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Original research article

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Please cite this article as: Balagny P, Vidal-Petiot E, Renuy A, *et al*. Prevalence, treatment and determinants of Obstructive Sleep Apnea and its symptoms in a population-based French cohort. *ERJ Open Res* 2023; in press (https://doi.org/10.1183/23120541.00053-2023).

Prevalence, treatment and determinants of Obstructive Sleep Apnea and its symptoms in a population-based French cohort

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Word count: 3000

"Take home" message: In the French population, prevalence of treated OSA was 3.5% but 18.5% of untreated patients had a positive Berlin questionnaire. Age, obesity, depression, poor health behaviors and socioeconomic conditions were associated with OSA or a high-risk for OSA.

Abstract (236 words)

Background: Obstructive Sleep Apnea (OSA) is associated with increased morbidity and mortality. Although the disorder has been well-studied in selected high-risk populations, few data exist on its prevalence in the general population. We aimed to assessed the prevalence and determinants of OSA in France.

Methods: Data from participants of the French population-based CONSTANCES cohort, aged 18-69 years at inclusion and being treated for sleep apnea or screened for OSA in 2017 using the Berlin questionnaire were analyzed. Weighted analyses were performed to provide recent and representative results in the general population.

Results: Among 20,151 participants, the prevalence of treated OSA was 3.5% [3.0;3.9]. The prevalence of untreated subjects with a positive Berlin questionnaire was 18.1% [17.3;19.2] for a total weighted prevalence of OSA or high-risk of OSA of 20.9% [20.0;21.9]. Regarding prevalence of OSA symptoms, it was 37.2% [36.1;38.3] for severe snoring and 14.6% [13.8;15.5] for hypersomnolence. In multivariable logistic regression analysis, male sex, age, previous cardiovascular events, smoking, low educational level, low physical activity and depressive symptoms were associated with having either treated OSA or a positive Berlin questionnaire.

Conclusion: In this large French population-based cohort, one in five participants had a high likelihood of OSA, whereas only 3.5% were treated for the disorder, suggesting major underdiagnosis in the general population. OSA diagnosis should be considered more often in people with risk factors such as depressive symptoms as well as unhealthy behaviors and socioeconomic conditions.

Introduction:

Obstructive Sleep Apnea (OSA) syndrome is defined by the association of symptoms (e.g., sleepiness, fatigue, insomnia, snoring, subjective nocturnal respiratory disturbance, or observed apnea) or disorders (i.e., hypertension, heart diseases, stroke, diabetes, cognitive dysfunction, or mood disorder) with an Apnea Hypopnea Index (AHI) ≥ 5 events per hour. Alternatively, an index ≥ 15 defines OSA, even in the absence of associated symptoms or disorders [1]. Untreated OSA is associated with increased risks of cardiovascular disease and neurocognitive sequelae. OSA is a frequent syndrome, although its reported prevalence varies greatly according to the population and diagnostic procedure [2]. In a seminal study conducted in the early 1990's, using an AHI cutoff of 5 combined with symptoms, OSA was reported to affect 4% of males and 2% of females in the general population [3]. In more recent population-based studies, the prevalence of OSA was estimated to be higher, from 14 to 50% in men and 5 to 23% in women [4, 5], likely reflecting the obesity epidemic .

Determining the prevalence of OSA, and characteristics of individuals at high risk of OSA will help improve targeted and efficient prevention and screening strategies. In France, the prevalence of treated OSA is estimated to be 2.4% [6, 7]. However, OSA is largely underdiagnosed and undertreated [8, 9] and the real prevalence of the disorder is thought to be higher [10, 11]. Male sex, age, and obesity are well-known determinants of OSA, but the role of other behavioral and socio-economic remains unclear [3, 5, 6, 10, 12–18].

Polysomnography is the gold-standard diagnostic procedure [19] but has limited availability. Alternatively, screening questionnaires such as the Berlin questionnaire have been developed. The Berlin questionnaire relies on the presence of heavy snoring and hypersomnolence (the most frequent symptoms of sleep apnea. [6, 10, 11, 18, 20, 21]), on

obesity (a major causal factor of the disorder), and on hypertension (a consequence of intermittent hypoxia). This questionnaire has been validated to diagnose an AHI≥ 5 with a sensitivity of 76-95% [22–26].

The aim of the study was to assess the prevalence and determinants of OSA assessed as treated sleep apnea and through the Berlin Questionnaire in the French population-based CONSTANCES cohort. Weighted analyses were performed to provide representative results in the general population.

Materials and methods:

Study design and participants

The CONSTANCES cohort included more of 200 000 volunteers aged 18-69 years from 21 departments throughout metropolitan France recruited between 2012 and 2020 [27]. Eligible individuals were selected from the adult population covered by the general insurance scheme (representing 85% of the French population) using a random sampling scheme stratified on place of residence, age, sex, occupation and socioeconomic status in order to be representative of the source population. At inclusion, participants underwent a clinical interview, examination, standard biology testing and completed questionnaires including sociodemographic characteristics. Follow up was performed through yearly self-questionnaires.

The present analyses were restricted to individuals invited to participate in 2013 and 2014 who had completed the 2017 follow-up questionnaire, which included items of the Berlin Questionnaire. This allowed the use of weighting coefficients (detailed below) to provide a representative sample of the general French population aged 18 to 69 years covered by the general insurance scheme in the selected departments of CONSTANCES (Figure 1).

The CONSTANCES cohort obtained the authorization of the National Data Protection Authority (Commission Nationale de l'Informatique et des Libertés, no. 910486) and was approved by the Institutional Review Board of the National Institute for Medical Research—INSERM (no. 01–011). Written informed consent was received from all participants.

OSA evaluation

Two situations were considered: either a confirmed prior diagnosis of sleep apnea with ongoing treatment, as self-reported by respondents in the 2017 CONSTANCES questionnaire, or being at high risk of OSA based on the Berlin questionnaire. This self-administered questionnaire consists of 10 questions covering three categories: 1) snoring and its loudness, frequency, and inconvenience to others, as well as witnessed apneas , 2) hypersomnolence and its severity, and 3) history of arterial hypertension or obesity, as defined by a body mass index (BMI) ≥ 30 kg/m² .Two or more positive categories are defined a high-risk for OSA [22]. History of arterial hypertension was either physician-reported at the inclusion visit or self-reported in the yearly questionnaires until 2017. BMI was calculated from the most-recent available weight until 2017 (either self-reported in the yearly follow-up questionnaire or measured at the inclusion visit) and from height measured at the inclusion visit.

Weighting coefficients

A weighting coefficient has been computed for each subject when data were available. This coefficient took into account both the survey weight and the non-participation correction factor, based on the follow-up of a control cohort of non-participants [28, 29]. In case the medico-administrative data of a participant could not be obtained, the weighting coefficient could not be calculated. However, participants with or without a weight had the same characteristics. Moreover, the probability of having completed the 2017 follow-up

questionnaire was estimated for each participant in order to compute a participation weight for this follow-up. The product of this weight with the weight at baseline provided the final weight.

Statistical analyses

Categorical variables were described as numbers and percentages with their 95% confidence intervals (CI), in the entire study population, and then according to the presence of sleep apnea, snoring or hypersomnolence. Groups were compared using chi square tests. We used logistic regressions to compute risks of sleep apnea, snoring and hypersomnolence. Multiple imputations by chained equations (10 imputations with 100 iterations) were performed to handle missing data for variables of the model.

All analyses were performed using STATA 15.1 (Statacorp College Station, Texas, USA).

Covariates

According to a directed acyclic graph, the following covariates (defined as detailed in Table 1) were retained: sex, age in 2017, marital status at baseline, household income at baseline, educational level at baseline. Smoking status and alcohol consumption (were defined by the last self-reported value in the inclusion or follow-up questionnaire until 2017. Self-reported physical activity at baseline was based on the following questions: (i) “in the past 12 months have you regularly engaged in gardening, cleaning or handy work?”, (ii)” in the past 12 months have you regularly practiced sport (aside from gardening, cleaning or handy work)?” and (iii) “in the past 12 months have you regularly gone on biking or walking trips (for work or leisure)?”. Depressive symptoms were collected at baseline using the Center of Epidemiologic Studies Depressive Scale (CES-D). A global score ≥ 19 was used to provide a proxy of depressive state [30]. History of myocardial infarction or stroke were physician-

reported at the inclusion visit or self-reported in the follow-up yearly questionnaires until 2017.

We did not adjust for hypertension, diabetes or dyslipidemia which in our directed acyclic graph were considered as a consequence and not a cause of sleep apnea, nor for obesity because it is part of the Berlin questionnaire.

When snoring and hypersomnolence were used as outcomes, the sample was restricted to participants without self-reported treated sleep apnea since symptoms could be modified by treatment, and an additional model was further adjusted for obesity.

Results

The flow diagram of the study population is shown in Figure 1. From the 25,491 participants invited in 2013 - 2014 and who responded to the 2017 CONSTANCES questionnaire, weighted data for OSA were available in 20,151 (79.0 %) participants.

Prevalence of sleep apnea and determinants

Characteristics of study participants are shown in Table 1. Treated OSA was reported by 608 participants, corresponding to a weighted prevalence of 3.5% [95%CI: 3.0;3.9], 5.0% [4.3;5.8] in men and 2.0% [1.6;2.6] in women. Among the remaining participants, 3,283 had a positive Berlin Questionnaire (18.1% [17.3;19.2], with 20.2% [18.9;21.6] in men and 16.4% [15.3;17.7] in women, respectively), resulting in a total weighted estimated prevalence of treated OSA or high risk of OSA of 20.9% [20.0;21.9] in the French population. This prevalence was higher in men (24.1% [22.7;25.6]) than in women (18.0% [16.8;19.3]) ($p<0.001$) and increased with age. It was 11.1% [9.7;12.8] in participants <40 y.o., 19.1% [17.1;21.2] in the 40-49 y.o., 25.0% [23.0;27.1] in the 50-59 y.o. and 31.3% [29.5;33.2] ≥60

y.o. (p for linear trend <0.001). Treated OSA or high-risk of OSA was also more frequent in smokers, in participants with no alcohol consumption or alcohol consumption above recommended thresholds (compared with moderate consumption) and those with a low level of physical activity. Finally, treated OSA or high-risk of OSA was more frequent in people with history of myocardial infarction and stroke, low income, low educational level and with symptoms of depression (Table 1).

Characteristics of participants with treated OSA compared to those with a positive Berlin Questionnaire are presented in Table S1 of the supplementary appendix. Participants with treated OSA were more often men, older, with a higher rate of myocardial infarction, stroke and obesity and lower educational and physical activity levels.

Unadjusted analyses are reported in supplementary Table S2. In multivariable analyses (Figure 2) treated OSA or high-risk of OSA were independently associated with male sex, higher age, previous cardiovascular events, lower socioeconomic status, former or current smoking, no alcohol consumption, a lower level of physical activity, depressive symptoms and marital status. Results were similar when excluding participants with treated OSA (supplementary Table S3).

Prevalence and determinants of symptoms of sleep apnea

Detailed results of all items and categories of the Berlin Questionnaire are shown in Figure 3. Prevalence of heavy snoring (positivity of the 1st category) was 37.2% [36.1;38.3]. It was higher in men (47.3% [45.6;49.0]) than in women (28.3% [26.9;29.7]) (p<0.001) and increased with age: 25.8% [23.8;27.9] in the <40 y.o., 39.1% [36.7;41.5] in the 40-49 y.o., 44.7% [42.4;46.9] in the 50-59 y.o. and 44.0% [42.1;45.9] in the ≥60 y.o. (p for trend<0.001). Prevalence of hypersomnolence (positive 2nd category) was 14.6% [13.8;15.5]. It was lower

in men (11.1% [9.9;12.3]) than in women 17.8 % [16.6;19.1] (p <0.001), and decreased with age (17.0% [15.3;18.9] in the <40 y.o., 15.6% [13.9;17.7] in the 40-49 y.o., 14.2% [12.6;16.0] in the 50-59 y.o., 10.7% [9.4;12.3] in the ≥60 y.o., p for trend <0.001). Characteristics of participants according to severe snoring and hypersomnolence are presented in supplementary Table S4.

In multivariate analysis (Table 2), heavy snoring was associated with male sex, higher age, lower educational level, smoking, lower level of physical activity, depressive symptoms and life in couple. Hypersomnolence was associated with female sex, younger age, previous cardiovascular events, a low educational level, smoking status, the absence of alcohol consumption, a low level of physical activity and depressive symptoms. Similar associations were observed whether or not the model was further adjusted for obesity except for the association with previous cardiovascular events which became non-significant for both symptoms. Obesity was also associated with snoring and hypersomnolence.

Discussion

Our study allowed to assess the prevalence and determinants of treated OSA and OSA as predicted by a positive Berlin Questionnaire in the French general population; data from each participant were weighted following a modelling process that allows to extend conclusions of the study to the French general population aged 18 to 69 years in the selected departments of CONSTANCES [28, 29, 31]. Our results show that 3.5% had a treated OSA and 18.2% had a positive Berlin Questionnaire. OSA and its cornerstone symptoms were more prevalent in older individuals, those with poorer health behaviors and socioeconomic conditions or those with depressive symptoms.

The first report sleep-disordered breathing prevalence, published almost 30 years ago, was based on the Wisconsin Cohort Study (WSCS) and reported a prevalence of 4% in men and 2% in women [3]. Since then, studies using various screening methodologies have reported a higher prevalence of the disorder. In 2001, Duran and reported a prevalence of mild sleep-disordered breathing (AHI≥5, based on polysomnography) of 26% in men and 28% in women in the general population of the Basque country, Spain [13]. In 2010, with the same recording method and threshold, a study among a representative sample of Sao Paulo inhabitants found a prevalence of 47% in men and 31% in women [15]. More recently, the HypnoLaus cohort reported a prevalence of moderate-to-severe sleep-disordered breathing (AHI≥15) that reached 23% (95% CI [21;26]) in women and 50% [47;53] in men [5]. A population-based study conducted in 27,210 adults in Canada, based on the STOP-BANG questionnaire, showed that one in five adult might suffer from sleep disordered breathing [32]. In a literature-based analysis published in 2019, Benjafield and colleagues estimated that OSA affected nearly 1 billion individuals worldwide, with a prevalence exceeding 50% in some countries, and concluded that effective diagnostic and treatment strategies were needed to minimize the burden of this disorder [9]. Noteworthy, European countries with specific estimates were Spain published in 2001 [13], Poland in 2008 [33], Switzerland in 2015 [5] and Germany in 2018 [34], with respective cohort sizes of 2148, 676, 2121 and 1208 subjects. Our study showing an overall OSA prevalence of 20.9 % in French adult population, with 24.1% in men and 18.0% in women, in a large contemporary cohort representative in the French general population adds to the existing knowledge regarding the prevalence of OSA in western Europe.

The prevalence of heavy snoring and hypersomnolence was 37.2% and 14.6%, respectively. A smaller French study using the Berlin Questionnaire among 776 hospital health workers

found similar results regarding sleep apnea and snoring (prevalence of 23.3% and 39.7%, respectively) while the prevalence of hypersomnolence was somewhat higher (20.3%)[11]. In the only previous study assessing the prevalence of symptoms of sleep apnea in the French general population in 2008, Fuhrman and colleagues found that 30% of the adult general population reported frequent snoring and 12% reported having non-restorative sleep [6]. Although symptoms were defined in a different manner, these data suggest that the prevalence of snoring and hypersomnolence (and thereby of OSA) may have increased over the past decade.

Besides recognized risk factors (male sex, age and obesity) [6, 35, 36], our study revealed that OSA and heavy snoring were associated with a low educational level, smoking, a lower level of physical activity and depressive symptoms. Although there is biological plausibility for a causal role of smoking in OSA, it is not established as a risk factor because of discrepant results [37]. To our knowledge, educational level has not previously been shown to be independently associated with OSA. Lack of physical activity has been shown to be associated with OSA, independently of measures of body habitus [38]. Previous studies have suggested a bidirectional association between depression and sleep apnea [39–42]. Our results are in accordance with a recent report, that used similar tools (Berlin and CES-D), indicating that depression, anxiety, and co-occurrence of both, were associated with an increased risk of OSA [43].

Association between OSA or snoring and marital status could reflect a reporting bias [44]. In our cohort as well as in previous studies [3, 10] , hypersomnolence was more frequent in women. In addition, we found that hypersomnolence decreased with age, which might reflect an adjustment of the perception of “acceptable” modifications of sleep and fatigue with aging [45–47]. The association of hypersomnolence with the absence of alcohol

consumption may be explained by the fact that this group includes abstainers, who quit drinking due to health reasons, a well-described paradox in epidemiological studies [48].

While OSA is recognized as a major health hazard, it remains majorly underdiagnosed. We found that despite 18.2% of the French general population being at high-risk of OSA, the prevalence of treated OSA was only 3.5%, suggesting that the vast majority of people with OSA are not diagnosed, and obviously not treated. Our study suggested an even greater underdiagnosis of OSA among women, as previously reported [8, 49] suggesting under-complaint for sleep apnea symptoms and/or less attention paid by healthcare providers to these symptoms among women [50]. Interestingly, Young and al. estimated that 93% of women and 82% of men with moderate to severe OSA were unaware of their disorder and reported the same risk factors of underdiagnosis [8]. Underdiagnosis is therefore a major issue in the general population, but also exists in groups at high-risk. For example, in a cohort of patients with newly diagnosed heart failure, Javaheri and colleagues found that OSA was rarely searched for and consequently subjects are underdiagnosed and not treated [51]. Meanwhile, the few subjects who were tested, diagnosed, and treated for OSA had a much better 2-year survival rate.

Given the burden of undiagnosed sleep apnea, such data and our study support the need for sleep-apnea awareness campaigns such as one implemented in Finland between 2001 and 2010. A recent analysis of the impact of this campaign and showed a massive and continuous increase in outpatient visits for sleep apnea, together with a decrease in apnea-related health cost attributable to better and earlier diagnosis [52].

The main limitation of our analysis is that we diagnosed a high-risk of OSA using the Berlin Questionnaire, and not OSA itself, using the gold-standard polysomnography. However,

polysomnography is not feasible in large epidemiological studies due to its high cost and limited availability and generally performed in subgroups of patients known to be at high-risk [26]. Amongst screening questionnaires, even though STOP BANG and NoSAS score are more sensitive than the Berlin questionnaire [53, 54], the latter (which does not include age and gender) was used here according to our study objective, to describe gender and age distribution of OSA as well as its determinants in a multivariate analysis adjusted on age and sex. The strengths of our study are the large population-based sample provided by the CONSTANCES cohort and the use of weighting coefficients at inclusion and follow-up. These weights allow an estimate of prevalence of treated OSA, high risk of OSA and its symptoms among the French adult population aged 18 to 69 years, in the selected departments of CONSTANCES, and covered by the general health insurance scheme. Using the Berlin questionnaire in such a large sample allowed to describe in-depth the prevalence and risk factors of OSA symptoms. Regarding these points our study provided recent, strong and unique data on OSA in the French adult population.

Conclusion

Symptoms that predict a high-risk of OSA were found in one in five participants in a French population-based cohort. This highly prevalent disorder is underdiagnosed: beyond well-known risk factors such as obesity, more attention should be given to less recognized high-risk groups such as depressive people, individuals with unhealthy behaviors and socioeconomic conditions.

Funding/acknowledgments

The CONSTANCES cohort benefits from a grant from the French National Research Agency. CONSTANCES is supported by the Caisse Nationale d'Assurance Maladie, the French Ministry of Health, the Ministry of Research, and the Institut National de la Santé et de la Recherche Médicale (INSERM). CONSTANCES is also partly funded by AstraZeneca, Lundbeck, L'Oréal, and Merck Sharp & Dohme Corp. This present study was sponsored by Assistance Publique – Hôpitaux de Paris (Paris, France), supported by the Recherche Hospitalo-Universitaire (RHU) iVASC grant (www.ivasc.eu) '#ANR-16-RHUS-00010' from the French National Research Agency (ANR) and funded by Plan d'Investissement d'Avenir-3 (PIA3-RHU, Ministry of Health).

Conflicts of interest

P. Balagny has received payment for presentation from Resmed.

E. Vidal-Petiot has received honoraria for lecture from Servier and support for attending meeting from Servier

A. Renuy declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

J. Matta declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

J. Frija-Masson has received research grants from LVL medical, support for attending meeting from LVL medical, VItalaire, ADEP assistance and SOS oxygène and fiduciary role in Digital Medical Hub SAS.

P.G. Steg has received grants from Amarin, AstraZeneca, Bayer, Sanofi and Servier, consulting fees from Amgen, AstraZeneca, BMS/Myokarddia, Merck, Novo-Nordisk and Regeneron, Steering Comitee or Critical Event Committee from Amarin, AstraZeneca, Bayer, Boerhriger Ingelheim, Bristo-Myers Squibb, Idorsia, Novartis, PhaseBio, Pfizer, Sanofi and Servier, payments for lectures from AstraZeneca, Novartis and Novo-Nordisk, support for attending meetings from AstraZeneca and participation on a Data Safety Monitoring Board or Advisory Board from Servier, Sanofi, PHRI and Monash University.

M. Goldberg declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

M. Zins declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

M.P.d'Ortho has received research grants from Sunrise medical, Desitin, ResMed, Lowenstein and Philips, honoraria for lecture from ResMed, Bioprojet, LVL medical, Viatalaire and Jazz Pharmaceuticals, payment for educational events from Jazz pharmaceutical and support for attending meeting from Bioprojet and Jazz pharmaceuticals.

E. Wiernik declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Table 1: Population characteristics

Variables	Total population n=20,151	Treated sleep apnea or positive Berlin Questionnaire n=3,914	No treated sleep apnea and negative Berlin Questionnaire n=16,237	P
Male sex	9,356 (47.8 [46.7;48.9])	2,193 (55.0 [52.5;57.6])	7,163 (45.8 [44.6;47.1])	<0.001
Age group				<0.001
<40 years old	1,555 (14.9 [14.0;15.9])	368 (16.1 [14.1;18.3])	3,414 (33.9 [32.6;35.2])	
40-49 years old	4,726 (23.5 [22.6;24.4])	598 (22.1 [19.9;24.5])	3,644 (24.9 [23.8;26.0])	
50-59 years old	5,110 (19.4 [18.6;20.2])	1,080 (24.7 [22.6;26.8])	4,039 (19.6 [18.7;20.6])	
≥60 years old	5,362 (18.8 [18.0;19.6])	1,868 (37.1 [34.8;39.5])	5,140 (21.6 [20.7;22.5])	
Myocardial infarction	234 (1.4 [1.2;1.8])	107 (3.2 [2.4;4.3])	127 (1.0 [0.7;1.3])	<0.001
Stroke	267 (1.3 [1.0;1.5])	109 (2.8 [2.0;3.9])	158 (0.9 [0.7;1.2])	<0.001
Household income				<0.001
Less than 1500€	1,625 (15.7 [14.8;16.7])	402 (19.8 [17.5;22.2])	1,223 (14.3 [13.3;15.3])	
1500 € to 2800 €	5,069(28.3 [27.3;29.3])	1,070 (30.8 [28.4;33.2])	3,999 (26.9 [25.8;28.0])	
More than 2800 €	12,304 (51.0 [49.8;52.1])	2,230 (43.4 [41.0;45.9])	10,074 (51.7 [50.4;52.9])	
Other	860 (5.0 [4.5;5.6])	163 (4.5 [3.5;5.7])	697 (5.0 [4.5;5.7])	
Missing n	293	49	244	
Educational level				<0.001
≤ High school degree	7,992 (46.4 [45.2;47.5])	2,001 (60.0 [57.5;62.3])	5,991 (41.9 [40.6;43.1])	
Undergraduate degree	6,970 (32.4 [31.4;33.4])	1,199 (25.6 [23.6;27.8])	5,771 (33.8 [32.4;34.7])	
Postgraduate degree	4,913 (21.2 [20.4;22.1])	658 (12.4 [11.1;13.9])	4,255 (23.3 [22.2;24.1])	
Missing n	276	56	220	

Smoking				<0.001
Non-smoker	9,193 (44.7[43.5;45.8])	1,525 (36.5 [34.0;39.0])	7,668 (46.8 [45.6;48.1])	
Ex-smoker	7,979 (36.2 [35.1;37.2])	1,726 (40.6 [38.1;43.1])	6,253 (35.0 [33.8;36.2])	
Current smoker	2,388 (19.2 [18.2;20.2])	517 (23.0 [21.0;25.5])	1,871 (18.2 [17.1;19.3])	
Missing n	591	146	445	
Alcohol consumption				<0.001
None	3,843 (22.0 [21.0;23.0])	731 (23.0 [20.8;25.4])	2,975 (20.8 [19.8;21.9])	
≤3/2 drinks per day in men/women	13,755 (64.7 [63.6;65.8])	2,432 (57.2 [54.6;59.7])	10,928 (62.8 [64.8;65.3])	
>3/2 drinks per day in men/women	2,773 (13.3 [12.6;14.1])	653 (15.6 [13.9;17.6])	2,035 (12.2 [11.4;13.0])	
Missing n	397	98	299	
Physical activity				<0.001
Few or none	5,139 (29.3 [28.2;30.3])	462 (15.1 [13.2;17.2])	1,239 (9.3 [8.5;10.1])	
Moderate	9,021 (45.6 [28.2;30.3])	2,411 (62.3 [59.8;64.8])	10,048 (64.9 [63.7;66.1])	
High	5,991 (25.2 [28.2;30.3])	899 (17.9 [16.2;19.7])	4,483 (23.0 [22.0;24.0])	
Missing n	609	142	467	
Obesity	2,259 (14.2 [13.4;15.1])	1,577 (46.2 [43.6;48.8])	840 (7.3 [6.6;8.1])	<0.001
Missing n	83	13	70	
Depressive symptoms	2,637 (8.3 [8.3;8.3])	813 (27.8 [25.4;30.3])	1,824 (13.5 [12.6;14.5])	<0.001
Missing n	985	252	733	
Married/in civil partnership	12,667 (55.1 [54.0;56.3])	2,580 (57.6 [55.0;60.1])	10,087 (54.5 [53.2;55.7])	<0.001
Missing n	312	57	255	

Data are n (% [95%CI]), % are weighted in order to provide results representative of the French general population aged 18 to 69 years old, in the selected departments of CONSTANCES, and covered by the general insurance scheme

Table 2: Associations between each variable and risk of heavy snoring or hypersomnolence

	Model 1 *		**Model 2****	
	Heavy snoring	Hypersomnolence	Heavy snoring	Hypersomnolence
Male sex	2.21 [2.00;2.44]	0.69 [0.59;0.80]	2.25 [2.03;2.49]	0.69 [0.59;0.81]
Age				
<40 years old	Ref	Ref	Ref	Ref
40-49 years old	1.59 [1.37;1.85]	0.90 [0.73;1.10]	1.55 [1.33;1.80]	0.87 [0.71;1.07]
50-59 years old	2.06 [1.77;2.39]	0.72 [0.59;0.89]	1.98 [1.70;2.30]	0.70 [0.57;0.86]
≥60 years old	1.94 [1.68;2.24]	0.59 [0.47;0.73]	1.85 [1.60;2.15]	0.57 [0.45;0.71]
Previous cardiovascular events	0.97 [0.71;1.33]	1.68 [1.03;2.71]	0.92 [0.68;1.25]	1.61 [1.00;2.63]
Household income				
Less than 1500€	0.83 [0.68;1.02]	1.10 [0.84;1.45]	0.81 [0.66;0.99]	1.09 [0.83;1.43]
1500 € to 2800€	0.98 [0.87;1.12]	1.16 [0.96;1.40]	0.97 [0.85;1.10]	1.15 [0.95;1.39]
More than 2800€	Ref	Ref	Ref	Ref
Other	0.81 [0.63;1.03]	1.29 [0.91;1.83]	0.80 [0.63;1.03]	1.27 [0.89;1.82]
Educational level				
≤ High school degree	1.13 [0.99;1.29]	1.51 [1.22;1.87]	1.08 [0.94;1.24]	1.47 [1.18;1.82]
Undergraduate degree	1.23 [1.08;1.39]	1.21 [0.98;1.50]	1.21 [1.06;1.38]	1.21 [0.98;1.49]
Postgraduate degree	Ref	Ref	Ref	Ref
Smoking				
Non-smoker	Ref	Ref	Ref	Ref
Ex-smoker	1.34 [1.20;1.49]	1.10 [0.93;1.29]	1.33 [1.20;1.48]	1.09 [0.93;1.29]
Current smoker	1.46 [1.24;1.70]	1.56 [1.26;1.92]	1.47 [1.26;1.73]	1.57 [1.27;1.94]
Alcohol consumption				
None	0.90 [0.79;1.04]	1.43 [1.19;1.71]	0.88 [0.77;1.02]	1.41 [1.17;1.69]

≤3/2 drinks per day in men/women	Ref	Ref	Ref	Ref
>3/2 drinks per day in men/women	1.13 [0.97;1.31]	1.00 [0.80;1.25]	1.13 [0.97;1.31]	1.00 [0.80;1.25]
Physical activity				
Few or not	1.29 [1.06;1.56]	1.50 [1.13;2.00]	1.21 [1.00;1.48]	1.44 [1.08;1.92]
Moderate	1.13 [1.01;1.27]	1.17 [0.96;1.42]	1.09 [0.97;1.23]	1.14 [0.94;1.38]
High	Ref	Ref	Ref	Ref
Depressive symptoms	1.36 [1.17;1.59]	3.84 [3.23;4.56]	1.33 [1.14;1.55]	3.79 [3.20;4.50]
Married/in civil partnership	1.44 [1.28;1.62]	0.89 [0.75;1.05]	1.43 [1.27;1.61]	0.88 [0.74;1.04]
Obesity			1.78 [1.52;2.07]	1.44 [1.18;1.76]

Results are (OR [95% CI], *Model 1: adjusted for age, sex, previous cardiovascular events, household income, educational level, smoking status, alcohol consumption, physical activity depressive symptoms and marital status; **Model 2: adjusted for age, sex, previous cardiovascular events, household income, educational level, smoking status, alcohol consumption, physical activity, depressive symptoms, marital status and obesity.

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Figure 1: Flow diagram of study population

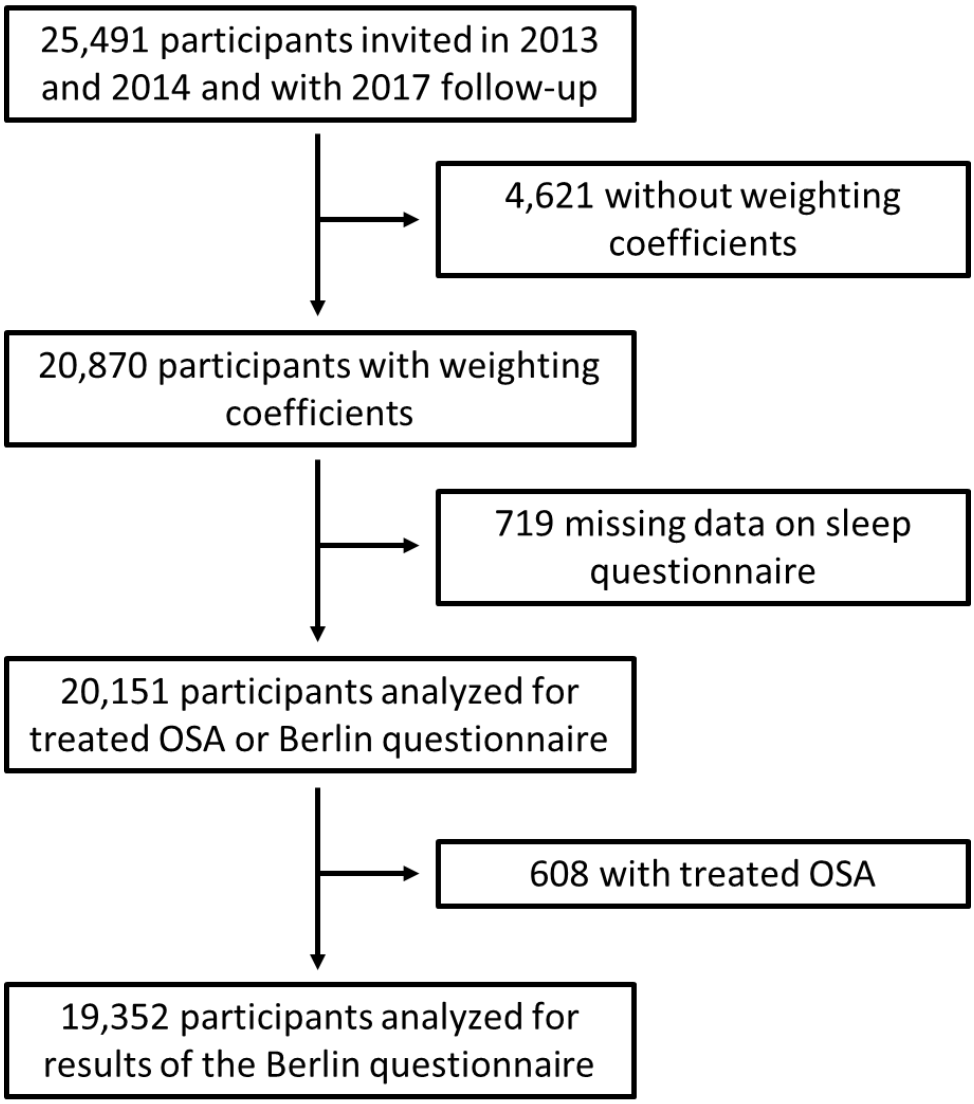
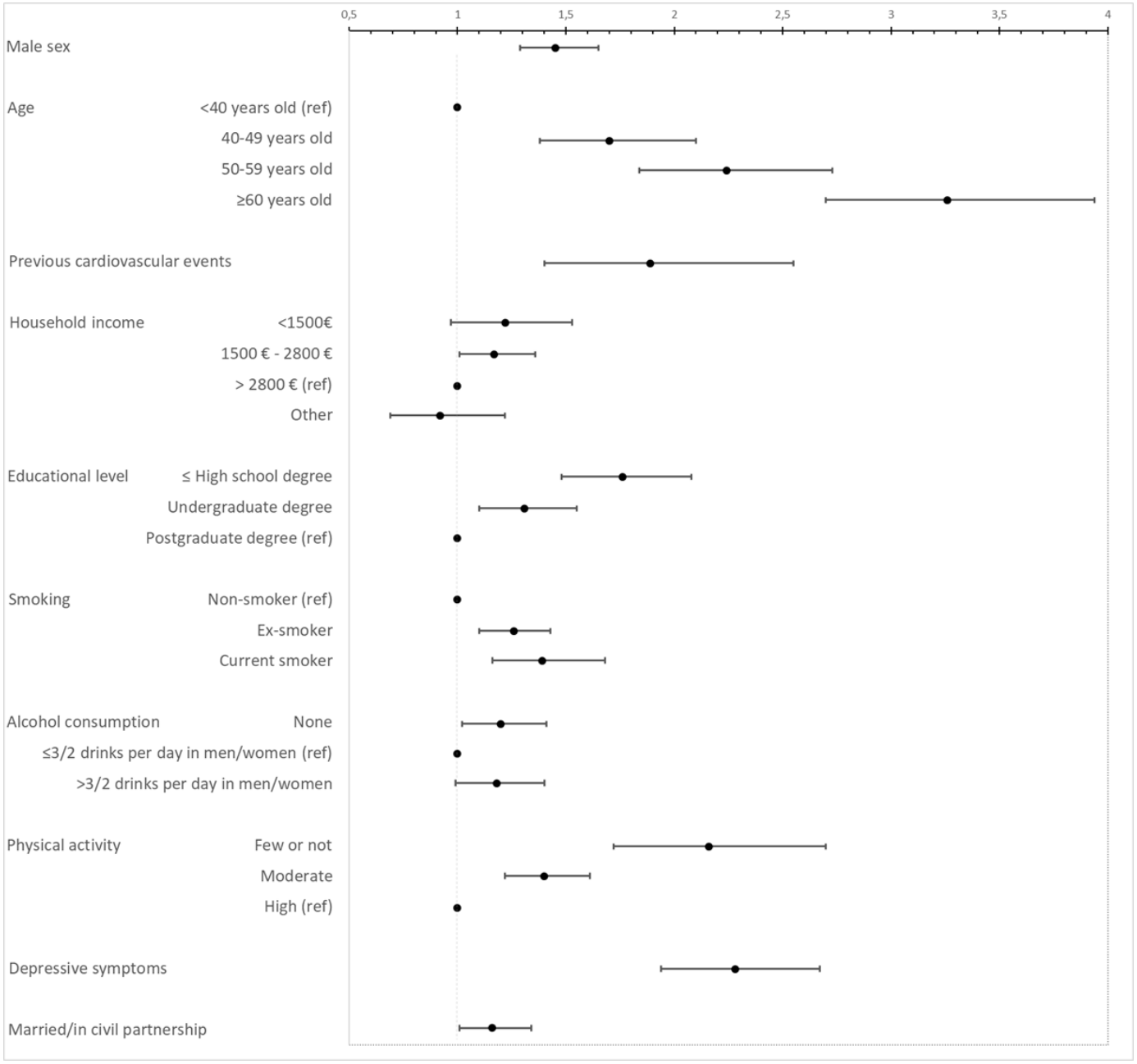
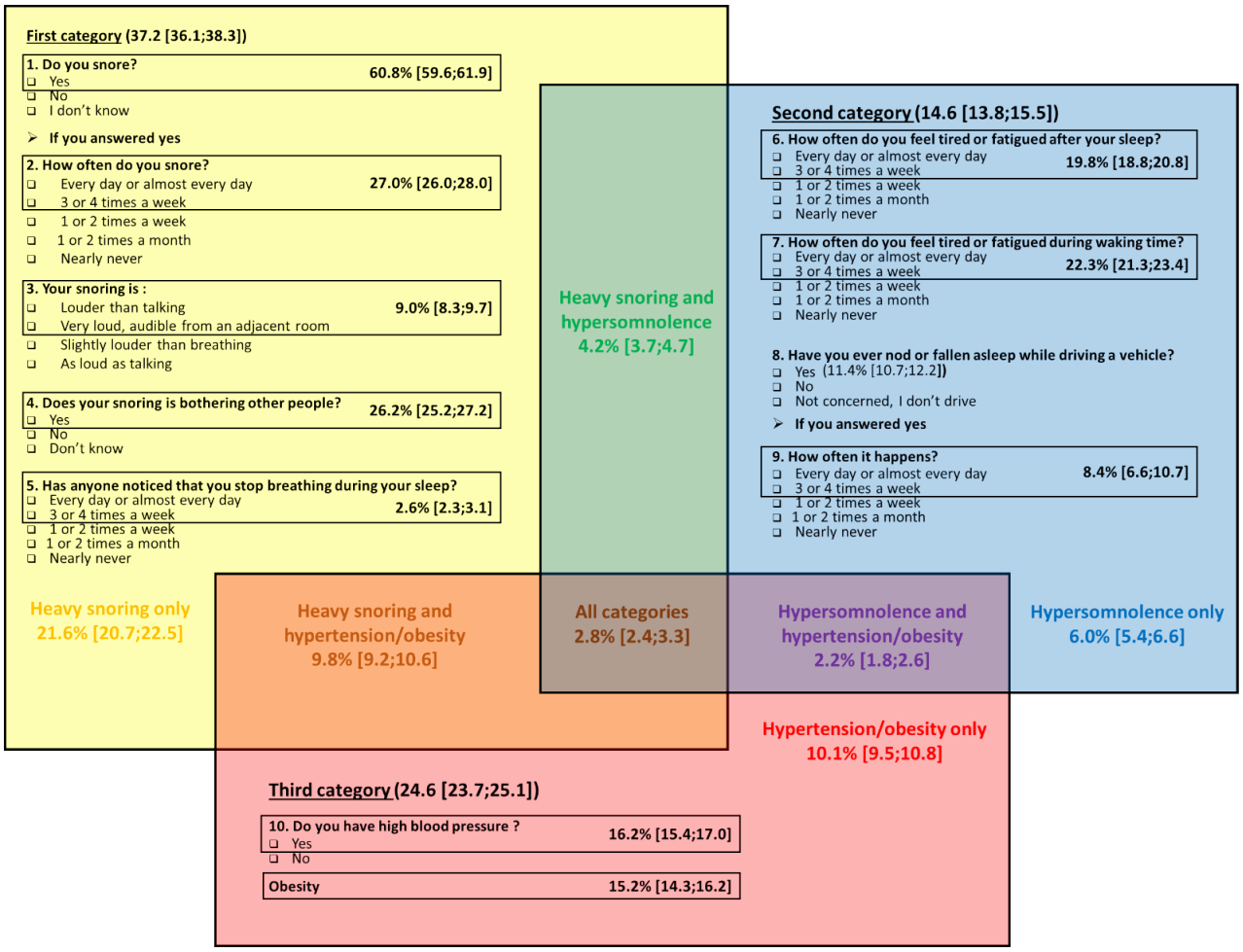


Figure 2: Associations between each variable and risk of sleep apnea



Results are (OR [95% CI], adjusted for age, sex, previous cardiovascular events, household income, educational level, smoking status, alcohol consumption, physical activity depressive symptoms and marital status

Figure 3: Results of the items and categories of the Berlin Questionnaire



Percentages refer to the number of participants who checked the items or the combination of items amongst the 19,352 participants. Any checked item in a framed area yields one point except for question 3 that yields 2 points, categories 1 and 2 are considered as positive if their total score is 2 or more points, category 3 is defined as positive if its total score is one point (either high blood pressure or obesity). Subjects with in at least two positive categories have a positive Berlin questionnaire and are considered at high risk for sleep apnea.Data are n (% [95%CI]), % are weighted in order to provide results representative of the French general population aged 18 to 69 years old, in the selected departments of CONSTANCES, and covered by the general insurance scheme

Supplementary appendix

Table S1: Characteristics of participants with treated sleep apnea compared to those with a positive Berlin Questionnaire

Variables	Total population n=3,914	Positive Berlin Questionnaire n=3,306	Self-declared treated sleep apnea n=608	p
Male sex	2,193 (55.0 [52.5;57.6])	9,356 (47.7 [49.5;55.0])	433 (69.3 [62.5;75.3])	<0.001
Age group				<0.001
<40 years old	368 (16.1 [14.1;18.3])	1,555 (17.7 [15.5;20.2])	24 (7.7 [4.4;13.1])	
40-49 years old	598 (22.1 [19.9;24.5])	4,726 (23.7 [21.3;26.4])	57 (14.0 [9.6;20.0])	
50-59 years old	1,080 (24.7 [22.6;26.8])	5,110 (23.8 [21.6;26.1])	164 (29.2[23.6;35.7])	
≥60 years old	1,868 (37.1 [34.8;39.5])	5,362 (34.8 [32.4;37.3])	353 (49.1 [42.5;35.7])	
Myocardial Infarction	107 (3.2 [2.4;4.3])	234 (3.0 [2.1;4.1])	23 (4.4 [2.4;8.2])	0.170
Stroke	109 (2.8 [2.0;3.9])	267 (2.4 [1.7;3.5])	26 (4.7 [2.4;8.8])	0.040
Household income				0.086
Less than 1500€	402 (20.1 [17.8;22.6])	1,625 (18.1 [15.8;20.7])	81 (30.5 [23.9;37.9])	

1500 € to 2800 €	1,070 (31.2 [28.9;33.7])	5,069 (32.0 [29.4;34.6])	163 (27.6 [22.2;33.7])	
More than 2800 €	2,230 (44.1 [41.6;46.6])	12,304 (45.4 [42.7;48.1])	325 (37.5 [31.6;43.7])	
Other	163 (4.5 [3.5;5.8])	860 (4.7 [3.4;6.0])	31 (4.4 [2.6;7.3])	
Missing	49	293	8	
Education level				0.02
≤ High school degree	2,001 (61.1 [58.7;63.5])	7,992 (59.0 [56.4;61.7])	345 (72.1 [66.5;77.1])	
Undergraduate degree	1,199 (26.2 [24.1;28.4])	6,970 (27.9 [25.6;30.3])	148 (17.2 [13.3;22.0])	
Postgraduate degree	658 (12.7 [11.3;14.2])	4,913 (13.1 [11.6;14.7])	100 (10.7 [7.8;14.4])	
Missing	56	276	15	
Smoking				0.052
Non-smoker	1,666 (38.5 [36.1;41.0])	9,767 (38.1 [35.5;40.7])	241 (40.9 [34.4;47.7])	
Ex-smoker	512 (22.1 [19.8;24.5])	2,377 (22.8 [20.3;25.5])	67 (18.2 [13.1;24.7])	
Current smoker	1,731 (39.4 [37.0;41.9])	7,990 (39.1[36.5;41.8])	299 (40.9 [34.8;47.4])	
Missing	5	17	1	
Alcohol consumption				0.488
None	731 (24.0 [21.8;26.5])	3,843 (23.0 [20.6;25.6])	120 (29.5 [23.4;36.5])	

Moderate	2,432 (59.7 [57.0;62.2])	13,755 (60.4 [57.6;63.2])	369 (55.6 [48.8;62.2])	
Not recommended	653 (16.3 [14.5;18.3])	2,773 (16.6 [14.6;18.8])	101 (14.9 [10.9;19.9])	
Missing	98	397	18	
Physical activity				0.028
Few or none	462 (15.8 [13.8;18.1])	5,139 (14.4 [12.4;16.8])	95 (23.0 [17.3;29.9])	
Moderate	2,411 (65.4 [62.9;67.8])	9,021 (66.3 [63.7;68.9])	351 (60.6 [53.8;67.1])	
High	899 (18.8 [17.0;20.6])	5,991 (19.2 [17.3;21.3])	142 (16.4 [12.6;21.0])	
Missing	142	609	20	
Obesity	1,577 (46.7 [44.1;49.2])	2,259 (46.1 [43.4;48.9])	260 (49.5 [42.8;56.1])	0.005
Missing	13	83	2	
Depressive symptoms	813 (29.9 [27.4;32.5])	2,637 (30.3 [27.5;33.1])	123 (28.0 [21.8;35.1])	0.221
Missing	252	985	44	
Married/in civil partnership	2,580 (58.7 [56.1;61.3])	12,667 (55.1 [54.0;56.3])	391 (52.6 [45.7;59.3])	0.066
Missing	57	312	16	

Data are n (% [95%CI]), % are weighted in order to provide results representative of the French general population aged 18 to 69 years old, in the selected departments of CONSTANCES, and covered by the general insurance scheme

Table S2: Associations between each variable and risk of sleep apnea, heavy snoring or hypersomnolence

	Sleep apnea	Severe snoring	Hypersomnolence
Male sex	1.45 [1.29;1.62]	2.27 [2.08;2.50]	0.57 [0.49;0.67]
Age			
<40 years old	Ref	Ref	Ref
40-49 years old	1.87 [1.53;2.29]	1.85 [1.60;2.14]	0.92 [0.76;1.11]
50-59 years old	2.65 [2.19;3.19]	2.32 [2.02;2.68]	0.81 [0.67;0.98]
>60 years old	3.63 [3.04;4.32]	2.26 [1.98;2.58]	0.59 [0.48;0.72]
Previous cardiovascular events	3.31 [2.46;4.44]	1.53 [1.13;2.07]	1.49 [0.98;2.27]
Household income			
Less than 1500€	1.62 [1.35;1.93]	0.70 [0.59;0.83]	2.28 [1.86;2.80]
1500 € to 2800 €	1.38 [1.21;1.58]	0.87 [0.78;0.97]	1.57 [1.34;1.84]
More than 2800 €	Ref	Ref	Ref
Other	1.05 [0.77;1.43]	0.70 [0.55;0.90]	1.71 [1.22;2.40]
Education level			
≤ High school degree	2.61 [2.23;3.04]	1.32 [1.17;1.48]	1.87 [1.56;2.24]
Undergraduate degree	1.44 [1.22;1.70]	1.17 [1.04;1.33]	1.41 [1.16;1.70]
Postgraduate degree	Ref	Ref	Ref
Smoking			
Non-smoker	Ref	Ref	Ref
Ex-smoker	1.56 [1.32;1.85]	1.57 [1.42;1.74]	1.02 [0.87;1.19]
Current smoker	1.44 [1.28;1.63]	1.47 [1.27;1.70]	1.94 [1.60;2.34]

Alcohol consumption			
None	1.23 [1.06;1.43]	0.76 [0.67;0.86]	1.74 [1.47;2.06]
≤3/2 drinks per day in men/women	Ref	Ref	Ref
>3/2 drinks per day in men/women	1.41 [1.20;1.66]	1.26 [1.09;1.45]	1.13 [0.91;1.39]
Physical activity			
Few or not	2.01 [1.62;2.49]	1.24 [1.03;1.49]	2.07 [1.59;2.68]
Moderate	1.22 [1.06;1.41]	1.04 [0.94;1.16]	1.34 [1.12;1.61]
High	Ref	Ref	Ref
Obesity	10.77 [9.24;12.55]	1.87 [1.61;2.16]	1.70 [1.40;2.06]
Depressive symptoms	2.47 [2.14;2.86]	1.15 [1.00;1.33]	4.81 [4.09;5.66]
Married/in civil partnership	1.14 [1.01;1.29]	1.66 [1.51;1.84]	0.63 [0.55;0.73]

Results are OR [95%CI]

Table S3 : Sensitivity analysis : aassociations between each variable and risk of sleep apnea in total population and after excluding self-declared treated sleep apnea

	Total population	**Positive Berlin Questionnaire only**
Male sex	1.45 [1.29;1.65]	1.31 [1.15;1.49]
Age		
<40 years old	Ref	Ref
40-49 years old	1.70 [1.38;2.10]	1.66 [1.34;2.06]
50-59 years old	2.24 [1.84;2.73]	1.99 [1.62;2.45]
>60 years old	3.26 [2.70;3.94]	2.75 [2.26;3.35]
Previous cardiovascular events	1.89 [1.40;2.55]	1.87 [1.36;2.60]
Household income		
Less than 1500€	1.22 [0.97;1.53]	1.11 [0.87;1.41]
1500 € to 2800 €	1.17 [1.01;1.36]	1.18 [1.01;1.38]
More than 2800 €	Ref	Ref
Other	0.92 [0.69;1.22]	0.93 [0.68;1.28]
Education level		
≤ High school degree	1.76 [1.48;2.08]	1.70 [1.42;2.03]
Undergraduate degree	1.31 [1.10;1.55]	1.33 [1.11;1.60]
Postgraduate degree	Ref	Ref
Smoking		
Non-smoker	Ref	Ref
Ex-smoker	1.26 [1.10;1.43]	1.44 [1.18;1.74]

Current smoker	1.39 [1.16;1.68]	1.28 [1.12;1.47]
Alcohol consumption		
None	1.20 [1.02;1.41]	1.14 [0.96;1.35]
≤3/2 drinks per day in men/women	Ref	Ref
>3/2 drinks per day in men/women	1.18 [0.99;1.40]	1.17 [0.97;1.39]
Physical activity		
Few or not	2.16 [1.72;2.70]	1.91 [1.50;2.44]
Moderate	1.40 [1.22;1.61]	1.33 [1.14;1.55]
High	Ref	Ref
Depressive symptoms	2.28 [1.94;2.67]	2.37 [2.01;2.80]
Married/in civil partnership	1.16 [1.01;1.34]	1.20 [1.03;1.40]

Results are (OR [95% CI], adjusted for age, sex, previous cardiovascular events, household income, educational level, smoking status, alcohol consumption, physical activity depressive symptoms and marital status

Table S4: Population characteristics according to heavy snoring or hypersomnolence

Variables	Heavy snoring + n=7,485	Heavy snoring – n=11,681	p	Hypersomnolence + n=2,218	Hypersomnolence – n=17,019	p
Male sex	4,414 (60.2 [58.4;61.9])	4,354 (40.2 [38.8;41.6])	<0.001	711 (35.6 [32.5;38.9])	8,089 (49.1 [47.9;50.3])	<0.001
Age group			<0.001			<0.001
<40 years old	949 (8.2 [7.1;9.5])	2,757 (19.2 [17.9;20.6])		594 (36.1 [32.9;39.4])	3,113 (14.9 [13.9;26.0])	
40-49 years old	1,533 (26.1 [24.5;27.7])	2,582 (21.9 [20.8;23.1])		524 (26.7 [23.8;29.8])	3,591 (23.2 [22.2;24.2])	
50-59 years old	2,146 (23.3 [21.9;24.7])	2,720 (16.9 [16.0;17.9])		601 (19.7 [17.4;22.2])	4,455 (19.2 [18.3;20.0])	
≥60 years old	2,857 (21.9 [20.6;23.2])	3,622 (16.7 [15.8;17.6])		499 (17.5 [15.3;20.0])	6,040 (19.8 [19.0;20.7])	
Myocardial Infarction	104 (1.8 [1.4;2.3])	102 (1.2 [0.9;1.7])	0.003	27 (2.3 [1.4;3.7])	211 (1.1 [0.9;1.4])	0.485
Stroke	121 (1.6 [1.2;2.2])	114 (1.1 [0.8;1.4])	<0.001	34 (1.2 [0.7;2.3])	173 (1.2 [0.9;1.4])	0.068
Household income			<0.001			<0.001
Less than 1500€	482 (14.1 [12.6;15.7])	1,015 (16.7 [15.5;18.0])		290 (22.7 [19.7;25.9])	1,213 (13.6 [12.6;14.7])	
1500 € to 2800€	1,760 (27.8 [26.1;29.5])	3,046 (28.5 [27.2;29.8])		668 (31.9 [28.9;35.1])	4,169 (27.8 [26.7;29.0])	
More than 2800€	4,857 (54.0 [52.2;55.8])	6,925 (49.3 [47.9;50.8])		1,122 (39.4 [36.3;42.5])	10,687 (53.7 [52.5;54.9])	
Other	288 (4.2 [3.5;5.0])	521 (5.5 [4.8;6.3])		106 (6.0 [4.5;8.1])	707 (4.8 [4.3;5.4])	
Missing	98	174		32	243	
Educational level			<0.001			<0.001
≤ High school degree	3,109 (49.3 [47.4;51.1])	4,375 (44.4 [42.9;45.9])		979 (54.0 [50.7;57.2])	6,535 (43.4 [42.5;45.0])	
Undergraduate degree	2,567 (31.8 [30.2;33.5])	4,131 (32.9 [31.6;34.2])		777 (31.0 [28.1;34.1])	5,954 (33.4 [32.2;34.5])	
Postgraduate degree	1,707 (18.9 [17.7;20.2])	3,024 (22.7 [21.6;23.9])		430 (15.0 [13.1;17.1])	4,308 (22.9 [21.9;23.8])	
Missing	102	151		32	222	

Smoking			<0.001			<0.001
Non-smoker	3,281 (39.9 [38.2;41.7])	6,040 (50.0 [48.6;51.4])		1,013 (40.3 [37.2;43.5])	8,343 (47.3 [46.1;48.6])	
Ex-smoker	954 (20.2 [18.6;21.9])	1,321 (17.5 [16.3;18.8])		409 (28.1 [25.1;31.4])	1,861 (16.9 [15.9;18.0])	
Current smoker	3,247 (39.8 [38.1;41.6])	4,308 (32.5 [31.2;33.8])		794 (31.6 [28.6;34.6])	6,802 (35.7 [34.6;36.9])	
Missing	3	12		2	13	
Alcohol consumption			<0.001			<0.001
None	1,129 (18.9 [17.5;20.5])	2,387 (23.8 [22.6;25.1])		567 (30.3 [27.1;33.6])	2,956 (20.2 [19.2;21.2])	
≤3/2 drinks per day in men/women	5,043 (65.6 [63.8;67.3])	7,701 (64.3 [62.8;65.7])		1,290 (56.7 [53.3;60.1])	11,507 (66.3 [65.3;67.6])	
>3/2 drinks per day in men/women	1,201 (15.5 [14.2;16.8])	1,346 (11.9 [11.0;12.9])		288 (13.0 [11.0;15.4])	2,265 (13.4 [12.6;14.2])	
Missing	112	247		73	291	
Physical activity			<0.001			<0.001
Few or non	2,054 (31.3 [29.6;33.0])	2,775 (28.0 [26.7;29.4])		783 (35.2 [32.1;38.5])	4,127 (27.8 [26.7;28.9])	
Moderate	3,303 (44.4 [42.6;41.2])	5,320 (46.5 [45.0;47.9])		991 (43.5 [40.3;46.8])	7,654 (46.2 [45.0;47.4])	
High	2,128 (24.3 [22.9;25.8])	3,586 (25.5 [24.3;26.7])		516 (21.3 [18.7;24.1])	5,238 (26.0 [25.0;27.1])	
Missing	207	362		72	499	
Obesity	1,191 (21.3 [19.7;22.9])	1,015 (10.0 [9.1;11.0])	<0.001	354 (21.4 [18.6;24.4])	1,846 (14.3 [13.3;15.2])	<0.001
Depressive symptoms	952 (19.0 [17.4;20.6])	1,502 (16.3 [15.2;17.5])	<0.001	774 (42.5 [39.1;45.9])	1,680 (12.6 [11.7;13.5])	0.001
Missing	378	523		113	799	
Married/in civil partnership	5,165	6,916	<0.001	10,892 (46.6 [43.4;49.9])	1,206 (57.9 [56.7;59.2])	<0.001
Missing	110	178		36	253	

Data are n (% [95%CI]), % are weighted in order to provide results representative of the French general population aged 18 to 69 years old, in the selected departments of CONSTANCES, and covered by the general insurance scheme