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

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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 behaviors such as smoking and alcohol, 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 behavior, alcohol, 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/hour: ≥15/≥30 events), and the ≥3% oxygen desaturation index (ODI: number of oxygen desaturation events/hour: ≥15/≥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.

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

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 characterized 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). While 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, and Sundquist 2008; Punjabi 2008; Tufik et al. 2010; Marti-Soler et al. 2016).

Risk factors for SDB include obesity, neck circumference, craniofacial characteristics, male sex, and age, whereas adverse health behaviors such as smoking and heavy drinking have also been suspected to play a role in the physiopathology of SDB (Li, Sundquist, and Sundquist 2008; Tufik et al. 2010; Tarasiuk et al. 2006; Scharf et al. 2004; Ulfberg et al. 1997; Young, Skatrud, and Peppard 2004). Furthermore, some studies have suggested that socioeconomic status (SES) could be involved in the occurrence and severity of SDB (Li, Sundquist, and Sundquist 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 for OSA (Tufik et al., 2010). Another Swedish study observed a higher risk for OSA among lower educated men and those occupying certain manual jobs, while 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 behavior, and BMI, as potential contributors to the socioeconomic gradient in SDB. We hypothesize that there is an inverse gradient between socioeconomic status and SDB, and that this association is explained by the lifestyle-related factors indicated above.

METHODS

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=5064) and comprises a random sample of CoLaus participants who agreed to undergo a level 2 polysomnogram (PSG) recording at home (N=2162) (Berry et al., 2012a; Stringhini et al., 2015). Included participants attended a medical visit which comprised an anthropometric exam, as well as blood and urine collection following an overnight fast. Information on demographic data, socioeconomic and marital status, health-related behaviors, personal and family history of disease, cardiovascular risk factors, and treatment was collected through 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).

Measures

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 et al., 2006; Stringhini et al., 2011). Occupational position was self-reported and grouped into three categories: "High" (Managers: liberal professions, directors, professors), "Middle" (Lower level executives: teachers, qualified technicians, nurses) and "Low" (Low qualified non-manuals and manuals: sales-assistants, clerks, 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 which reflects individual's intellectual resources, as well as future employment and income (Galobardes et al., 2006). 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).

Sleep-disordered breathing

During a visit at the Center for Investigation and Research in Sleep (Lausanne University Hospital, Switzerland), certified technicians equipped the participants with a PSG recorder (Titanium, Embla® Flaga, Reykyavik, Iceland). The recorder was set between 5 and 8 pm 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 surface electromyography channels (one submental region, two anterior tibialis muscle), one for electrocardiogram, nasal pressure, thoracic and abdominal belts, body position, oxygen saturation, and pulse rate in accordance with the American Association of Sleep Medicine

(AASM) recommended setup (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 10s or longer, whereas hypopnea was defined as ≥30% drop of airflow lasting at least 10s with either an arousal or ≥3% oxygen saturation drop, following the 2.4 AASM criteria 1A (Berry et al., 2012b; Heinzer et al., 2015). In the present analyses, we used the Apnea-Hypopnea Index (AHI) and the ≥3% Oxygen Desaturation Index (ODI) as outcome variables. AHI represents the number apneas and hypopneas per hour of sleep, including both obstructive and central events (Heinzer et al., 2015; Punjabi, 2008). AHI was dichotomized into ≥15 events/hour vs. less (AHI15), and into ≥30 events/h vs. less (AHI30) following the definition of moderate and severe SDB in the ICSDIII manual (American Academy of Sleep Medicine, 2014). ODI represents the number of desaturation events per hour of sleep, which are defined as ≥3% decrease in oxygen saturation (SpO_2) (Heinzer et al., 2015). ODI was also dichotomized into ≥15 events/h vs. less (ODI15), and ≥30 events/h vs. less (ODI30) following the definition of moderate and severe SDB in the ICSDIII manual (American Academy of Sleep Medicine, 2014).

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 behavior, and BMI, and were assessed through questionnaire and medical examination. Smoking status was categorized as current and noncurrent 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 categorized as hazardous intake (>3 daily alcoholic drinks for men, >2 daily alcoholic drinks for women) vs. non-hazardous intake. Sedentary behavior was defined as lower tertile vs. 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 meters.

Statistical analyses

The associations between SES indicators, lifestyle-related factors, and AHI/ODI were analyzed using linear and logistic regression models. First, the association between SES and AHI/ODI was analyzed, 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 by selected lifestyle-related factors were assessed by applying the counterfactual mediation method (Valeri and 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 which is mediated by the mediator of interest (proportion mediated – PM). When compared to other mediation approaches, the counterfactual method is valid in 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” (Valeri and VanderWeele 2013; VanderWeele and Vansteelandt 2010; Jiang and VanderWeele 2015). 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-value <0.05.

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 to the included participants, those excluded were more frequently women (57% vs. 43%, p<0.05), were older (mean age 65 vs. 52 years, p<0.05), were more frequently Swiss-born (72% vs. 58%, p<0.05), had a lower education (17% vs. 25% in the high education group, p<0.05), had a higher mean BMI (27 vs. 26 kg/m^2, p<0.05), were less frequently smokers (15% vs. 21%, p<0.05), were more sedentary (46% vs. 24%, p<0.05) and had more apnea-hypopnea events per hour of sleep (mean AHI 19 vs. 14/h, p<0.05), as well as more oxygen desaturation events (mean ODI 18 vs. 13/h, p<0.05) than included participants.

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

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]).

Selection of lifestyle-related factors as potential mediators

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 for an increased BMI (occupational position (lowest vs. highest) – BMI, β_{M1} = 1.59, 95% confidence interval [0.94;2.24]; education (lowest vs. highest) – BMI, β_{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.

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: β_{M1} = 1.16, 95%CI [1.13;1.19]; BMI – AHI30: β_{M1} = 1.16, 95%CI [1.13;1.20]; BMI – ODI15: β_{M1} = 1.21, 95%CI [1.18;1.24]; BMI – ODI30: β_{M1} = 1.21, 95%CI [1.18;1.26]), whereas there were inconsistent associations between the remaining lifestyle-related factors and AHI/ODI. Sedentary behavior was associated with a lower risk of experiencing ≥30 ODI events/h (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/h (OR_{M1} = 1.56, 95%CI [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/h (OR_{M1} = 1.45, 95%CI [0.99;2.13]; OR_{M2} = 1.52, 95%CI [1.01;2.30]).

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 for 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.

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 Bonferroni threshold. In women, occupational position tended to be associated with an increased risk of AHI30, while education was associated with an increased risk of ODI15 (Supplementary table 1). 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 for an increased BMI, with stronger associations in women than in men. In both men and women, BMI was associated with an increased risk for AHI/ODI, whereas there were no meaningful associations between smoking, sedentary behavior and hazardous alcohol intake, and AHI/ODI (Supplementary table 2). Low occupational position was associated with a higher risk of ODI30 in men, with a mediating effect of 49% by BMI (Supplementary Figure 1). In women, low occupational position was strongly associated with a higher risk of having ≥ 30 AHI events/h and ≥ 30 ODI events/h, 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 dichotomized BMI (<25 kg/m^2, ≥25 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).

DISCUSSION

In this study, we found that individuals with low occupational position and low educational level were at a higher risk for SDB as measured by AHI and ODI. As BMI was also strongly related to AHI/ODI and SES, a substantial part (43% to 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, Sundquist, and Sundquist 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 for hospitalization for obstructive sleep apnea, whereas no meaningful associations were observed in women (Li, Sundquist, and Sundquist 2008). Further, another study conducted in the United States has shown that neighborhood 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 for 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 (Wilkinson 1994; Petrovic et al. 2018).

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 airway anatomy alters the upper respiratory function and increases the airway collapsibility, eventually resulting in breathing cessation during sleep (Wolk, Shamsuzzaman, and Somers 2003; Benumof 2004; Young, Skatrud, and Peppard 2004). Another mechanism linking obesity to SDB may be related to leptin, a hormone which is produced by the adipose tissue, and which was found to play an important role in central respiratory control mechanisms (Wolk, Shamsuzzaman, and Somers 2003; O'Donnell et al. 2000).

Furthermore, we observed that smoking, sedentary behavior, and hazardous alcohol intake were not strongly related to AHI and ODI. The lack of association between adverse lifestyle behaviors 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 (Punjabi 2008; Young, Peppard, and Gottlieb 2002; Hong and Dimsdale 2003). However, our results may be explained by the lack of statistical power and the small sample size of this study.

Health behaviors 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 (Pampel, Krueger, and Denney 2010; McLaren 2007), as a result of lack of resources, knowledge, and the motivation to afford a healthy lifestyle and are also more exposed to obesogenic environments ('Diet, nutrition and the prevention of chronic diseases' 2003; Adam and Epel 2007; Pampel, Krueger, and Denney 2010; Stringhini et al. 2012).

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 to men, and may be related to the epidemiologic transition of chronic diseases and lifestyle-related risk factors, in particular obesity and obstructive sleep apnea (Stringhini et al. 2012; Wilkinson 1994; Gaziano 2010). Another explanation may be that low SES women often have to combine the psychosocial strain of unqualified, less paid jobs to that of household responsibilities, resulting in higher stress and obesogenic behaviors such as overeating and energy-dense diets (Petrovic et al. 2016; Artazcoz et al. 2004).

Our findings have important research and clinical implications. First, this study provides a comprehensive understanding about the underlying mechanisms of socioeconomic inequalities in sleep-disordered breathing. Further, this study shall also help improve clinical practices which 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.

Strengths and limitations

Our study has several strengths. To our knowledge, this 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 cross-sectional data which does not allow determining 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 has been initially developed for rare outcomes, and may thus not be valid for lower thresholds of AHI and ODI (i.e. <15 events/h, vs. ≥15 events/h) whose prevalence estimates are higher than more severe indexes (i.e. <30 events/h, vs. ≥30 events/h) 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.

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 shall 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.

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CONFLICT OF INTEREST

None to declare

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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, PV critically revised the manuscript.

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

	Men (N=1055)	Women (N=1106)	P-value [a,b]
Age, mean±SD (y)	56.8 (±10.5)	57.6 (±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)	
BMI, mean±SD (kg/m^2)	26.9 (±4)	25.6 (±4.7)	<0.001
Overweight (BMI>25), N (%)	716 (68)	534 (48)	<0.001
Health behaviors, N (%)			
Current smoking	200 (19)	204 (18)	0.760
Hazardous alcohol consumption[c]	85 (8)	56 (5)	0.005
Sedentary behavior	344 (33)	371 (34)	0.643
Apnea-hypopnea index (AHI)			
AHI - continuous score, mean±SD (events/h)	20.4 (±18.2)	10.9 (±12.7)	<0.001
≥15 AHI events/h (N,%)	530 (50%)	260 (24%)	<0.001
≥30 AHI events/h, N (%)	239 (23)	84 (8)	<0.001
Oxygen desaturation index (ODI)			
ODI - continuous score, mean±SD (events/h)	19.1 (±17)	10.6 (±12)	<0.001
≥15 ODI events/h, N (%)	512 (48)	244 (22)	<0.001
≥30 ODI events/h, N (%)	201 (19)	72 (7)	<0.001

Data are mean±SD for continuous variables and N (%) for categorical variables
[a] Mann-Whitney U test was performed between men and women for continuous variables
[b] Chi2 contingency test was performed between men and women for categorical variables
[c] Hazardous alcohol was defined as having >3 alcoholic drinks per day for men and >2 alcoholic drinks per day in women

Table 2: Association between SES indicators (occupational position, educational attainment) and AHI/ODI

		M1: OR [95%CI][a]	***P*-value[b]**	**N**
Occupational position	≥15 AHI events/h	1.31 [0.91;1.90]	0.149	1311
	≥30 AHI events/h	1.79 [1.05;3.03]	0.032	1311
	≥15 ODI events/h	1.40 [0.96;2.04]	0.080	1311
	≥30 ODI events/h	2.07 [1.14;3.73]	0.016	1311
Education	≥15 AHI events/h	1.20 [0.94;1.53]	0.147	2160
	≥30 AHI events/h	1.20 [0.87;1.65]	0.270	2160
	≥15 ODI events/h	1.50 [1.17;1.93]	0.001	2160
	≥30 ODI events/h	1.31 [0.92;1.85]	0.132	2160

[a] Regression coefficients for the association between SES indicator (predictor-Lowest vs. Highest) and AHI/ODI , adjusted for age, sex, country of birth, and marital status

[b] Significance threshold for the association SES indicators and AHI/ODI was set at P-value <0.0125 (0.05/4) due to multiple comparisons

Table 3: Association between SES indicators (occupational position, education) and lifestyle-related factors (smoking, sedentary behavior, hazardous alcohol intake, BMI)

		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	1311
	Sedentary behavior	0.86 [0.58;1.25]	0.420	1.04 [0.70;1.53]	0.850	1311
	Hazardous alcohol intake	0.53 [0.29;0.96]	0.036	0.51 [0.28;0.94]	0.030	1311
	BMI [c]	1.59 [0.94;2.24]	<0.001	1.56 [0.92;2.20]	<0.001	1311
Education	Smoking	1.55 [1.16;2.06]	0.003	1.71 [1.28;2.28]	<0.001	2160
	Sedentary behavior	0.79 [0.62;1.01]	0.063	0.95 [0.74;1.23]	0.713	2160
	Hazardous alcohol intake	0.68 [0.45;1.03]	0.070	0.62 [0.40;0.95]	0.028	2160
	BMI [c]	1.77 [1.31;2.23]	<0.001	1.75 [1.30;2.20]	<0.001	2160

OR, odds ratio; CI, confidence interval

[a] Regression coefficients for the association between SES indicator (predictor-Lowest vs. Highest) and lifestyle-related factor, adjusted for age, sex, country of birth, and marital status

[b] Regression coefficients for the association between SES indicator (predictor-Lowest vs. Highest) and lifestyle-related factor, adjusted for age, sex, country of birth, marital status, and the three remaining lifestyle-related factors

[c] Linear regression model was performed for the association between SES indicator and BMI, and logistic regression models for associations using smoking, sedentary behavior, and hazardous alcohol intake

[d] Significance threshold was set at P-value <0.0125 (0.05/4) due to multiple comparisons

Table 4: Association between lifestyle-related behaviors and AHI/ODI indexes

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

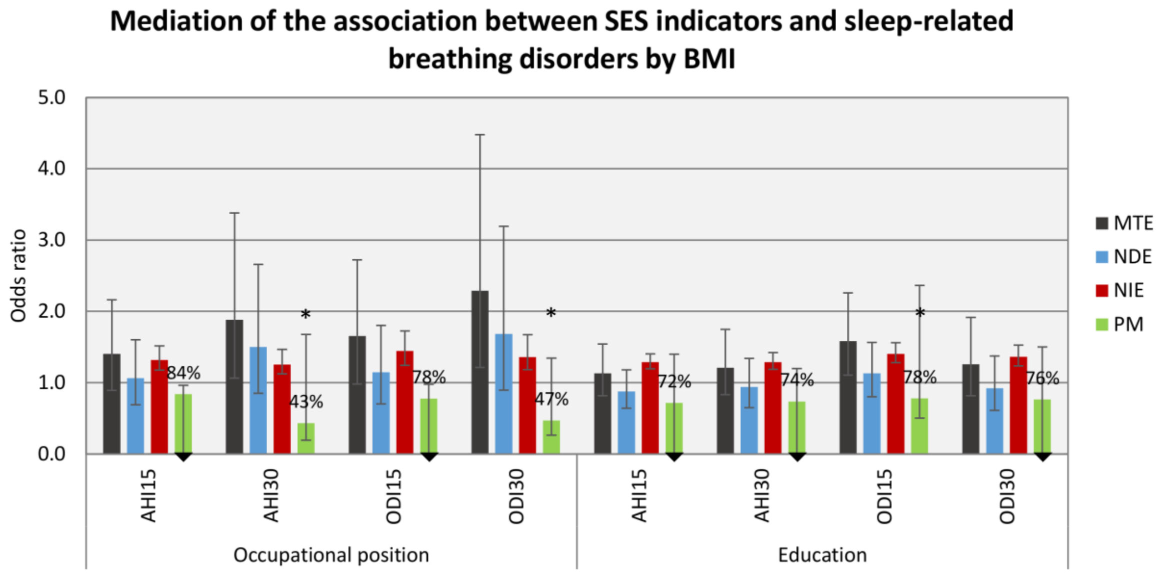
OR, odds ratio; CI, confidence interval

[a] Logistic regression (OR) for the association between lifestyle-related factors and AHI/ODI, adjusted for age, sex, country of birth, and marital status

[b] Logistic 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

[c] Significance threshold was set at P-value <0.0125 (0.05/4) due to multiple comparisons

Figure 1: Counterfactual mediation by BMI for the association between two SES indicators, and AHI and ODI



MTE: Marginal total effect (OR 95%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 which is mediated by continuous or dichotomized BMI (* significant mediation)

Lower ▼ and upper ▲ arrow indicate that CIs extend beyond the limits of the graph.

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Supplementary table 1: Association between SES indicators (occupational position, educational attainment) and AHI/ODI in men and women

Men		**OR [95%CI][a]**	***P*-value[b]**	**N**
Occupational position	≥15 AHI events/h	1.15 [0.75;1.76]	0.525	688
	≥30 AHI events/h	1.61 [0.92;2.82]	0.094	688
	≥15 ODI events/h	1.31 [0.86;2.02]	0.212	688
	≥30 ODI events/h	1.86 [1.00;3.45]	0.050	688
Education	≥15 AHI events/h	1.02 [0.75;1.38]	0.886	1054
	≥30 AHI events/h	1.21 [0.84;1.75]	0.304	1054
	≥15 ODI events/h	1.31 [0.96;1.77]	0.084	1054
	≥30 ODI events/h	1.33 [0.89;1.98]	0.158	1054
Women		**OR [95%CI][a]**	***P*-value[b]**	**N**
Occupational position	≥15 AHI events/h	1.96 [0.91;4.20]	0.085	623
	≥30 AHI events/h	6.62 [1.01;43.52]	0.049	623
	≥15 ODI events/h	1.80 [0.80;4.06]	0.155	623
	≥30 ODI events/h	6.84 [0.85;55.31]	0.071	623
Education	≥15 AHI events/h	1.59 [1.04;2.43]	0.033	1106
	≥30 AHI events/h	1.14 [0.58;2.26]	0.701	1106
	≥15 ODI events/h	1.96 [1.25;3.07]	0.003	1106
	≥30 ODI events/h	1.22 [0.59;2.55]	0.592	1106

[a] Regression coefficients for the association between SES indicator (predictor-Lowest vs. Highest) and AHI/ODI , adjusted for age, country of birth, and marital status

[b] Significance threshold for the association SES indicators and AHI/ODI was set at P-value <0.0125 (0.05/4) due to multiple comparisons

Supplementary table 2: Association between SES indicators (occupational position and education) and lifestyle-related factors in men and women

Men		**M1: OR [95%CI][a]**	***P*-value[d]**	**M2: OR [95%CI][b]**	***P*-value[d]**	**N**
Occupational position	Smoking	1.36 [0.81;2.28]	0.245	1.46 [0.86;2.46]	0.162	688
	Sedentary behavior	0.79 [0.48;1.32]	0.369	0.86 [0.52;1.44]	0.569	688
	Haz. alcohol intake [e]	0.77 [0.36;1.62]	0.486	0.74 [0.34;1.61]	0.453	688
	BMI [c]	1.19 [0.42;1.96]	0.003	1.17 [0.40;1.94]	0.003	688
Education	Smoking	1.54 [1.05;2.27]	0.028	1.63 [1.10;2.41]	0.015	1054
	Sedentary behavior	0.81 [0.58;1.14]	0.225	0.88 [0.62;1.24]	0.453	1054
	Haz. alcohol intake [e]	1.05 [0.61;1.80]	0.870	0.95 [0.54;1.64]	0.844	1054
	BMI [c]	1.25 [0.68;1.82]	<0.001	1.24 [0.68;1.81]	<0.001	1054

Women		**M1: OR [95%CI][a]**	***P*-value[d]**	**M2: OR [95%CI][b]**	***P*-value[d]**	**N**
Occupational position	Smoking	1.19 [0.63;2.24]	0.599	1.44 [0.75;2.76]	0.273	623
	Sedentary behavior	0.95 [0.53;1.71]	0.864	1.32 [0.71;2.46]	0.375	623
	Haz. alcohol intake [e]	0.26 [0.10;0.69]	0.007	0.27 [0.10;0.70]	0.007	623
	BMI [c]	2.29 [1.16;3.42]	<0.001	2.28 [1.19;3.38]	<0.001	623
Education	Smoking	1.61 [1.05;2.47]	0.029	1.90 [1.22;2.94]	0.004	1106
	Sedentary behavior	0.80 [0.56;1.14]	0.217	1.09 [0.75;1.58]	0.654	1106
	Haz. alcohol intake [e]	0.36 [0.18;0.70]	0.003	0.32 [0.16;0.65]	0.002	1106
	BMI [c]	2.40 [1.68;3.13]	<0.001	2.36 [1.64;3.07]	<0.001	1106

OR, odds ratio; CI, confidence interval

[a] Regression coefficients for the association between SES indicator (predictor-Lowest vs. Highest) and lifestyle-related factor, adjusted for age, sex, country of birth, and marital status

[b] Regression coefficients for the association between SES indicator (predictor-Lowest vs. Highest) and lifestyle-related factor, adjusted for age, sex, country of birth, marital status, and the three remaining lifestyle-related factors

[c] Linear regression model was performed for the association between SES indicator and BMI, and logistic regression models for associations using smoking, sedentary behavior, and hazardous alcohol intake

[d] Significance threshold was set at P-value <0.0125 (0.05/4) due to multiple comparisons

[e] Hazardous alcohol intake

Supplementary table 3: Association between lifestyle-related factors and AHI/ODI indexes in men and women

Men		**M1: OR [95%CI]** [a]	***P*-value** [c]	**M2: OR [95%CI]** [b]	***P*-value** [c]	***N***
Smoking	≥15 AHI events/h	0.86 [0.62;1.19]	0.373	0.9 [0.64;1.26]	0.524	1055
	≥30 AHI events/h	0.71 [0.47;1.08]	0.113	0.73 [0.47;1.13]	0.158	1055
	≥15 ODI events/h	0.84 [0.61;1.16]	0.301	0.87 [0.62;1.23]	0.428	1055
	≥30 ODI events/h	0.72 [0.46;1.13]	0.155	0.75 [0.46;1.22]	0.241	1055
Sedentary behavior	≥15 AHI events/h	0.89 [0.66;1.19]	0.436	1.04 [0.77;1.42]	0.788	1055
	≥30 AHI events/h	0.79 [0.56;1.11]	0.179	0.96 [0.67;1.37]	0.819	1055
	≥15 ODI events/h	0.94 [0.7;1.25]	0.656	1.14 [0.84;1.56]	0.401	1055
	≥30 ODI events/h	0.62 [0.43;0.9]	0.012	0.78 [0.53;1.17]	0.231	1055
Hazardous alcohol intake	≥15 AHI events/h	1.28 [0.81;2.04]	0.296	1.23 [0.76;2]	0.407	1055
	≥30 AHI events/h	1.48 [0.9;2.45]	0.121	1.46 [0.86;2.5]	0.162	1055
	≥15 ODI events/h	1.48 [0.93;2.35]	0.099	1.42 [0.86;2.33]	0.167	1055
	≥30 ODI events/h	1.57 [0.93;2.66]	0.089	1.55 [0.86;2.78]	0.142	1055
BMI	≥15 AHI events/h	1.17 [1.13;1.22]	<0.001	1.17 [1.13;1.22]	<0.001	1055
	≥30 AHI events/h	1.19 [1.14;1.24]	<0.001	1.18 [1.14;1.23]	<0.001	1055
	≥15 ODI events/h	1.23 [1.18;1.28]	<0.001	1.23 [1.18;1.28]	<0.001	1055
	≥30 ODI events/h	1.26 [1.21;1.32]	<0.001	1.26 [1.2;1.32]	<0.001	1055
Women		**M1: OR [95%CI]** [a]	***P*-value** [c]	**M2: OR [95%CI]** [b]	***P*-value** [c]	***N***
Smoking	≥15 AHI events/h	1.22 [0.82;1.81]	0.320	1.42 [0.94;2.15]	0.100	1106
	≥30 AHI events/h	0.93 [0.45;1.89]	0.832	1.02 [0.49;2.13]	0.953	1106
	≥15 ODI events/h	1.14 [0.76;1.73]	0.525	1.38 [0.88;2.16]	0.157	1106
	≥30 ODI events/h	1.16 [0.57;2.4]	0.679	1.44 [0.68;3.05]	0.339	1106
Sedentary behavior	≥15 AHI events/h	0.75 [0.54;1.03]	0.079	1.03 [0.73;1.45]	0.882	1106
	≥30 AHI events/h	0.91 [0.56;1.48]	0.690	1.22 [0.72;2.07]	0.451	1106
	≥15 ODI events/h	0.84 [0.61;1.17]	0.300	1.28 [0.89;1.84]	0.178	1106
	≥30 ODI events/h	0.85 [0.51;1.44]	0.557	1.27 [0.72;2.26]	0.406	1106
Hazardous alcohol intake	≥15 AHI events/h	1.38 [0.71;2.68]	0.336	1.57 [0.79;3.14]	0.200	1106
	≥30 AHI events/h	2.06 [0.8;5.33]	0.136	2.62 [0.98;6.98]	0.054	1106
	≥15 ODI events/h	1.56 [0.8;3.05]	0.193	1.91 [0.93;3.93]	0.079	1106
	≥30 ODI events/h	1.01 [0.29;3.53]	0.986	1.26 [0.35;4.56]	0.729	1106
BMI	≥15 AHI events/h	1.16 [1.12;1.2]	<0.001	1.16 [1.12;1.2]	<0.001	1106
	≥30 AHI events/h	1.13 [1.08;1.19]	<0.001	1.14 [1.09;1.2]	<0.001	1106
	≥15 ODI events/h	1.2 [1.16;1.25]	<0.001	1.22 [1.17;1.26]	<0.001	1106
	≥30 ODI events/h	1.16 [1.11;1.22]	<0.001	1.17 [1.11;1.23]	<0.001	1106

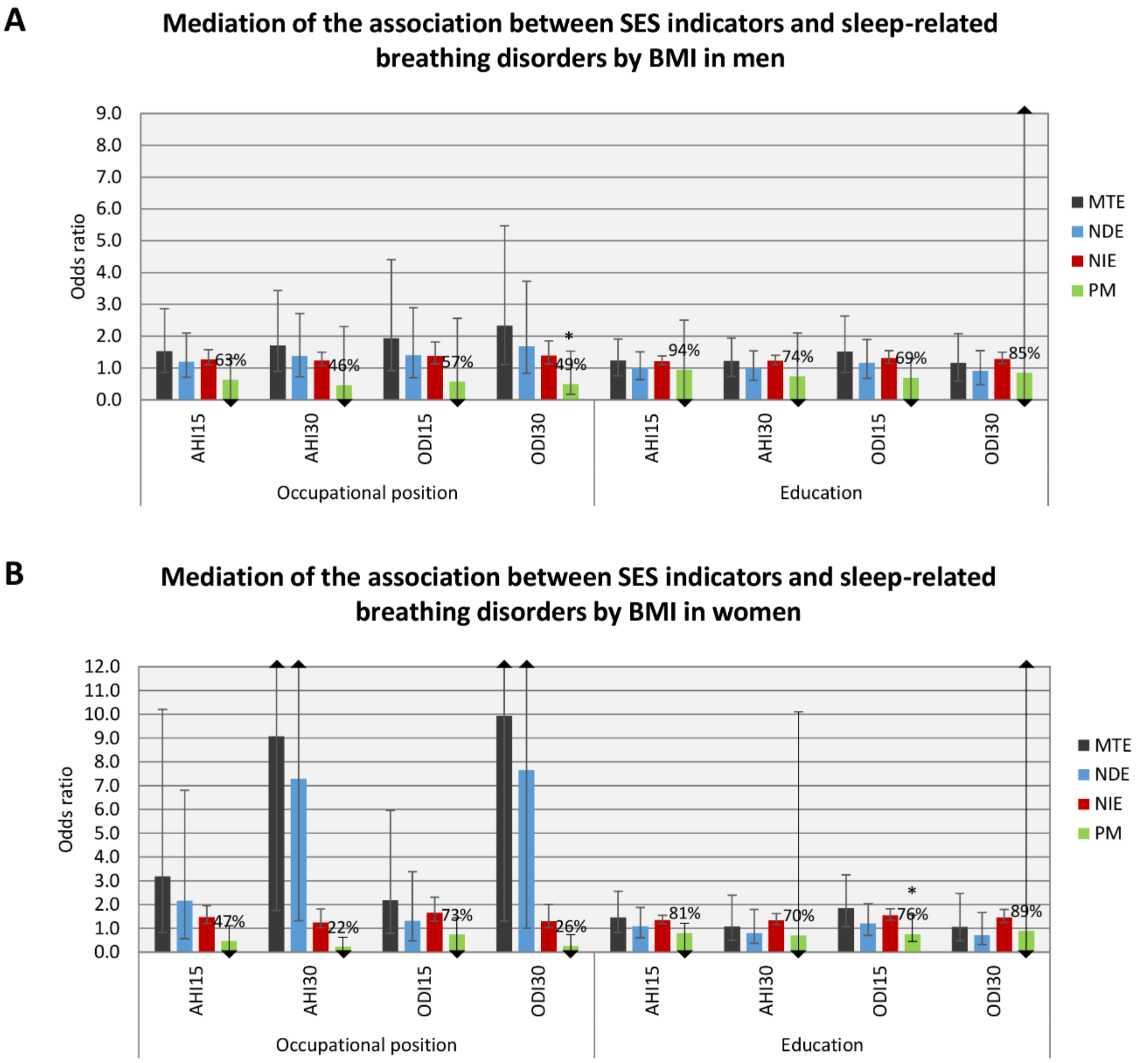
OR, odds ratio; CI, confidence interval

[a] Logistic regression (OR) for the association between lifestyle-related factors and AHI/ODI index, adjusted for age, sex, country of birth, and marital status

[b] Logistic regression (OR) for the association between lifestyle-related factors and AHI/ODI index, adjusted for age, sex, country of birth, marital status, and the remaining lifestyle-related factors

[c] Significance threshold was set at P-value <0.0125 (0.05/4) due to multiple comparisons

Supplementary figure 1: Counterfactual mediation by BMI for the association between two SES indicators, and AHI and ODI indexes in men (A) and women (B)



MTE: Marginal total effect (OR 95%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 indexes which is mediated by continuous or dichotomized BMI (* significant mediation)

Lower ▼ and upper ▲ arrow indicate that CIs extend beyond the limits of the graph.