Published in final edited form as:

Menopause. 2018 April ; 25(4): 391–398. doi:10.1097/GME.0000000000001020.

Association of vasomotor symptoms and sleep apnea risk in midlife women

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Abstract

Objective—To determine the association between self-reported vasomotor symptoms (VMS) and obstructive sleep apnea (OSA) risk.

Methods—The STOP-BANG to evaluate OSA and Menopause Rating Scale (MRS) were administered to 2,935 women seen in the Women's Health Clinic at Mayo Clinic in Rochester, MN between May 2015 and December 2016. Of these, 1,691 women were included in the analysis. Total MRS and VMS ratings were compared using logistic regression, with age, smoking, and body mass index (BMI) included as covariates between women at intermediate/high risk versus low risk for OSA.

Results—Total MRS scores were significantly higher in women with intermediate/high risk OSA scores versus those with low risk scores [mean (SD): 16.8 (8.0) vs 12.9 (7.0), P<0.001]. Women at intermediate/high OSA risk were older, had more education, self-reported hypertension, BMI >35 kg/m^2, and were less likely to be married or employed. Self-reported severe/very severe VMS were significantly associated with intermediate/high risk vs low risk for OSA (26.6% vs 15.0%; P<0.001). After adjusting for age, BMI, and smoking status, the odds of having intermediate/high risk for OSA were 1.87 times higher for those with severe/very severe VMS compared to those with none/mild/moderate VMS (95% CI: 1.29–2.71, P<0.001). This association persisted upon subgroup analysis based on BMI <25 kg/m^2 (OR 2.15; 95% CI: 1.12–4.16, P=0.022).

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Financial disclosure/conflicts of interest: S.S.F. is a consultant for Mithra Pharmaceuticals.

Conclusion—Self-reported severe/very severe VMS were associated with intermediate/high risk for obstructive sleep apnea in midlife women, even in women with BMI <25 kg/m^2. However, given the limitations of the STOP-BANG tool, OSA risk may have been overestimated.

Keywords

Vasomotor symptoms; menopause; obstructive sleep apnea; sleep disturbance; hot flashes

Introduction

The menopause transition is independently associated with poor sleep[1–3] and appears to be associated with increased risk for obstructive sleep apnea (OSA).[4–7] In addition, up to 80% of midlife women experience hot flashes or night sweats (vasomotor symptoms-VMS).[8] Although there is an association between the presence of VMS and sleep disturbances in midlife women, it may be clinically difficult to distinguish sleep disturbances directly related to menopausal symptoms from those due to an underlying primary sleep disorder such as OSA.[9,10]

Although OSA is more common in men than women, the risk for OSA in women increases with age, obesity, and peri- and postmenopausal status.[11,12] For example, the prevalence of OSA increases from 6.5% in women in their 30s to 16% in women in their 50s.[13] In a sample of peri- and postmenopausal women who experienced disturbed sleep, 53% were found to have a primary sleep disorder (OSA, restless leg syndrome or both).[10] The Sleep in Midlife Women Study also found that progression through the menopausal transition was associated with increasing severity of sleep disordered breathing.[14]

While men with OSA tend to have loud snoring, witnessed apneas, and snort arousals, women often present with atypical symptoms such as insomnia, headache, night sweats, nocturnal enuresis, fatigue, depression, and anxiety.[15–19] These differences in clinical presentation may lead to under-diagnosis of OSA in women.[11] Identifying OSA is important because it is associated with significantly increased risk for coronary heart disease, hypertension, stroke, atrial fibrillation, carotid atherosclerosis, depression and death.[20–27] Although OSA and VMS have both been independently associated with menopause and with cardiovascular risk, the association between VMS and OSA in midlife women is unclear (Figure 1).[28] The purpose of this study was to explore the relationship between self-reported VMS and OSA risk in midlife women using commonly available questionnaires in the clinical setting.

Methods

The Women's Health Clinic (WHC) at Mayo Clinic, Rochester, MN is a subspecialty clinic that provides consultative care to women presenting with menopausal symptoms or sexual health concerns. Women seen in the WHC between May 2015 and December 2016 provided self-reported responses to the Menopause Rating Scale (MRS) and the STOP-BANG questionnaires as part of their clinical visit. Responses to these questionnaires are contained in a database called Data Registry on Experiences of Aging, Menopause and Sexuality (DREAMS). For the purposes of this study, only midlife women between the ages of 40 and

65 years were included in the analysis. Additional information about body mass index (BMI), current tobacco use, education, relationship status, employment status, race/ethnicity, menopausal status, menopausal hormone therapy use, and diagnoses of sleep disorders (using ICD codes) was obtained from the electronic medical record. Women provided written, informed consent for the use of their medical records for research purposes.

The MRS assesses the presence and severity of menopausal symptoms with 11 questions, each rated on a scale of 0–4 for severity (0=none; 1=mild; 2=moderate; 3=severe; 4=very severe). In addition to total MRS score, the questions assessing hot flashes/sweating and sleep problems (difficulty falling asleep, difficulty sleeping through the night, waking up early) were assessed individually.

OSA risk was assessed with the STOP-BANG questionnaire, which consists of 8 questions with self-reported yes/no answers to **S**noring, **T**ired, **O**bserved apneas, **P**ressure (hypertension), **B**ody mass index >35 kg/m^2, and numerical responses to **A**ge, **N**eck size, and categorical response to **G**ender. Based on studies which included both men and women, the STOP-BANG has a high sensitivity of 87% and modest specificity of 43% for detection of moderate to severe OSA, which increases the risk of false positive screening results.[29] As sensitivity and specificity data for the questionnaire are not available for women, for the purposes of the current study, scores were derived according to published formulation: low risk=yes to 0–2 questions; intermediate risk=yes to 3–4 questions; high risk=yes to 5–8 questions *or* yes to 2 or more STOP questions and BMI > 35 kg/m^2.[30] Unless otherwise specified, data are presented using mean ± standard deviation for continuous variables, and frequency percentages for categorical variables. The intermediate and high risk groups were combined to compare to the low risk group for a binary variable indicating OSA risk (yes versus no).

The answers to the individual MRS questions pertaining to hot flashes/sweating and sleep problems were grouped to produce binary variables: moderate/severe/very severe versus none/mild; severe/very severe versus none/mild/moderate. Univariate logistic regression was then performed with OSA risk as the dependent variable, and demographics or MRS measures as the explanatory variable. Multivariable logistic regression was used to assess the association between OSA risk and MRS measures after adjusting for age, smoking and BMI. All statistical tests were two-sided and the threshold statistical significance was set at $p<0.05$. All analyses were conducted using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Results

Of the 2,935 women between the ages of 40 and 65 years seen in consultation in WHC at Mayo Clinic in Rochester, MN between May 2015 and December 2016, 1,691 completed both the STOP-BANG and MRS questionnaires and provided consent for the use of their medical records for research. Of those, 147 (8.7%) had STOP-BANG scores representing high risk for OSA, 274 (16.2%) had intermediate risk scores, and 1,270 (75.1%) had low risk scores. Together, the intermediate and high risk categories added up to 24.9% of the women. Women with intermediate/high OSA risk scores were more likely to be older, have a higher BMI, and have self-reported hypertension. They were more likely to have education

beyond high school, and were less likely to be married or to be employed. Women in the intermediate/high risk OSA group were more likely to be postmenopausal compared to those in the low risk group. The use of menopausal hormone therapy was similar across all STOP-BANG score groups (Tables 1 and 2).

Total MRS scores were significantly higher in women at intermediate/high risk for OSA compared to those at low risk [mean (SD): 16.8 (8.0) vs 12.9 (7.0), P<0.001] (Table 3). After adjusting for age, BMI, smoking status, and self-reported hypertension, the odds of having an intermediate/high risk score for OSA are 1.34 times higher for women with moderate/severe/very severe VMS compared to those with none/mild VMS (95% CI: 0.99–1.81, P=0.063) and 1.87 times higher for women with severe/very severe hot flashes compared to those with none/mild/moderate VMS (95% CI: 1.29–2.71, p<0.001) (Table 4).

In a post-facto subgroup analysis in women with BMI <25 kg/m^2, there was a significant association between severe/very severe VMS and intermediate/high risk of OSA after adjusting for age and smoking status (95% CI: 1.12–4.16, P=0.022). However, no significant association between moderate/severe/very severe VMS and intermediate/high risk of OSA was identified after adjusting for age and smoking status (Table 5).

In women with intermediate/high OSA risk scores, 23% had a diagnosis of OSA by ICD codes prior to the WHC consultation, and another 11.7% received a diagnosis in the 2 years following their WHC visit (Table 3).

Discussion

In this large cross-sectional cohort of midlife women, total MRS scores and self-reported severe and very severe VMS ratings were significantly associated with intermediate/high risk for OSA as assessed by the highly sensitive, moderately specific STOP-BANG screening tool which may overestimate OSA risk. The nature of this association is unclear, but shared risks such as age, smoking status, and BMI do not fully account for the association because the findings persist after adjusting for these factors. Furthermore, an association between severe/very severe VMS and intermediate/high OSA risk persisted in subgroup analysis of women with BMI <25 kg/m^2. This relationship most likely reflects interactions among neuronal circuits associated with temperature regulation (as might be related to vasomotor symptoms), those regulating sleep, and those controlling respiration as well as alterations in peripheral or central chemo-sensor sensitivity and their modulation by hormone status (e.g., levels of estrogen, progesterone or follicle stimulating hormone).[31,32] Different patterns of VMS have been described in postmenopausal women,[33] suggesting differences in neurovascular dysregulation or perhaps more general autonomic dysregulation that warrants further investigation.

Consistent with population-based data,[11] about one-quarter (24.9%) of women in our cohort were at intermediate/high risk for OSA. An important finding of this study is that 65% of women in the intermediate/high risk OSA group remained without a diagnosis of OSA up to 2 years after their clinical consultation, which is also consistent with population-based data regarding the under-diagnosis of OSA in women.[11] Our results underscore the importance of

having a high level of clinical suspicion for the presence of OSA in menopausal women, particularly given the significant morbidity and mortality associated with untreated disease.[34] For example, in a study of 207 pre- and postmenopausal women that assessed hypertension prevalence, BMI was the only factor that affected the blood pressure profile in premenopausal women, while both BMI and apnea hypopnea index affected the blood pressure profile in postmenopausal women.[35] Another study of 277 midlife women concluded that OSA is underdiagnosed and independently associated with hypertension and increased arterial stiffness in perimenopausal women.[36] The results of the present study suggest that the intensity of VMS might be a factor that links OSA and increased cardiovascular risk in menopausal women, thereby alerting the clinician to the need for further evaluation.

The conclusion that VMS may alert clinicians to increased cardiovascular risk is not new. Indeed, in a large population-based study involving 11,725 midlife women followed for 14 years, those reporting frequent VMS had an increased risk for incident CHD compared to those who did not, even after adjusting for multiple factors including age, menopausal status, lifestyle, BMI, diabetes and hypertension.[37] Reduced flow-mediated vasodilatation was also associated with VMS in recent (<10 years from last menstrual period) and late (>10 years from last menstrual period) postmenopause phases in one study,[38] but only among younger midlife women in another study.[20] In the Women's Ischemia Syndrome Evaluation (WISE) study, women with early onset VMS (first occurring before the age of 42 years) had lower flow-mediated dilatation and higher cardiovascular mortality than those who experienced later onset VMS.[21] Overall, the aggregate data support an association between VMS and CHD risk,[39,40] with a suggestion that night sweats more than daytime hot flashes may be associated with increases in blood pressure.[41,42]

The STOP-BANG self-report was used in the present study to assess OSA risk. Although in a community-based sample STOP-BANG is sensitive (87%) for detection of moderate to severe OSA in both men and women, the specificity is modest (43%) for detection of moderate to severe OSA and increases the risk of false positive screening results.[29] In individuals with mid-range STOP-BANG scores (at lower risk for moderate to severe OSA), the specificity for OSA at any level is increased when combined with BMI ≥ 35 kg/m^2.[30] However, these studies may not be entirely applicable to the women as The Sleep Heart Health study showed that weight changes led to more significant changes in apnea hypopnea index in men than women.[43] In addition, several studies have validated versions of the STOP-BANG in specific populations, including those of Chinese, Indian, and Danish descent, in whom BMI tends to be lower than in the US population.[44–48] Yet, even at a lower BMI, the STOP-BANG remains a sensitive screening tool.[47,48]

While it is clear that menopausal hormone therapy (MHT) is helpful for VMS management and may mitigate CHD risk in younger postmenopausal women,[49] the question of whether there is a role for MHT in the management of OSA or sleep disordered breathing in menopausal women is still unanswered. One study demonstrated that the prevalence of OSA was greater in postmenopausal women who did not receive MHT compared to premenopausal women and postmenopausal women on MHT.[12] Estrogen and progesterone have been associated with increased sensitivity to hypercapnia and hypoxia, whereas

ovariectomy has been associated with decreased sensitivity to hypoxia.[50–52] One prospective randomized controlled trial investigating the impact of estrogen on sleep-related disordered breathing revealed that 3 months of unopposed transdermal estradiol was associated with decreased occurrence (P=0.047) and frequency (P=0.049) of sleep apnea in healthy postmenopausal women, but had no effect on partial upper airway obstruction.[53] Further, lower estradiol levels were shown to be associated with increased OSA risk in a study of 30 depressed peri-/postmenopausal women.[6] Another small study involving nine postmenopausal women showed that treatment with conjugated equine estrogens and medroxyprogesterone acetate was associated with reduced risk of sleep-related disordered breathing.[54] However, given the lack of randomized controlled clinical trial data, no definitive conclusions can be made regarding the role of MHT for management of OSA or sleep-related disordered breathing.

To the best of our knowledge, this hypothesis generating study is the first to examine the association between VMS and OSA in midlife women. The strength of the study is the relatively large size of our cohort. As this is a cross-sectional study, causality cannot be determined. A potential limitation of this study is the lack of racial diversity in the cohort as the majority of women were white, educated, married, and employed, thus limiting the generalizability of the findings to other ethnic and socioeconomic groups. In addition, the MRS does not distinguish between daytime and nighttime symptoms, and distinguishing between the two may be helpful to identify women who are experiencing sleep disruption due to OSA and who may be more aware of nighttime VMS. The STOP-BANG questionnaire may underestimate risk for OSA in some women as the question about witnessed apneic events may not be accurate in women without bed partners, and 20% of participants did not know their neck size.

Although the STOP-BANG questionnaire has not been validated in women as a specific subpopulation, the validation studies for this tool have included large numbers of women. One study compared STOP-BANG with three other OSA screeners in a community-based sample of 4,770 individuals, 48.5% of whom were women, and found that STOP-BANG had the highest sensitivity in predicting moderate and severe sleep disordered breathing.[29] Several studies have shown that the STOP-BANG tool has high sensitivity and moderate specificity and thus may overestimate OSA risk. Though sex-specific data are not available, studies involving more women than men have supported this conclusion.[55–57]

Additionally, VMS were self-reported and subjective rather than objectively measured and thus, subject to recall bias. We do not have specific information on which menopausal symptom caused women to seek care in the Women’s Health Clinic (e.g., VMS or sleep disturbance), which may have biased the findings. Also, we did not have access to data regarding referrals for additional testing to confirm the diagnosis of sleep disordered breathing or for treatment.

Conclusions

The results of the present study suggest that women reporting severe or very severe VMS in midlife may be at higher risk for OSA, particularly those with hypertension and obesity.

Further, this risk is often unrecognized. An association between severe/very severe hot flashes and high OSA risk persisted in subgroup analysis of women with BMI <25 kg/m^2 after adjustment for age and smoking status, suggesting the possibility that factors other than obesity may be contributing to this association. Given the low specificity of STOP-BANG in mixed populations of men and women and the lack of validation in women as a specific population, a critical need exists for a brief, validated screening tool that can be used for clinical assessment of women.

Both VMS and OSA are associated with cardiovascular risk,[58] and increased clinical visibility of these associations is necessary to facilitate evaluation for and treatment of OSA in midlife women. It is important to note that not all sleep disturbances in midlife women relate directly to VMS, and primary sleep disorders may co-exist. Distinguishing between sleep disturbances secondary to OSA versus those predominantly related to VMS is critical in order to determine appropriate treatment in women.

Acknowledgments

Funding/support: This study was sponsored by Women's Health Research Center, National Institutes of Health P50 AG44170, the Mayo School of Education, and the Mayo Foundation; The DREAMS database is supported by a grant to Dr. Faubion from a grateful patient.

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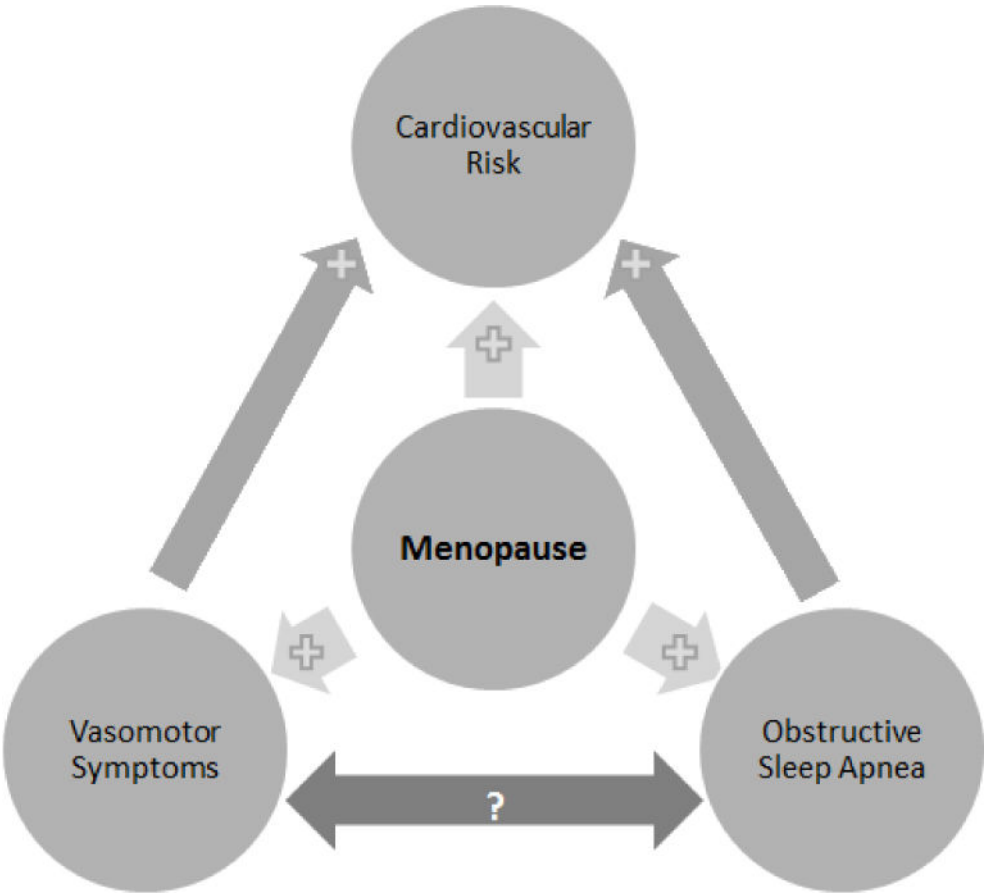

Figure 1. Associations between vasomotor symptoms, cardiovascular risk, obstructive sleep apnea, and *menopause*

Light grey arrows between variables indicate a positive association in the direction of the plus sign, while the bidirectional dark grey arrow between vasomotor symptoms and obstructive sleep apnea indicate a potential association.

Table 1

Participant Demographics by OSA risk group based on STOP-BANG scores and BMI>35kg/m^2

Summary of demographics for the 1,691 women in the study cohort from May 2015 through December 2016.

	Total (N=1691)	Low (N=1270)	Intermediate (N=274)	High (N=147)	p-value[a]	Intermediate/High (N=421)	p-value[b]
Age, Mean (SD)	53.3 (6.1)	52.9 (6.2)	55.8 (4.8)	52.3 (6.5)	<0.001	54.6 (5.7)	<0.001
BMI, Mean (SD)	26.7 (6.0)	25.4 (4.9)	28.4 (6.0)	35.7 (6.4)	<0.001	31.0 (7.1)	<0.001
Race					0.35		0.12
White	1576 (93.2%)	1181 (93.0%)	258 (94.2%)	137 (93.2%)		395 (93.8%)	
Black or African American	18 (1.1%)	10 (0.8%)	4 (1.5%)	4 (2.7%)		8 (1.9%)	
Asian	33 (2.0%)	29 (2.3%)	3 (1.1%)	1 (0.7%)		4 (1.0%)	
Other	28 (1.7%)	23 (1.8%)	3 (1.1%)	2 (1.4%)		5 (1.2%)	
Unknown/Choose Not to Disclose	36 (2.1%)	27 (2.1%)	6 (2.2%)	3 (2.0%)		9 (2.2%)	
Menopausal Status							
Missing	1259	946	200	113	0.002	313	0.002
Premenopausal	44 (10.2%)	42 (13.0%)	1 (1.4%)	1 (2.9%)		2 (1.9%)	
Perimenopausal	62 (14.4%)	51 (15.7%)	6 (8.1%)	5 (14.7%)		11 (10.2%)	
Postmenopausal	293 (67.8%)	208 (64.2%)	63 (85.1%)	22 (64.7%)		85 (78.7%)	
Unknown Menopause Status	33 (7.6%)	23 (7.1%)	4 (5.4%)	6 (17.7%)		10 (9.3%)	
Menopausal Hormone Therapy					0.31		0.17
Missing	236	187	30	19		49	
No	1030 (70.8%)	777 (71.8%)	163 (66.8%)	90 (70.3%)		253 (68.0%)	
Yes	425 (29.2%)	306 (28.3%)	81 (33.2%)	38 (29.7%)		119 (32.0%)	
Marital Status					0.004		0.021
Married	1407 (83.2%)	1076 (84.7%)	226 (82.5%)	105 (71.4%)		331 (78.6%)	
Committed Relationship	7 (0.4%)	6 (0.5%)	1 (0.4%)	0 (0.0%)		1 (0.2%)	
Single	121 (7.2%)	83 (6.5%)	18 (6.6%)	20 (13.6%)		38 (9.0%)	
Separated	8 (0.5%)	3 (0.2%)	2 (0.7%)	3 (2.0%)		5 (1.2%)	
Divorced	115 (6.8%)	79 (6.2%)	23 (8.4%)	13 (8.8%)		36 (8.6%)	
Widowed	18 (1.1%)	13 (1.0%)	2 (0.7%)	3 (2.0%)		5 (1.2%)	
Unknown	15 (0.9%)	10 (0.8%)	2 (0.7%)	3 (2.0%)		5 (1.2%)	
Education					<0.001		<0.001

	Total (N=1691)	Low (N=1270)	Intermediate (N=274)	High (N=147)	p-value[a]	Intermediate/High (N=421)	p-value[b]
High school graduate/GED or lower	123 (7.7%)	81 (67.1%)	17 (6.7%)	25 (17.7%)		42 (10.6%)	
Some College or 2 year degree	446 (27.5%)	311 (15.6%)	85 (33.2%)	50 (35.5%)		135 (34.0%)	
4-year college graduate	543 (33.5%)	432 (9.5%)	79 (30.9%)	32 (22.7%)		111 (28.0%)	
Post graduate studies	507 (31.3%)	398 (7.8%)	75 (29.3%)	34 (24.1%)		109 (27.4%)	
Employment Status					<0.001		<0.001
Employed	1071 (65.3%)	829 (67.1%)	160 (61.3%)	82 (57.7%)		242 (60.0%)	
Full time homemaker	229 (14.0%)	193 (15.6%)	24 (9.2%)	12 (8.5%)		36 (8.9%)	
Retired	174 (10.6%)	118 (15.6%)	37 (14.2%)	19 (13.4%)		56 (13.9%)	
Other	165 (10.1%)	96 (9.5%)	40 (15.3%)	29 (20.4%)		69 (17.1%)	
How often do you have a drink containing alcohol					0.052		0.20
Never	272 (18.0%)	193 (17.2%)	45 (18.0%)	34 (24.6%)		79 (20.4%)	
≤ 1 per month	336 (22.3%)	240 (21.4%)	56 (22.4%)	40 (29.0%)		96 (24.7%)	
2–4 per month	362 (24.0%)	281 (25.1%)	55 (22.0%)	26 (18.8%)		81 (20.9%)	
2–3 per week	324 (21.5%)	248 (22.1%)	50 (20.0%)	26 (18.8%)		76 (19.6%)	
4+ per month	215 (14.3%)	159 (14.2%)	44 (17.6%)	12 (8.7%)		56 (14.4%)	
Smoking Status					0.007		0.010
Never	1210 (73.9%)	932 (75.8%)	183 (69.3%)	95 (66.4%)		278 (68.3%)	
Former	351 (21.4%)	246 (20.0%)	70 (26.5%)	35 (24.5%)		105 (25.8%)	
Current	76 (4.7%)	52 (4.2%)	11 (4.2%)	13 (9.1%)		24 (5.9%)	

[a] p-value comparing Low vs Intermediate vs High

[b] p-value comparing Low vs Intermediate/High

Table 2

Responses to components of the STOP-BANG questionnaire by OSA risk defined by STOP-BANG scores and BMI>35 kg/m^2

Summary of study cohort responses to the STOP-BANG questionnaire by low versus intermediate/high OSA risk groups.

	Total (N=1691)	Low (N=1270)	Intermediate (N=274)	High (N=147)	Intermediate/High (N=421)
STOP BANG total					
Mean (SD)	1.9 (1.2)	1.3 (0.7)	3.2 (0.4)	4.3 (0.9)	3.6 (0.8)
Median	2.0	1.0	3.0	4.0	3.0
Snore loudly					
Missing	8	6	1	1	2
No	1237 (73.5%)	1109 (87.7%)	95 (34.8%)	33 (22.6%)	128 (30.5%)
Yes	446 (26.5%)	155 (12.3%)	178 (65.2%)	113 (77.4%)	291 (69.5%)
Tired, fatigued, sleepy					
Missing	9	7	2	0	2
No	868 (51.6%)	773 (61.2%)	78 (28.7%)	17 (11.6%)	95 (22.7%)
Yes	814 (48.4%)	490 (38.8%)	194 (71.3%)	130 (88.4%)	324 (77.3%)
Observed stop breathing or choking/gasping during sleep					
Missing	5	0	1	4	5
No	1547 (91.8%)	1246 (98.1%)	212 (77.7%)	89 (62.2%)	301 (72.4%)
Yes	139 (8.2%)	24 (1.9%)	61 (22.3%)	54 (37.8%)	115 (27.6%)
Hypertension[d]					
Missing	5	4	0	1	1
No	1425 (84.5%)	1181 (93.3%)	171 (62.4%)	73 (50.0%)	244 (58.1%)
Yes	261 (15.5%)	85 (6.7%)	103 (37.6%)	73 (50.0%)	176 (41.9%)
Body mass index > 35 kg/m^2					
Missing	332	260	68	4	72
No	1066 (78.4%)	923 (91.4%)	138 (67.0%)	5 (3.5%)	143 (41.0%)
Yes	293 (21.6%)	87 (8.6%)	68 (33.0%)	138 (96.5%)	206 (59.0%)
Age > 50					
No	545 (32.2%)	463 (36.5%)	25 (9.1%)	57 (38.8%)	82 (19.5%)
Yes	1146 (67.8%)	807 (63.5%)	249 (90.9%)	90 (61.2%)	339 (80.5%)
Neck size (≥16 inches/41cm)					

	Total (N=1691)	Low (N=1270)	Intermediate (N=274)	High (N=147)	Intermediate/High (N=421)
Missing	343	205	76	62	138
No	1300 (96.4%)	1061 (99.6%)	181 (91.4%)	58 (68.2%)	239 (84.5%)
Yes	48 (3.6%)	4 (0.4%)	17 (8.6%)	27 (31.8%)	44 (15.5%)
Gender					
Female	1691 (100.0%)	1270 (100.0%)	274 (100.0%)	147 (100.0%)	421 (100.0%)

[a]Hypertension as self-reported on STOP-BANG

Table 3

MRS responses by OSA risk group based on STOP-BANG scores and BMI>35kg/m^2

Summary of study cohort responses to the MRS questionnaire by low versus intermediate/high OSA risk groups.

	Total (N=1691)	Low (N=1270)	Intermediate (N=274)	High (N=147)	p-value[a]	Intermediate/High (N=421)	p-value[b]
MRS #1 - VMS[c]					<0.001		<0.001
Mean (SD)	1.4 (1.1)	1.4 (1.1)	1.4 (1.1)	1.9 (1.3)		1.7 (1.3)	
Median (IQR)	1.0 (1.0, 2.0)	1.0 (0.0, 2.0)	1.0 (1.0, 2.0)	2.0 (1.0, 3.0)		2.0 (1.0, 3.0)	
MRS #1 - VMS[c]					<0.001		<0.001
0	403 (23.8%)	319 (25.1%)	58 (21.2%)	26 (17.7%)		84 (20.0%)	
1	537 (31.8%)	419 (33.0%)	86 (31.4%)	32 (21.8%)		118 (28.0%)	
2	448 (26.5%)	341 (26.9%)	63 (23.0%)	44 (29.9%)		107 (25.4%)	
3	206 (12.2%)	139 (10.9%)	41 (15.0%)	26 (17.7%)		67 (15.9%)	
4	97 (5.7%)	52 (4.1%)	26 (9.5%)	19 (12.9%)		45 (10.7%)	
MRS #1 - VMS[c]					<0.001		<0.001
None/Mild	940 (55.6%)	738 (58.1%)	144 (52.6%)	58 (39.5%)		202 (48.0%)	
Moderate/Severe/Very Severe	751 (44.4%)	532 (41.9%)	130 (47.4%)	89 (60.5%)		219 (52.0%)	
MRS #1 - VMS[c]					<0.001		<0.001
None/Mild/Moderate	1388 (82.1%)	1079 (85.0%)	102 (69.4%)	207 (75.5%)		309 (73.4%)	
Severe/Very Severe	303 (17.9%)	191 (15.0%)	45 (30.6%)	67 (24.5%)		112 (26.6%)	
MRS #3 – Sleep problems							<0.001
Mean (SD)	1.9 (1.2)	1.8 (1.2)	1.6 (1.2)	1.9 (1.3)		2.1 (1.2)	
Median (IQR)	2.0 (1.0, 3.0)	2.0 (1.0, 3.0)	1.0 (1.0, 2.0)	2.0 (1.0, 3.0)		2.0 (1.0, 3.0)	
MRS #3 – Sleep problems					<0.001		<0.001
0	251 (14.9%)	203 (16.0%)	32 (11.7%)	16 (10.9%)		48 (11.5%)	
1	412 (24.5%)	330 (26.1%)	56 (20.4%)	26 (17.7%)		82 (19.7%)	
2	503 (29.9%)	387 (30.6%)	73 (26.6%)	43 (29.3%)		116 (27.8%)	
3	342 (20.3%)	237 (18.7%)	68 (24.8%)	37 (25.2%)		105 (25.2%)	
4	174 (10.3%)	108 (8.5%)	41 (15.0%)	25 (17.0%)		66 (15.8%)	
MRS #3 – Sleep problems					<0.001		<0.001
None/Mild	663 (39.4%)	533 (42.1%)	88 (32.6%)	42 (28.6%)		130 (31.2%)	

	Total (N=1691)	Low (N=1270)	Intermediate (N=274)	High (N=147)	p-value[a]	Intermediate/High (N=421)	p-value[b]
Moderate/Severe/Very Severe	1019 (60.6%)	732 (57.9%)	182 (67.4%)	105 (71.4%)		287 (68.8%)	
MRS #3 – Sleep problems					<0.001		<0.001
None/Mild/Moderate	1166 (69.3%)	920 (72.7%)	161 (59.6%)	85 (57.8%)		246 (59.0%)	
Severe/Very Severe	516 (30.7%)	345 (27.3%)	109 (40.4%)	62 (42.2%)		171 (41.0%)	
MRS Total					<0.001		<0.001
Mean (SD)	13.9 (7.5)	12.9 (7.0)	15.7 (7.7)	18.9 (8.2)		16.8 (8.0)	
Median (IQR)	13.0 (9.0, 18.0)	12.0 (8.0, 17.0)	15.0 (11.0, 20.0)	18.0 (13.0 (24.0)		16.0 (12.0, 22.0)	
Sleep Diagnosis prior to visit?					<0.001		<0.001
Yes	154 (9.1%)	57 (4.5%)	54 (19.7%)	43 (29.3%)		97 (23.0%)	
No	1537 (90.9%)	1213 (95.5%)	220 (80.3%)	104 (70.8%)		324 (77.0%)	
Sleep Diagnosis prior to or up to 2 years after visit?					<0.001		<0.001
Yes	225 (13.3%)	79 (6.2%)	77 (28.1%)	69 (46.9%)		146 (34.7%)	
No	1466 (86.7%)	1191 (93.8%)	197 (71.9%)	78 (53.1%)		275 (65.3%)	

[a] p-value comparing Low vs Intermediate vs High

[b] p-value comparing Low vs Intermediate/High

[c] Vasomotor symptoms (VMS): hot flashes and night sweats

Table 4

Univariate and multivariable models comparing OSA risk based on STOP-BANG scores and BMI>35kg/m^{2}by VMS severity

Analysis adjusted for age, BMI, and smoking status.

			Univariate Analysis			Multivariable Analysis (using none/mild vs Moderate/severe/very severe)			Multivariable Analysis (using none/ mild/moderate vs Severe/very severe)		
	Intermediate/ High OSA Risk (N=421) Mean (SD)	**Low OSA Risk (N=1270) Mean (SD)**	**Odds Ratio**	**95% CI**	**p value**	**Odds Ratio**	**95% CI**	**p-value**	**Odds Ratio**	**95% CI**	**p-value**
Age	54.6 (6.2)	52.9 (6.2)	1.05	(1.03, 1.07)	<0.001	1.05	(1.03, 1.08)	<0.001	1.06	(1.03, 1.08)	<0.001
BMI	31.0 (7.1)	25.4 (4.9)	1.17	(1.14, 1.20)	<0.001	1.17	(1.14, 1.20)	<0.001	1.17	(1.14, 1.20)	<0.001
Smoking Status, N (%)											
Never	278 (23.0%)	932 (77.0%)	Reference			Reference			Reference		
Former	105 (29.9%)	246 (70.1%)	1.43	(1.10, 1.87)	0.42	1.10	(0.77, 1.58)	0.34	1.12	(0.78, 1.61)	0.41
Current	24 (31.6%)	52 (68.4%)	1.55	(0.94, 2.56)	0.31	1.88	(0.97, 3.66)	0.084	1.83	(0.94, 3.59	0.11
Hypertension[a], N (%)											
No	244 (17.1%)	1181 (82.9%)	Reference			Reference			Reference		
Yes	176 (67.4%)	85 (32.6%)	10.02	(7.47, 13.44)	<0.001	8.23	(5.71, 11.85)	<0.001	8.34	(5.78, 12.0)	<0.001
MRS Total	16.8 (8.0)	12.9 (7.0)	1.07	(1.05, 1.09)	<0.001						
VMS[b], N (%)											
None/Mild	202 (21.5%)	738 (78.5%)	Reference			Reference					
Moderate/severe/very severe	219 (29.2%)	532 (70.8%)	1.54	(1.23, 1.93)	<0.001	1.34	(0.99, 1.81)	0.063			
VMS[b], N (%)											
None/Mild/Moderate	309 (22.3%)	1079 (77.7%)	Reference						Reference		
Severe/very severe	112 (37.0%)	191 (63.0%)	2.15	(1.64, 2.81)	<0.001				1.87	(1.29, 2.71)	<0.001

[a]Hypertension as self-reported on STOP-BANG

[b]Vasomotor symptoms (VMS): hot flashes and night sweats

Table 5

Univariate and multivariable models comparing OSA risk based on STOP-BANG scores and BMI>35kg/m^2 by VMS severity: BMI subgroup analysis

BMI subgroup analysis adjusted for age and smoking status.

BMI < 25											
			Univariate Analysis			Multivariable Analysis (using none/mild vs Moderate/severe/very severe)			Multivariable Analysis (using none/ mild/moderate vs Severe/very severe)		
	Intermediate/ High OSA Risk (N=64) Mean (SD)	Low OSA Risk (N=569) Mean (SD)	Odds Ratio	95% CI	p value	Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
Age	55.1 (5.1)	53.2 (6.2)	1.05	(1.01, 1.10)	0.031	1.05	(1.004, 1.10)	0.034	1.06	(1.01, 1.11)	0.024
Smoking Status, N (%)											
Never	49 (10.4%)	423 (89.6%)	Reference			Reference			Reference		
Former	12 (10.6%)	101 (89.4%)	1.03	(0.53, 2.00)	0.35	0.94	(0.48, 1.85)	0.47	0.93	(0.47, 1.82)	0.46
Current	1 (3.8%)	25 (96.2%)	0.35	(0.05, 2.61)	0.30	0.37	(0.05, 2.83)	0.35	0.36	(0.05, 2.72)	0.34
MRS Total	15.3 (7.9)	12.9 (6.9)	1.04	(1.004, 1.08)	0.028						
VMS[a], N (%)											
None/Mild	36 (9.4%)	346 (90.6%)	Reference			Reference					
Moderate/severe/very severe	28 (11.2%)	223 (88.8%)	1.12	(0.66, 1.91)	0.67	1.22	(0.71, 2.09)	0.47			
VMS[a], N (%)											
None/Mild/Moderate	50 (9.2%)	495 (90.8%)	Reference						Reference		
Severe/very severe	14 (15.9%)	74 (84.1%)	1.90	(0.999, 3.62)	0.051				2.15	(1.12, 4.16)	0.022

BMI ≥ 25											
			Univariate Analysis			Multivariable Analysis (using none/mild vs Moderate/severe/very severe)			Multivariable Analysis (using none/ mild/moderate vs Severe/very severe)		
	Intermediate/ High OSA Risk (N=264) Mean (SD)	Low OSA Risk (N=471) Mean (SD)	Odds Ratio	95% CI	p value	Odds Ratio	95% CI	p-value	Odds Ratio	95% CI	p-value
Age	54.5 (5.8)	53.0 (6.3)	1.04	(1.02, 1.07)	<0.001	1.05	(1.02, 1.08)	<0.001	1.05	(1.02, 1.08)	<0.001
Smoking Status, N (%)											
Never	171 (33.9%)	334 (66.1%)	Reference			Reference			Reference		

BMI ≥ 25											
			Univariate Analysis			Multivariable Analysis (using none/mild vs Moderate/severe/very severe)			Multivariable Analysis (using none/ mild/moderate vs Severe/very severe)		
	Intermediate/ High OSA Risk (N=264) Mean (SD)	**Low OSA Risk (N=471) Mean (SD)**	**Odds Ratio**	**95% CI**	**p value**	**Odds Ratio**	**95% CI**	**p-value**	**Odds Ratio**	**95% CI**	**p-value**
Former	67 (38.3%)	108 (61.7%)	1.21	(0.85, 1.73)	0.23	1.15	(0.80, 1.65)	0.14	1.15	(0.80, 1.66)	0.15
Current	21 (56.8%)	16 (43.2%)	2.56	(1.30, 5.04)	0.014	2.66	(1.33, 5.31)	0.010	2.62	(1.31, 5.25)	0.012
MRS Total	17.2 (8.2)	12.6 (7.0)	1.08	(1.06, 1.11)	<0.001						
VMS[a], N (%)											
None/Mild	120 (31.3%)	264 (68.8%)	Reference			Reference					
Moderate/severe/very severe	144 (41.0%)	207 (59.0%)	1.59	(1.17, 2.17)	0.003	1.61	(1.18, 2.20)	0.003			
VMS[a], N (%)											
None/Mild/Moderate	189 (32.7%)	389 (67.3%)	Reference						Reference		
Severe/very severe	75 (47.8%)	82 (52.2%)	2.01	(1.40, 2.90)	<0.001				2.03	(1.39, 2.94)	<0.001

[a]Vasomotor symptoms (VMS): hot flashes and night sweats