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ORIGINAL STUDY

Association of menopausal vasomotor symptom severity with sleep and work impairments: a US survey

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Abstract

Objective: Menopausal vasomotor symptoms commonly disrupt sleep and affect daytime productivity. This online survey evaluated associations between vasomotor symptom severity and perceived sleep quality and work productivity.

Methods: Participants were perimenopausal or postmenopausal US women aged 40 to 65 years with ≥14 vasomotor symptom episodes per week for ≥1 week in the past month. The women, who were recruited from Dynata panels via email invitation and categorized by vasomotor symptom severity based on the Menopause Rating Scale, were surveyed about sleep and work productivity and completed the Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b (primary outcome) and Sleep-Related Impairment Short Form 8a, Pittsburgh Sleep Quality Index, and Work Productivity and Activity Impairment questionnaire.

Results: Among 619 respondents (mean age, 53 y; White, 91%; perimenopausal, 34%; postmenopausal, 66%; 57.5% were never treated for vasomotor symptoms), vasomotor symptoms were mild in 88, moderate in 266, and severe in 265. A majority (58% overall) were employed, including 64.8%, 49.6%, and 64.2% of women with mild, moderate, and severe VMS, respectively. Of the 90.8% who reported that vasomotor symptoms affect sleep (81.8%, 86.8%, and 97.7% of those with mild, moderate, and severe VMS), 83.1% reported sleep-related changes in productivity (75.0%, 73.2%, and 94.2%, respectively). Patient-Reported Outcomes Measurement Information System Sleep Disturbance Short Form 8b mean T scores in the mild (T score, 53.5), moderate (57.3), and severe (59.8) VMS cohorts indicated more sleep disturbance than in the general population (T score, 50; overall $P < 0.001$ before and after controlling for confounding variables). Sleep-Related Impairment 8a results were similar. Vasomotor symptom severity was positively associated with Pittsburgh Sleep Quality Index mean scores, presenteeism, absenteeism, overall work impairment, and impairment in general activities.

Conclusions: Greater vasomotor symptom severity was associated with more sleep disturbance, more sleep-related impairment, worse sleep quality, and greater impairment in daytime activities and work productivity.

Key Words: Hot flashes – Menopause – Presenteeism – Sleep – Vasomotor symptoms – Work.

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Vasomotor symptoms (VMS), comprising hot flashes and night sweats, are the primary symptoms of the menopause transition and can last for many years postmenopause.[1-3] Peak prevalence rates of VMS in the United States are about 60% to 80%.[3-5] Some people experience no or mild VMS, whereas 32% to 46% experience moderate to severe VMS during perimenopause and/or postmenopause.[3,6]

VMS can cause sleep interruptions, and both VMS and impaired sleep can interfere with daily activities, quality of life, and productivity at home and work.[6-12] Nearly half of postmenopausal individuals in one study had sleep impairment. VMS were further associated with poor sleep quality and excessive daytime sleepiness.[13] Night sweats commonly interrupt sleep and cause difficulty returning to sleep.[11] Such new-onset sleep disturbances in midlife are associated with reduced productivity and an increased risk of job loss.[14] Daytime hot flashes also can impair concentration and interfere with productivity at work.[8,9,11] The median age at natural menopause is 51.4 years,[15] and 71% of women aged 50 to 54 years are employed[16]; thus, most individuals affected by VMS and related sleep difficulties must balance their symptoms with the demands of their jobs.

This online survey was conducted to evaluate the association between VMS severity and perceived sleep quality (primary outcome), and between VMS severity and work productivity (secondary outcome), among US women with symptoms related to perimenopause or postmenopause. We hypothesized that differences in perceived sleep and work productivity would be found between at least one of the severity cohorts (mild, moderate, or severe VMS) versus the other(s).

METHODS

Study design and survey population

This noninterventional, cross-sectional, online survey was conducted in English from March 17, 2021, to June 7, 2021. A large first-party data provider (Dynata) recruited US women aged 40 to 65 years from their existing national panel. Recruitment was carried out exclusively via direct email including a link to the survey. Dynata recruits panelists through Websites, social media, and direct email to participants in various consumer brand loyalty programs that have partnerships with Dynata (eg, Hertz, American Airlines, Accor, Honda). Participants receive reward points for their participation, which can be redeemed for cash, airline miles, or other prizes. A control system prevented unauthorized access to the survey questionnaire, and duplicate records from the same participant were not permitted.

Eligible participants were in perimenopause or postmenopause and experiencing at least 14 episodes per week of VMS (hot flashes and/or night sweats) of any severity for at least 1 week in the month before the survey. Menopause stage was based on self-reported responses to survey questions about menstrual, surgical, and symptom history. For women older than 40 years of age with a uterus and at least one ovary, perimenopause was defined as the onset of intermenstrual cycle irregularities of ±7 days and other symptoms of menopause for 2 to 12 months. Postmenopause was defined as permanent cessation of menstruation for at least 12 months for women with a uterus. Women who had undergone hysterectomy and bilateral oophorectomy were considered to be in postmenopause as of the date of the surgery. Exclusion criteria were hysterectomy without oophorectomy within 5 years, hysterectomy with unilateral oophorectomy, history of endometrial ablation, current hormonal intrauterine device use, VMS induced by medication (eg, endocrine therapy or chemotherapy for breast cancer), or participation in a clinical trial for VMS within 5 years. Women were neither selected nor excluded based on use of hormone and nonhormone treatments for VMS; such use (current/former/never) was captured in the survey.

Although this publication uses gender-specific language aligned with the referenced publications and survey protocol, the authors recognize that some individuals who experience VMS associated with menopause may identify differently than the gender/pronouns used herein.

Ethical considerations

The study received institutional review board (IRB) exemption from WCG IRB,[17] as surveys are an exempt category. An informed consent form was presented at the beginning of the online survey, and only women who provided consent were able to proceed to the survey questions. WCG IRB approved the informed consent form. Participation was voluntary, but survey questions could not be skipped. Data were collected automatically via the online portal and stored in secure databases encrypted using Secure Sockets Layer technology.

Survey design and outcome measures

The survey took about 20 minutes to complete. One survey question asked women whether VMS impact their sleep; women who responded affirmatively then were asked whether the VMS-induced sleep disturbance impacted their productivity. Women also completed three sleep-related questionnaires: Patient-Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance Short Form (SF) 8b (primary outcome),[18] PROMIS Sleep-Related Impairment SF 8a (secondary outcome),[19] and the Pittsburgh Sleep Quality Index (PSQI; secondary outcome).[20] The effects of VMS on daily activities and work productivity were assessed using the Work Productivity and Activity Impairment (WPAI) questionnaire (secondary outcome).[21,22] Survey questions were presented in the same order for all participants, with the measures of sleep and work productivity preceding questions about sociodemographic characteristics to minimize the potential for survey fatigue that could affect the main outcomes. Adaptive question processes were used such that certain questions were displayed only after specific responses to other questions.

PROMIS Sleep Disturbance SF 8b contains eight items, rated on a scale of 1 to 5, assessing sleep difficulties and quality in the past 7 days.[18] A total score (8-40, with higher scores indicating greater sleep disturbance) was derived by summing the scores of the individual items[23] and was converted to a T score based on the conversion table in the scoring manual.[23] T scores rescale the raw scores into standardized scores with a mean of 50 and SD of 10, such that a T score of 60 indicates one SD worse sleep

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disturbance than that of the general US population of adult women and men.[23] The T score was the primary outcome for this analysis.

PROMIS Sleep-Related Impairment SF 8a contains eight items, rated on a scale of 1 to 5, assessing daytime sleepiness and related functional impairments in the past 7 days resulting from poor sleep.[19] Scoring is the same as that described for PROMIS Sleep Disturbance SF 8b.[24] Based on a previous qualitative validation analysis, postmenopausal women with moderate to severe VMS found both of these PROMIS sleep measures to be relevant to the effects of VMS on sleep and sleep-related daytime impairments.[11]

The PSQI has 19 self-rated questions relating to sleep quality, duration, latency, and frequency/severity of specific sleep problems during the past month.[20] The 19 items are grouped into 7 domains, with scores each weighted equally on a scale of 0 (no difficulty) to 3 (severe difficulty); the 7 domain scores are summed to derive a total ranging from 0 (no difficulty) to 21 (severe difficulty).[20] Higher scores indicate worse sleep quality. The PSQI has been validated in adult populations with mean ages of 42 to 60 years,[20] as well as in White and Black women aged at least 65 years (with the exception of the Sleep Medications and Daytime Dysfunction subscales).[25]

The WPAI questionnaire asks six questions related to employment status, time devoted to work, time missed from work (absenteeism), effect on productivity while at work (presenteeism; scale: 0 [no effect] to 10 [VMS completely prevented me from working]), and extent to which performance of daily nonwork activities was impaired by VMS (same scale of 0-10) in the past 7 days.[21,26] The scores are percentages of hours missed from work (absenteeism), impairment at work (presenteeism), overall work impairment (absenteeism and presenteeism), and impairment in general activities outside of work.[27] WPAI outcomes are expressed as percentages of impairment, with higher values indicating greater impairment. Percent overall work impairment due to VMS was calculated as (absenteeism + [1 − absenteeism] × presenteeism). Absenteeism and presenteeism were assessed only in employed participants; activity impairment was assessed in all participants. To our knowledge, the WPAI has not been validated in midlife and older women or women with VMS due to menopause specifically.

Results for each outcome above are reported for three cohorts based on self-reported VMS severity (mild, moderate, or severe). The VMS severity rating was based on responses to the Menopause Rating Scale (MRS)[28] item 1: "Which of the following symptoms apply to you at this time? 1. Hot flushes, sweating (episodes of sweating)" with answer choices of 0 (none), 1 (mild), 2 (moderate), 3 (severe), and 4 (very severe). For the purposes of this analysis, women with scores of 3 or 4 on this item were combined and considered to have severe VMS.

In addition, a subgroup analysis was conducted looking at the outcomes described previously in women who had at least 25 VMS episodes per week.

Statistical methods

Target sample size was 600 women, with 200 per VMS severity cohort. This sample size was selected to provide adequate power to investigate associations using analysis of covariance (ANCOVA); at a significance level of 0.05, the target sample size would provide 80% power to detect an effect size of 0.13 across cohorts for the primary outcome of PROMIS Sleep Disturbance SF 8b total score.

Respondent characteristics were summarized descriptively for the overall sample and each of the three cohorts (mild, moderate, and severe VMS). *P* values for respondents' comorbidities and other categorical variables were calculated using χ^2 tests, and *P* values for continuous baseline variables were derived using analysis of variance (ANOVA).

T scores on the PROMIS Sleep Disturbance SF 8b and PROMIS Sleep-Related Impairment SF 8a, total and domain scores on the PSQI, and domain scores on the WPAI were summarized descriptively for each VMS severity cohort. Comparisons among the three severity cohorts (mild, moderate, and severe) were made using one-way ANOVA, with the null hypothesis being that the scores for each study outcome were equal for the three cohorts. If the null hypothesis was rejected, pairwise tests comparing findings between each of the severity cohorts were conducted using *t* tests with adjustments for multiple comparisons (Bonferroni correction). Associations of VMS severity for the entire sample and primary/secondary outcomes were made using ANCOVA, with mild VMS as the reference category and adjustments for sociodemographic characteristics (age, race/ethnicity, education, and marital status; employment status was included for sleep outcomes since work-related outcomes on the WPAI were assessed only among respondents who were employed), clinical characteristics (time since onset of VMS, menopause stage, smoking status, caffeine use, body mass index, and comorbidities), and current treatment status (pharmacologic and nonpharmacologic treatment use). The associations between frequency of severe VMS episodes experienced in the past week during the daytime and (separately) at nighttime and scores on each sleep and work questionnaire were evaluated using multivariable linear regression models, adjusting for the same sociodemographic characteristics, clinical characteristics, and treatment status as in the ANCOVA model. The terms selected for adjustment in these models were chosen a priori and specified in the statistical analysis plan. Decisions on what to adjust for were made based on the authors' clinical experience of relevance to the outcome(s). All statistical comparisons were conducted using two-sided tests at the 5% significance level.

The online survey did not permit respondents to skip questions; however, a few questions included "not sure" or "prefer not to answer" as answer choices, which were reported as separate categories.

Data analyses were conducted using R (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

Participants

A total of 7,671 women accessed the survey, of whom 6,878 (89.7%) consented to participate and 793 (10.3%) declined and therefore did not complete the survey. Of 679 women who

passed the screening questions and met the eligibility criteria, 619 (91.2%) completed the survey and composed the analysis population. Among the 619 respondents, VMS severity was mild in 88, moderate in 266, and severe in 265.

Respondent characteristics are summarized in Table 1 for the overall sample and each VMS severity cohort. For the overall sample, the mean age was 53 years, with women with mild VMS being slightly older than those with moderate or severe VMS. Most respondents had at least one comorbidity, with the most common being arthritis in the mild and moderate VMS cohorts and depression in the severe VMS cohort (Table 2). A majority of survey respondents were employed (64.8% with mild VMS, 49.6% with moderate VMS, and 64.2% with severe VMS). Few were currently being treated with hormone therapy (14.8%) or nonhormone prescription therapy (eg, selective serotonin reuptake inhibitors, serotonin and norepinephrine reuptake inhibitors, gabapentin, clonidine) for VMS (13.7%); 57.5% had never been treated for VMS (Table 3).

Impact of VMS on sleep and work productivity (survey questions)

A majority of women (90.8%), including 81.8%, 86.8%, and 97.7% of those with mild, moderate, and severe VMS, respectively, reported that VMS impairs their sleep (Fig. 1A). Most of those whose sleep was affected reported that the VMS-related sleep interference affected their productivity (83.1% overall and 75.0%, 73.2%, and 94.2% of those with mild, moderate, and severe VMS, respectively) (Fig. 1B). For both of these outcomes, the differences across VMS severity cohorts were statistically significant ($P < 0.001$).

Association of VMS severity and sleep outcomes (standardized sleep scales)

The mean PROMIS Sleep Disturbance SF 8b T scores were >50, indicating more sleep disturbance than in the general population. Sleep disturbance significantly increased with greater VMS severity (Fig. 2A). A similar pattern was seen in the PROMIS Sleep-Related Impairment SF 8a T scores (Fig. 2B). Mean PSQI total scores (Fig. 3A) and all seven domain scores (Fig. 3B) were positively associated with VMS severity as well.

The number of severe VMS episodes per night was significantly associated with PROMIS Sleep Disturbance SF 8b T scores, such that one severe nighttime episode was associated with a 0.38 (95% CI, 0.19-0.56) increase in T score ($P < 0.001$). Similarly, the number of severe nighttime VMS episodes was significantly associated with PSQI total score, such that one

TABLE 1. *Respondent characteristics*

Characteristics	Overall (N = 619)	Mild VMS (n = 88)	Moderate VMS (n = 266)	Severe VMS (n = 265)	*P*
Age at survey date (y), mean ± SD	53.0 ± 5.6	54.9 ± 6.0	53.6 ± 5.8	51.7 ± 5.1	<0.001
Race, n (%)					
American Indian or Alaska Native	14 (2.3)	3 (3.4)	7 (2.6)	4 (1.5)	0.5
Black	32 (5.2)	6 (6.8)	15 (5.6)	11 (4.2)	0.6
White	562 (90.8)	78 (88.6)	236 (88.7)	248 (93.6)	0.1
Other or prefer not to answer	17 (2.7)	2 (2.3)	10 (3.8)	5 (1.9)	
Hispanic ethnicity, n (%)	39 (6.3)	8 (9.1)	15 (5.6)	16 (6.0)	0.7
Menopause stage, n (%)					<0.001
Perimenopause	210 (33.9)	8 (9.1)	82 (30.8)	120 (45.3)	
Postmenopause	409 (66.1)	80 (90.9)	184 (69.2)	145 (54.7)	
Time since last menstrual period (y), mean ± SD	5.7 ± 5.1	5.2 ± 5.6	6.3 ± 5.6	5.1 ± 4.2	0.1
BMI[a] (kg/m^2), mean ± SD	25.4 ± 6.9	25.3 ± 5.2	25.8 ± 6.6	25.1 ± 7.6	0.5
Current caffeine users, n (%)	321 (51.9)	37 (42.0)	173 (65.0)	111 (41.9)	<0.001
Current tobacco users, n (%)	118 (19.1)	10 (11.4)	51 (19.2)	57 (21.5)	0.1
Education level, n (%)					0.3
Less than high school	4 (0.6)	0 (0.0)	1 (0.4)	3 (1.1)	
High school diploma or equivalent	83 (13.4)	14 (15.9)	37 (13.9)	32 (12.1)	
Some college or associate's degree	222 (35.9)	25 (28.4)	100 (37.6)	97 (36.6)	
College graduate/bachelor's degree	227 (36.7)	33 (37.5)	89 (33.5)	105 (39.6)	
Advanced degree	83 (13.4)	16 (18.2)	39 (14.7)	28 (10.6)	
Marital status, n (%)					<0.01
Married/domestic partnership	483 (78.0)	74 (84.1)	189 (71.1)	220 (83.0)	
Not currently married or prefer not to answer	136 (22.0)	14 (15.9)	77 (28.9)	45 (17.0)	
Employed, n (%)	359 (58.0)	57 (64.8)	132 (49.6)	170 (64.2)	
Employment status, n (%)[b]					
Employed full-time	339 (54.8)	56 (63.6)	130 (48.9)	153 (57.7)	<0.05
Employed part-time	36 (5.8)	3 (3.4)	21 (7.9)	12 (4.5)	0.2
Self-employed	28 (4.5)	3 (3.4)	12 (4.5)	13 (4.9)	0.9
Retired	79 (12.8)	12 (13.6)	40 (15.0)	27 (10.2)	0.2
Homemaker	66 (10.7)	8 (9.1)	30 (11.3)	28 (10.6)	0.8
Disabled	38 (6.1)	3 (3.4)	20 (7.5)	15 (5.7)	0.4
Unemployed	37 (6.0)	3 (3.4)	15 (5.6)	19 (7.2)	0.5
Student	3 (0.5)	0	0	3 (1.1)	0.1

Percentages in each category may not total exactly 100% because of rounding.
BMI, body mass index; VMS, vasomotor symptoms.
[a]BMI was available for 547 respondents overall and for 68, 236, and 243 respondents with mild, moderate, and severe VMS, respectively.
[b]Respondents were allowed to select more than one employment category.

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TABLE 2. *Respondent comorbidities*

Comorbidities, n (%)	Overall (N = 619)	Mild VMS (n = 88)	Moderate VMS (n = 266)	Severe VMS (n = 265)	*P*
None	155 (25.0)	27 (30.7)	70 (26.3)	58 (21.9)	0.2
Depression	172 (27.8)	8 (9.1)	73 (27.4)	91 (34.3)	<0.001
Arthritis	167 (27.0)	32 (36.4)	74 (27.8)	61 (23.0)	<0.05
Migraines	138 (22.3)	25 (28.4)	61 (22.9)	52 (19.6)	0.2
Hypertension	133 (21.5)	15 (17.0)	54 (20.3)	64 (24.2)	0.3
Diabetes	68 (11.0)	1 (1.1)	20 (7.5)	47 (17.7)	<0.001
Thyroid disease	57 (9.2)	5 (5.7)	29 (10.9)	23 (8.7)	0.3
Osteoporosis	52 (8.4)	8 (9.1)	26 (9.8)	18 (6.8)	0.4
Gynecologic conditions	48 (7.8)	4 (4.5)	24 (9.0)	20 (7.5)	0.4
Other	41 (6.6)	3 (3.4)	24 (9.0)	14 (5.3)	0.1
Cardiovascular disease	36 (5.8)	2 (2.3)	17 (6.4)	17 (6.4)	0.3
Deep vein thrombosis	31 (5.0)	4 (4.5)	17 (6.4)	10 (3.8)	0.4
Obstructive sleep apnea	31 (5.0)	5 (5.7)	14 (5.3)	12 (4.5)	0.9
Gynecologic cancer	21 (3.4)	4 (4.5)	9 (3.4)	8 (3.0)	0.8
Breast cancer	14 (2.3)	1 (1.1)	10 (3.8)	3 (1.1)	0.1
Pulmonary embolism	9 (1.5)	1 (1.1)	4 (1.5)	4 (1.5)	1.0

Participants may have had more than one comorbidity.
VMS, vasomotor symptoms.

severe episode was associated with an increase of 0.13 (95% CI, 0.03-0.23) in PSQI total score ($P < 0.05$). The number of severe nighttime VMS episodes was not significantly associated with PROMIS Sleep-Related Impairment SF 8a scores, nor was number of severe daytime VMS episodes significantly associated with scores on either PROMIS measure or the PSQI.

Association of VMS severity and work productivity (WPAI)

A total of 57 respondents with mild VMS, 132 with moderate VMS, and 170 with severe VMS reported employment and therefore responded to the work-related questions in the WPAI; all respondents answered the question regarding daily activities. Presenteeism (impairment at work), overall work impairment (absenteeism + presenteeism), and impairment in general activities increased with greater VMS severity, an association that was statistically significant with and without adjusting for confounding factors (Fig. 4). There was less absenteeism than presenteeism related to VMS. Severe VMS were associated with more absenteeism than mild VMS, and the association between absenteeism and VMS severity was statistically significant after adjusting for confounding factors (Fig. 4).

There was a significant ($P < 0.05$) association between the number of severe daytime but not nighttime VMS episodes and impairment in general activity, such that one severe daytime episode was associated with a 0.63 percentage point increase (95% CI, 0.08-1.18) in the activity domain score. There were no significant associations between the number of severe daytime or nighttime VMS episodes and the other WPAI domains.

TABLE 3. *VMS and treatment history*

VMS and treatment history	Overall (N = 619)	Mild VMS (n = 88)	Moderate VMS (n = 266)	Severe VMS (n = 265)	*P*
Time since VMS onset (y), median (range)	2.3 (0.1-38.0)	2.3 (0.1-27.0)	3.0 (0.1-38.0)	2.0 (0.2-25.0)	<0.001
No. VMS in past week, median (range)	22.0 (3.0-510.0)	22.0 (3.0-298.0)	23.0 (3.0-510.0)	22.0 (3.0-190.0)	<0.01
VMS treatment history, n (%)					<0.01
Never treated	356 (57.5)	62 (70.5)	133 (50.0)	161 (60.8)	
Ever treated	256 (41.4)	26 (29.5)	129 (48.5)	101 (38.1)	
Not sure	7 (1.1)	0 (0.0)	4 (1.5)	3 (1.1)	
HT[a]					
Current users	38 (14.8)	3 (11.5)	21 (16.3)	14 (13.9)	0.8
Former users	51 (19.9)	5 (19.2)	20 (15.5)	26 (25.7)	0.2
Never users	160 (62.5)	16 (61.5)	85 (65.9)	59 (58.4)	0.5
Not sure	7 (2.7)	2 (7.7)	3 (2.3)	2 (2.0)	0.2
Prescription non-HT[a]					
Current users	35 (13.7)	3 (11.5)	14 (10.9)	18 (17.8)	0.3
Former users	40 (15.6)	1 (3.8)	15 (11.6)	24 (23.8)	<0.01
Never users	169 (66.0)	18 (69.2)	94 (72.9)	57 (56.4)	<0.05
Not sure	12 (4.7)	4 (15.4)	6 (4.7)	2 (2.0)	<0.05
Nonprescription pharmacologic therapies[a]					
Current users	78 (30.5)	7 (26.9)	27 (20.9)	44 (43.6)	<0.001
Former users	85 (33.2)	9 (34.6)	45 (34.9)	31 (30.7)	0.8
Never users	73 (28.5)	6 (23.1)	44 (34.1)	23 (22.8)	0.1
Not sure	20 (7.8)	4 (15.4)	13 (10.1)	3 (3.0)	<0.05

HT, hormone therapy; non-HT, nonhormone therapy; VMS, vasomotor symptoms.
[a]All percentages are of those who were ever treated for VMS: 256 respondents overall and 26, 129, and 101 respondents with mild, moderate, and severe VMS, respectively.

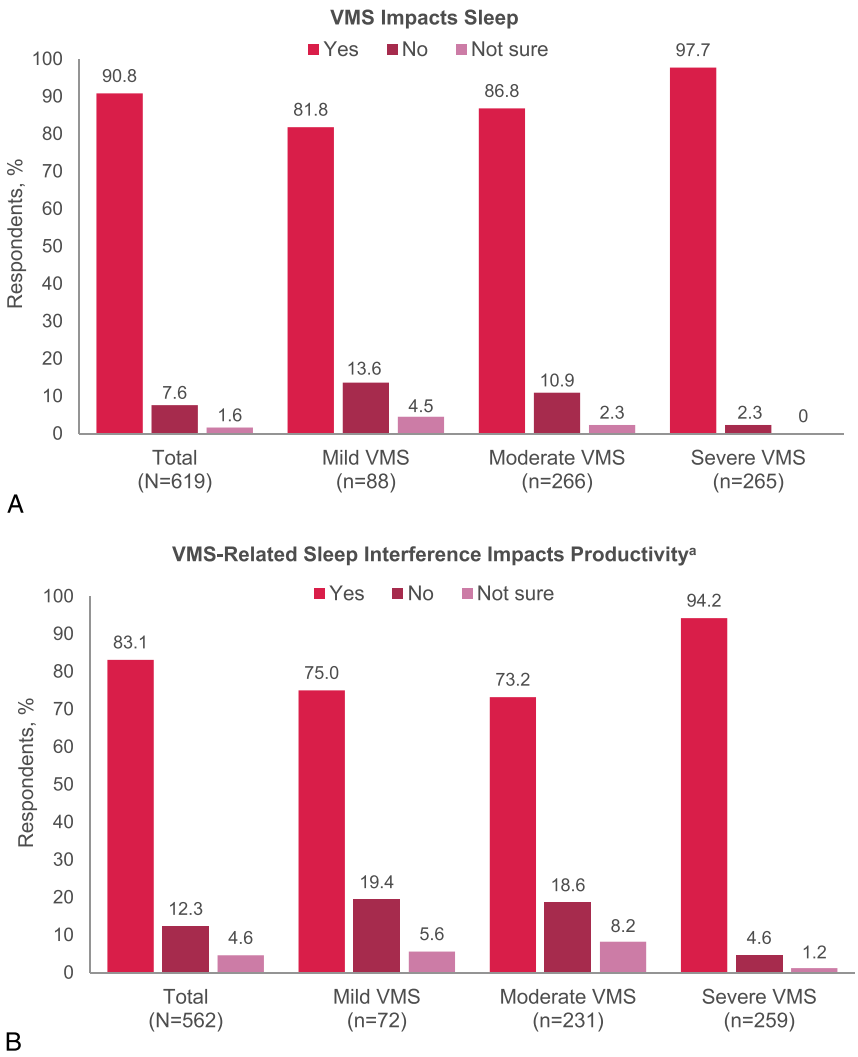

FIG. 1. Self-reported impact of VMS on sleep (**A**) and those sleep impacts on work productivity (**B**), by VMS severity. [a]This question was asked only of those who responded affirmatively to the question of whether VMS impacts sleep. VMS, vasomotor symptoms.

Subgroup analysis

In the subgroup of women with ≥25 VMS episodes per week (n = 279; mild, 32; moderate, 128; severe, 119), relationships between VMS severity and perceived sleep outcomes were similar to those in the main analysis (Supplemental Digital Content, Supplementary Table S1, http://links.lww.com/MENO/B156). Total scores on all three standardized sleep measures were significantly different (ANOVA $P < 0.05$) across levels of self-reported VMS severity, with greater effects on sleep seen among those with the most severe VMS. The number of severe nighttime but not daytime VMS episodes was positively associated with PROMIS Sleep Disturbance SF 8b T scores such that one severe nighttime VMS episode was associated with a 0.37 (95% CI, 0.16-0.57) increase in PROMIS score ($P < 0.001$). There were no significant associations between number of severe daytime or nighttime VMS episodes and the other two sleep measures. WPAI results for this subgroup were also similar to those in the main analysis (Supplemental Digital Content, Supplementary Table S1, http://links.lww.com/MENO/B156). Among women with ≥25 VMS episodes per week, the mean presenteeism, overall work impairment, and activity impairment were significantly different (ANOVA $P < 0.05$) across levels of self-reported VMS, with the greatest impairments among those with severe VMS. However, differences in the domain scores across severity cohorts were no longer significant after adjusting for baseline characteristics, potentially because of small sample sizes. The number of severe daytime VMS episodes was significantly ($P < 0.05$) associated with activity impairment, such that one severe daytime episode was associated with a 0.71 (95% CI, 0.04-1.37) increase in percentage activity impairment. There were no other significant associations between number of daytime or nighttime VMS episodes and the other WPAI domains.

DISCUSSION

Results of this survey of 619 US women with VMS provide insight into women's perceptions of how VMS associated with perimenopause or postmenopause affect sleep and work productivity and how these effects vary by VMS severity. As VMS severity increased, reported sleep disturbance and sleep-related impairment rose and perceived sleep quality worsened. More

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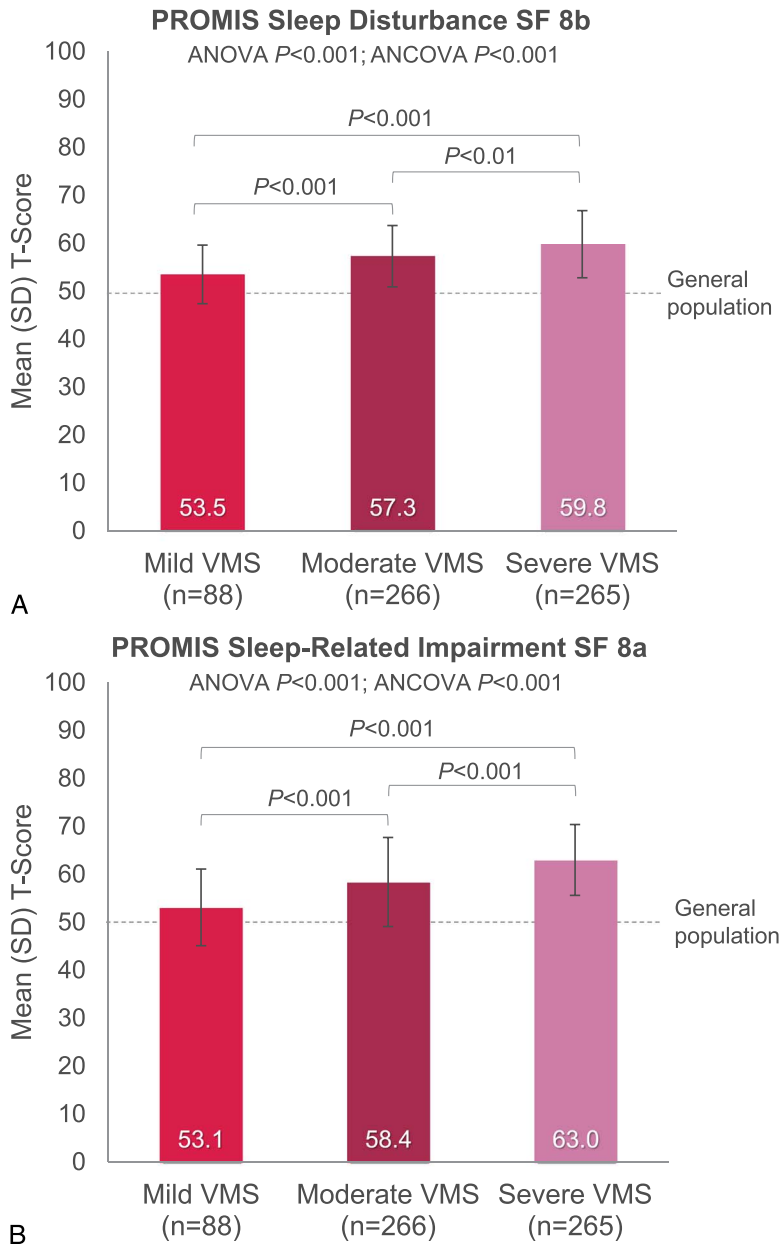

FIG. 2. PROMIS Sleep Disturbance SF 8b (**A**) and Sleep-Related Impairment SF 8a (**B**) T scores by VMS severity. ANCOVA, analysis of covariance; ANOVA, analysis of variance; PROMIS, Patient-Reported Outcomes Measures Information System; SF, short form; VMS, vasomotor symptoms.

severe VMS were associated with greater impairments in daytime activities and work productivity. The vast majority of women and almost all of those with severe VMS said that VMS had a detrimental effect on sleep and that the resulting sleep impairments in turn affected their daytime productivity. The prevalence of moderate to severe VMS during perimenopause or postmenopause in the United States ranges from 32% to 46%,[3] indicating that VMS-related sleep and productivity impacts could affect a large number of midlife women. Our findings point to unmet needs for this population.

The association between nighttime VMS and poor sleep quality reported in our study expands on initial findings from previous research. Previously, a qualitative study was conducted to validate the PROMIS Sleep Disturbance SF 8b and PROMIS Sleep-Related Impairment SF 8a for assessment of VMS effects on sleep. That study included interviews with 32 US and European women with moderate to severe VMS about the effects of VMS on sleep and next-day functioning. They self-reported in the interviews and also indicated on the PROMIS measures that VMS result in nighttime awakenings and poor sleep quality, contributing to sleepiness and impairments in daytime functioning.[11] In a survey of 163 postmenopausal women from Greece, VMS were reported to be associated with nighttime awakenings, premature final awakenings, shorter sleep duration, worse sleep quality, decreased sense of well-being and functioning during the day, and daytime sleepiness based on the Athens Insomnia Scale.[29]

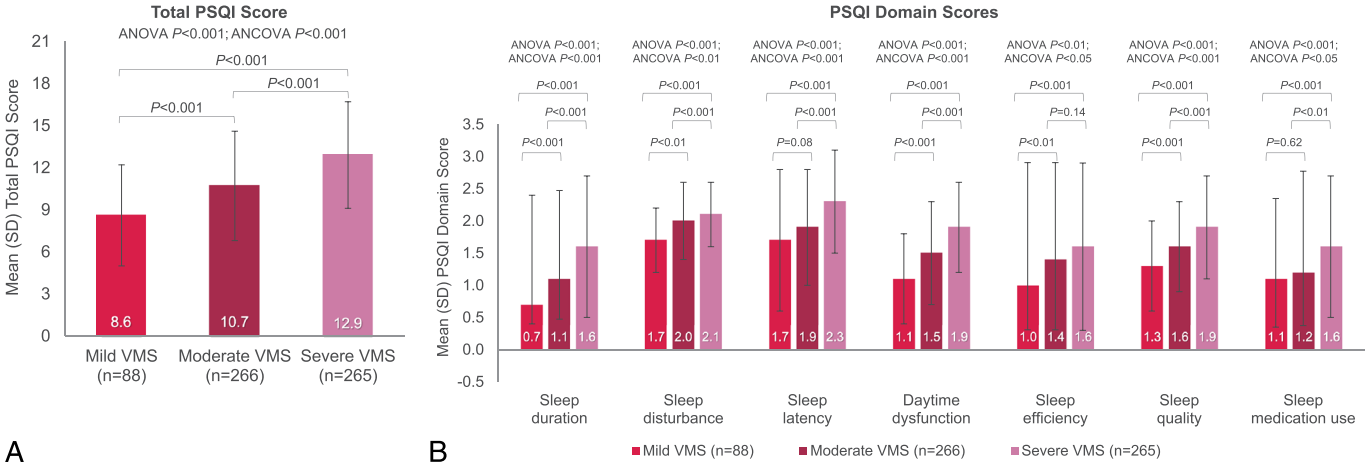

FIG. 3. PSQI total score (**A**) and domain scores (**B**), by VMS severity. ANCOVA, analysis of covariance; ANOVA, analysis of variance; PSQI, Pittsburgh Sleep Quality Index; VMS, vasomotor symptoms.

Our analysis confirmed the association between VMS and sleep impairment in a larger sample of women using multiple standardized instruments (PROMIS Sleep Disturbance SF 8b, PROMIS Sleep-Related Impairment SF 8a, and PSQI) to measure subjective sleep effects. Our findings are consistent with those of studies using objective sleep assessments (actigraphy ± polysomnography), which have associated VMS with motor restlessness, wakefulness, and sleep fragmentation and also decreased likelihood of having good sleep efficiency or feeling well rested upon awakening.[30,31]

Our analysis also builds on prior evidence suggesting an association between VMS severity and self-reported sleep quality. In the Midlife Women's Health Study, US (Maryland) women aged 45 to 54 years (with or without VMS symptoms) rated the frequency of sleep disturbance, insomnia, and restless sleep on Likert scales.[32] Frequencies of sleep disturbance and insomnia were highly associated with self-reported severity, frequency, and number of night sweats among perimenopausal and postmenopausal women; similar associations were found for restless sleep among perimenopausal women.[32] In that study, VMS severity was self-rated using definitions consistent with those in the US FDA Guidance for Industry[33]: "none, mild (sensation of heat without sweating), moderate (sensation of heat with sweating), and severe (sensation of heat with sweating that disrupts your usual activity)."[32] The Midlife Women's Health survey used US FDA Guidance for Industry to define VMS severity. Our more recent survey exclusively enrolled women with VMS and used multiple standardized patient-reported outcome scales (PROMIS and PSQI) and defined severity based on responses to the MRS item 1. We also used ANCOVA to compare sleep quality/disturbance between the three severity cohorts while controlling for sociodemographic characteristics, clinical characteristics, and current treatment status. We found similar trends in both the overall population and the subset of women with ≥25 VMS episodes per week, thereby further validating the findings from the Midlife Women's Health Study.[32]

The association between VMS severity and work and VMS severity and activity impairment on the WPAI in the current survey are also consistent with findings from previous surveys that used the WPAI. Whiteley et al[8] surveyed 3,267 postmenopausal

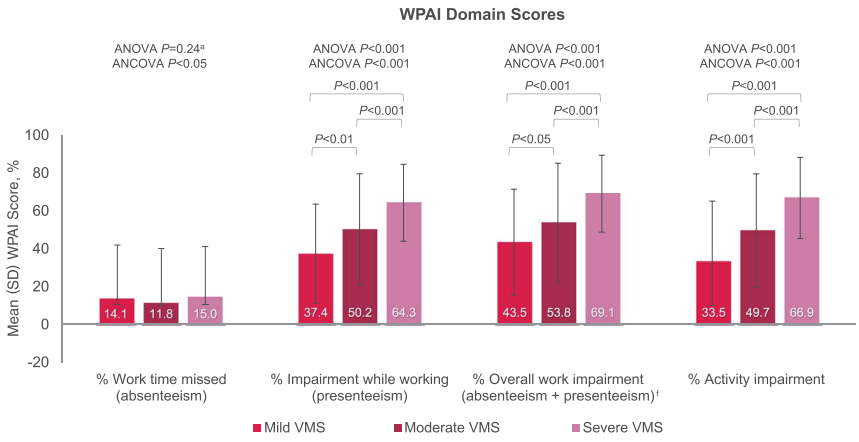

FIG. 4. VMS-related WPAI in the past week, by VMS severity. [a]Pairwise tests were not conducted for absenteeism, since the null hypothesis of the one-way ANOVA was not rejected. ANCOVA, analysis of covariance; ANOVA, analysis of variance; VMS, vasomotor symptoms; WPAI, Work Productivity and Activity Impairment questionnaire.

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US women aged 40 to 75 years who participated in the 2010 US National Health and Wellness Survey and classified them by VMS severity based on MRS item 1. Increasing VMS severity among those who were employed was associated with increases in WPAI scores for presenteeism (mild, 4.0%; moderate, 14.5%; severe, 24.3%; $P < 0.0001$) and overall work impairment (mild, 4.3%; moderate, 14.3%; severe, 24.6%; $P < 0.0001$). Among all women with VMS, irrespective of employment status, severity was associated with impairment in general activities based on the WPAI (mild, 6.2%; moderate, 17.1%; severe, 31.7%; $P < 0.0001$). A survey of postmenopausal women from five European countries similarly found that VMS severity was associated with level of work and activity impairments on the WPAI.[10] Although the pattern of results is similar, the degrees of work- and activity-related impairments on the WPAI in the current survey are greater than those reported by Whiteley et al,[8] likely owing to the inclusion criterion requiring at least 14 VMS episodes per week for at least 1 week in the past month.

Although daytime hot flashes may directly affect work productivity, responses to our survey questions suggest that VMS-related sleep impairments also affect next-day functioning. This finding is consistent with that of previous reports that sleep impairments in general[34-36] and VMS-related sleep impairments specifically[11] are associated with impaired functioning at work. Strategies are needed to improve sleep quality among women with VMS and support employees who are affected by VMS.

One potential strategy is use of pharmacologic treatment to ameliorate VMS. Our survey did not assess the effect of VMS treatment on sleep or work productivity; however, studies of a wide range of hormone and nonhormone treatments for VMS report that effective therapies produced at least partial improvements in sleep.[37-43] Pinkerton et al[44] concluded that treatment for VMS producing a reduction of at least five hot flashes per day or a reduction of 1.0 point in VMS severity would lead to a clinically meaningful improvement in sleep on the Sleep Problems Index II, with particular improvements in sleep disturbance and sleep adequacy. Although available treatments for VMS may provide sleep benefits, as well as symptom relief, about 50% of those with moderate VMS and about 61% of those with severe VMS in our study reported that they had never received treatment for VMS. Concerns about long-term safety of hormone therapy and moderate efficacy of available nonhormone treatment for VMS may be contributing to low usage rates of these therapies.[45-50] Therefore, new therapies that are safe and effective in reducing hot flashes and night sweats could be beneficial in improving sleep quality among women with VMS.

One strength of our analysis is that the ANCOVA model allowed us to control for a variety of factors that could affect sleep (eg, comorbidities, caffeine use, body mass index, sociodemographic factors, current treatment status). In addition, we used multiple standardized patient-reported outcomes (PROMIS, PSQI, and WPAI) and comprehensively assessed the impact of VMS severity on sleep, productivity, and daily activities. This survey also has several limitations. It should be noted that sleep disturbances are multifactorial and may not be exclusively attributable to VMS,[32,51] and although associations were found between VMS severity and sleep/work impacts, we cannot directly determine causality. Another limitation is that the survey sample may not fully represent the general population of US women with VMS. A potential exists for selection bias among women who decided to participate in the Dynata panel or participate in the survey. In addition, less than 10% of women who accessed the survey met the eligibility criteria, allowing for a possibility of inclusion bias. A majority of participants had moderate or severe VMS, which is not representative of the distribution of VMS severity in the general population. Recruitment difficulties led to a smaller-than-target number of women with mild VMS, possibly as a result of the requirement to have at least 14 VMS episodes per week for at least 1 week in the past month or to women's underrecognition that they have VMS when symptoms are mild. Calculation of T scores using the conversion tables in the PROMIS measure scoring manual meant that the scores were standardized to that of adult women and men of all ages rather than an age- and sex-matched population without VMS. Self-reports of VMS severity, sleep, and daytime functioning in the past 7 days (PROMIS or WPAI) or 1 month (PSQI) were subject to potential recall bias, whereas the MRS on which the severity classification was based is less prone to recall bias because it asks about symptoms that "apply to you at this time." There is also a potential for bias inherent in surveys in general in that the respondent can readily identify what is being investigated based on the questions, which could potentially influence responses. Finally, it is unknown whether the concurrent coronavirus disease 2019 pandemic directly or indirectly affected sleep and work productivity responses.

CONCLUSIONS

A large majority of perimenopausal and postmenopausal women in the United States who participated in this online survey said that VMS, especially more severe VMS, impair their sleep and that this sleep impairment then affects their productivity. Additional results from the survey using standardized questionnaires (PROMIS sleep measures, PSQI, and WPAI) further confirmed that women with more severe VMS also have greater sleep disturbance and sleep-related daytime impairment, worse perceived sleep quality, and greater impairment in daytime activities and work productivity. These findings point to a need to ensure access to safe and effective VMS therapies that can also reduce the effect of VMS on sleep, for appropriate patients in perimenopause or postmenopause. Future research should determine whether treatment of VMS also ameliorates the effect of VMS on work productivity and identify approaches that employers can use to accommodate and support workers affected by VMS.

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