149, 342–347. <https://doi.org/10.1016/j.jpeds.2006.04.061>
- Stringhini, S., Dugravot, A., Shipley, M., Goldberg, M., Zins, M., Kivimäki, M., ... Singh-Manoux, A. (2011). Health behaviours, socioeconomic status, and mortality: Further analyses of the British Whitehall II and the French GAZEL prospective cohorts. *PLoS Medicine*, 8, e1000419.
- Stringhini, S., Haba-Rubio, J., Marques-Vidal, P., Waeber, G., Preisig, M., Guessous, I., ... Heinzer, R. (2015). Association of socioeconomic status with sleep disturbances in the Swiss population-based CoLaus study. *Sleep Medicine*, 16, 469–476. <https://doi.org/10.1016/j.sleep.2014.12.014>
- Stringhini, S., Spencer, B., Marques-Vidal, P., Waeber, G., Vollenweider, P., Paccaud, F., & Bovet, P. (2012). Age and gender differences in the social patterning of cardiovascular risk factors in Switzerland: The CoLaus study. *PLoS ONE*, 7, e49443. <https://doi.org/10.1371/journal.pone.0049443>
- Tarasiuk, A., Greenberg-Dotan, S., Simon, T., Tal, A., Oksenberg, A., & Reuveni, H. (2006). Low socioeconomic status is a risk factor for cardiovascular disease among adult obstructive sleep apnea syndrome patients requiring treatment. *Chest*, 130, 766–773. <https://doi.org/10.1378/chest.130.3.766>
- Tufik, S., Santos-Silva, R., Taddei, J. A., & Bittencourt, L. R. A. (2010). Obstructive sleep apnea syndrome in the Sao Paulo epidemiologic sleep study. *Sleep Medicine*, 11, 441–446. <https://doi.org/10.1016/j.sleep.2009.10.005>
- Ulfberg, J., Carter, N., Talback, M., & Edling, C. (1997). Occupational exposure to organic solvents and sleep-disordered breathing. *Neuroepidemiology*, 16, 317–326. <https://doi.org/10.1159/000109704>
- Valeri, L., & VanderWeele, T. J. (2013). Mediation analysis allowing for exposure-mediator interactions and causal interpretation: Theoretical assumptions and implementation with SAS and SPSS macros. *Psychological Methods*, 18, 137. <https://doi.org/10.1037/a0031034>
- VanderWeele, T. J., & Vansteelandt, S. (2010). Odds ratios for mediation analysis for a dichotomous outcome. *American Journal of Epidemiology*, 172, 1339–1348. <https://doi.org/10.1093/aje/kwq332>
- Wilkinson, R. G. (1994). The epidemiological transition: From material scarcity to social disadvantage? *Daedalus*, 123, 61–77.
- Wolk, R., Shamsuzzaman, A. S. M., & Somers, V. K. (2003). Obesity, sleep apnea, and hypertension. *Hypertension*, 42, 1067–1074. <https://doi.org/10.1161/01.hyp.0000101686.98973.a3>
- World Health Organization (2003). Diet, nutrition and the prevention of chronic diseases. *World Health Organization Technical Report Series*, 916, i–viii, 1–149, backcover.
- Young, T., Peppard, P. E., & Gottlieb, D. J. (2002). Epidemiology of obstructive sleep apnea: A population health perspective. *American Journal of Respiratory and Critical Care Medicine*, 165, 1217–1239. <https://doi.org/10.1164/rccm.2109080>
- Young, T., Skatrud, J., & Peppard, P. E. (2004). Risk factors for obstructive sleep apnea in adults. *JAMA*, 291, 2013–2016. <https://doi.org/10.1001/jama.291.16.2013>

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

How to cite this article: Petrovic D, Haba-Rubio J, Carmeli C, Vollenweider P, Heinzer R, Stringhini S. Social inequalities in sleep-disordered breathing: Evidence from the CoLaus|HypnoLaus study. *J Sleep Res*. 2019;28:e12799. <https://doi.org/10.1111/jsr.12799>