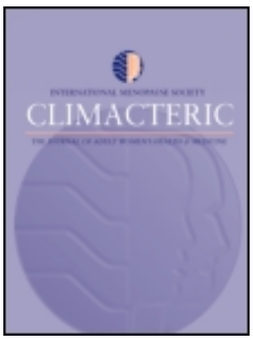

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MsFLASH participants' priorities for alleviating menopausal symptoms

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Key words: MENOPAUSE, SYMPTOMS, VASOMOTOR SYMPTOMS, SLEEP DISTURBANCES, FATIGUE, COGNITIVE FUNCTIONING

ABSTRACT

Objective To describe self-reported menopausal symptom priorities and their association with demographics and other symptoms among participants in an intervention trial for vasomotor symptoms (VMS).

Methods Cross-sectional study embedded in the MsFLASH 02 trial, a three-by-two factorial design of yoga vs. exercise vs. usual activity and omega-3-fatty acid vs. placebo. At baseline, women ($n = 354$) completed hot flush diaries, a card sort task to prioritize symptoms they would most like to alleviate, and standardized questionnaires.

Results The most common symptom priorities were: VMS ($n = 322$), sleep ($n = 191$), concentration ($n = 140$), and fatigue ($n = 116$). In multivariate models, women who chose VMS as their top priority symptom ($n = 210$) reported significantly greater VMS severity ($p = 0.004$) and never smoking ($p = 0.012$), and women who chose sleep as their top priority symptom ($n = 100$) were more educated ($p \leq 0.001$) and had worse sleep quality ($p < 0.001$). ROC curves identified sleep scale scores that were highly predictive of ranking sleep as a top priority symptom.

Conclusions Among women entering an intervention trial for VMS and with relatively low prevalence of depression and anxiety, VMS was the priority symptom for treatment. A card sort may be a valid tool for quickly assessing symptom priorities in clinical practice and research.

INTRODUCTION

Most women experience multiple, concurrent menopausal symptoms at midlife[1–5]. Although vasomotor symptoms (VMS) have been the focus of most intervention studies[6,7], they do not occur in isolation. VMS frequently co-occur with disturbed sleep and mood, fatigue, trouble remembering or concentrating, and/or sexual difficulties[1–3,8–10]. These co-occurring symptoms are typically not assessed or are considered secondary outcomes, with few trials specifically targeting more than one symptom[6,7,11,12]. Research shows that symptoms act synergistically and that the impact of co-occurring symptoms on an individual is multiplicative rather than additive[9,13]. Thus, addressing multiple co-occurring symptoms is vital to improving midlife women's quality of life.

Little is known about how women view the relative importance of their menopausal symptoms[14]. During clinic visits, symptoms are often discussed with providers but not necessarily ranked by relative importance, which may result in under-treatment of the symptom women would most like to alleviate. Investigating the relative importance of menopausal symptoms to each woman would provide useful information for understanding how to design research trials to alleviate

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co-occurring symptoms and prioritize therapeutic discussions and treatment recommendations by providers in clinical practice. Furthermore, understanding demographic correlates of symptom priorities would be informative for identifying at-risk patients in clinical practice and designing research sampling plans. For example, it is likely that symptom priorities vary by race given that higher rates of VMS[15] and disturbed sleep[16–18] are reported by African-American women compared to white women. In addition, understanding whether symptom priorities are correlated with ratings and scores on other symptom measures, such as diaries or standardized scales, is important for both research and practice. Symptoms that exceed cut-off scores (i.e. those that are more severe) are likely to be more salient, but when several symptoms exceed cut-off scores, women may differ on how they prioritize each symptom's relative importance.

The study objective was to describe menopausal symptom priorities among women participating in a behavioral intervention trial for VMS treatment and their association with demographic characteristics and other symptom measures. We anticipated that distinct patterns of symptom priorities would emerge and that these would be associated with demographic correlates and cut-off scores.

METHODS

Design

This cross-sectional study was embedded within the second trial conducted by the United States research network, MsFLASH (Menopause Strategies Finding Lasting Answers to Symptoms and Health). Details of the MsFLASH protocol and research study are published elsewhere[19,20]. Briefly, the trial was a three-by-two factorial design comparing yoga and exercise vs. usual activity and omega-3 supplements vs. placebo for the treatment of VMS (primary outcome) and menopausal symptoms of disturbed sleep and mood, pain, sexual function, and quality of life (secondary outcomes). All data reported here are from the baseline data collection. Procedures were approved by the institutional review boards at each clinical site (Indianapolis, Oakland, and Seattle) and the Data Coordinating Center in Seattle. All research participants provided written, informed consent and authorization to use protected health information.

Sample

Participants were recruited between February 2011 and January 2012. Mass mailings were sent to women aged 40–62 years using purchased lists and health-plan enrollment files. Women were screened via telephone for eligibility and then via a 2-week VMS diary and questionnaire. Potentially eligible women completed a 3rd week of diaries. Eligible women were 40–62 years old; in the menopausal transition or early postmenopause or had had a hysterectomy with follicle stimulating hormone >20 mIU/ml and estradiol $\leq$50 pg/ml; and in generally good health. The VMS eligibility criteria were: $\geq$14 hot flushes/night sweats per week recorded on daily VMS diaries for 3 weeks; VMS rated as bothersome or severe on four or more occasions per week; and the VMS frequency in week 3 did not decrease by >50% from the average weekly levels in weeks 1 and 2. Exclusion criteria included: body mass index (BMI) >37 kg/m^2; use of hormonal contraceptives or hormones in the past month; use of prescription or over-the-counter treatments for VMS in the past month; unstable medical conditions; current user of one of the study interventions or a related activity (i.e. yoga, tai chi, qi gong, meditation, regular exercise, omega-3 fatty acid supplements, frequent consumption of fish); contraindications to exercise (e.g. physical limitations), yoga, or omega-3 (e.g. allergy to soy or fish); or a major depressive episode in the past 3 months.

Procedures

Study screening was done via telephone followed by 2 weeks of at-home daily VMS diaries. Women whose diaries indicated they met VMS inclusion criteria completed two baseline clinic visits scheduled 1 week apart before being randomized to the interventions. All measures used for this study were collected during the trial's baseline data collection period.

Measures

Symptom priorities were assessed using a card sort methodology. Women were given a set of 12 symptom cards: hot flushes or night sweats; disturbed sleep; feeling tired or worn out (fatigue); trouble remembering or concentrating (concentration); loss of interest in sex; vaginal dryness or pain with sexual intercourse; uncontrollable loss of urine; mood swings; feeling irritable; aches and pains; headaches; or heart palpitations. Research staff instructed women to select three cards representing the top three symptoms they would 'most like to get rid of or be free of'. Once the three cards were selected from the deck, research staff then asked women to rank order the cards from one to three, with one representing the top symptom, two the second symptom, and three the third symptom they would most like to alleviate. Responses were recorded onto a paper form and data entered by study staff.

VMS frequency, severity and bother were recorded twice daily for 3 weeks: 2 weeks prior to the first baseline visit and during the 1 week between the two baseline visits. Women were instructed to use the diaries in the morning to write down the number, severity rating, and bother rating of their nighttime VMS and similarly to use the diaries at bedtime to record daytime VMS. Severity was rated as mild, moderate, or severe. Bother was rated as not at all, a little, moderate, or a lot. Ratings were used to calculate daily mean frequency, severity, and bother.

Hot flush interference was assessed with the 10-item Hot Flash Related Daily Interference Scale (HFRDIS)[21]. Participants rated the degree to which hot flushes interfered with each item during the previous week using a scale of 0 (do not interfere) to 10 (completely interfere). This one-dimensional scale is best represented by an overall mean score (sum of items/10) with higher scores representing higher levels of daily interference[22].

Sleep was assessed using two scales: the 18-item Pittsburgh Sleep Quality Index (PSQI)[23,24] and the 7-item Insomnia Severity Index (ISI)[25,26]. Both were used since the PSQI focuses broadly on overall sleep quality and the ISI is more specific to insomnia symptoms. PSQI global scores above 5 indicate poor sleep quality and above 8 indicate very poor sleep quality and daytime fatigue[27]. ISI insomnia severity is interpreted using total scores as none (0–7), subthreshold (8–14), moderate (15–21), and severe (22–28)[25,26].

Data analysis

Analyses were conducted using SAS version 9.3. Sample demographics were analyzed using descriptive statistics ($n = 355$). Symptoms were ranked by number of top-priority symptoms and the total number of first-, second-, and third-priority symptoms. Frequencies and a Venn diagram were used to evaluate how symptoms were prioritized and how the overlap among symptoms was distributed within the sample. Participants were categorized by top-priority symptoms. VMS and disturbed sleep were the most highly prioritized symptoms (VMS: 210 first- + 78 second-place votes; disturbed sleep: 48 first- + 100 second-place votes).

The sample was divided based on symptom priorities. We performed several analyses between (1) women who did and did not pick VMS as their top-priority symptom and (2) women who did and did not pick disturbed sleep as their top-priority symptom. Univariate and then multivariate comparisons and receiver operating characteristic (ROC) curve analyses were performed as outlined below.

Demographics, hot flush diary, and hot flush interference scores were compared using χ^2 and t-tests between women who rated VMS as their first-priority symptom to alleviate ($n = 210$) and women who did not ($n = 144$). We fitted a logistic regression model estimating the probability of picking VMS symptoms as the first priority to alleviate as a function of VMS frequency, severity, and interference, adjusted for those baseline characteristics with a p value less than 0.2 from the univariate tests. VMS bother was not included in the model because of its high correlation with VMS severity.

Similarly, we compared participant characteristics, PSQI and ISI scores using χ^2 and t-tests between women who rated disturbed sleep as their first-priority symptom to alleviate ($n = 48$) and those who did not ($n = 296$). We fitted two logistic regression models – one as a function of PSQI scores and one as a function of ISI scores – both controlling for baseline characteristics with p values less than 0.2 from univariate tests.

We plotted ROC curves and calculated the area under the ROC curves (AUC) from three unadjusted logistic regression models – one estimating the probability of choosing VMS as the priority symptom as a function of HFRDIS, and two models estimating the probability of choosing disturbed sleep as the priority symptom as a function of PSQI and ISI, respectively. If AUC ≥ 0.7, indicating that the measurement had at least a fair level of efficacy in predicting participant choice, then we applied the ROC curve to select an optimal cut-off point in the scale for predicting a participant's choice, treating sensitivity and specificity as equally important.

RESULTS

The sample included 354 women with card sort data. Most of the women were in their fifties (82%), white (64%) or African-American (26%), college graduates (62%) and married or partnered (66%). The majority had never smoked (65%) and were non-drinkers (38%) or reported drinking one to seven alcoholic beverages per week (44%). BMI varied: 34% had a BMI $<25\,kg/m^2$, 41% had a BMI from 25 to $30\,kg/m^2$, and 25% had a BMI $>30\,kg/m^2$. Most (82%) were postmenopausal, and reported fair/good (37%) or very good (45%) health.

Table 1 shows the total number of first-, second-, and third-ranked symptom priorities. The top four symptoms women most wanted to alleviate were hot flushes ($n = 322$), disturbed sleep ($n = 191$), trouble remembering or concentrating ($n = 140$), and fatigue (feeling tired/worn out) ($n = 116$). VMS was the most highly prioritized symptom yet only 59% ($n = 210$) of our study sample rated VMS as the top symptom they would most like to eliminate whereas 41% ($n = 144$) picked another symptom. Disturbed sleep was the second most highly prioritized: 48 women picked disturbed sleep as the symptom they would most like to alleviate versus 296 who picked another symptom.

Figure 1 shows co-occurrence among the top four symptoms. All but two participants selected at least one of the top four symptoms, and thus the sample size for this figure is $n = 353$. The most common co-occurrence was to select both VMS and disturbed sleep ($n = 96$, 27% of the total sample) as two of the three priority symptoms to alleviate. In contrast, only one person picked disturbed sleep but not one of the other most highly prioritized symptoms.

VMS as the top symptom priority

Tables 2 and 3 show unadjusted differences between women who selected VMS and those that did not. Compared to women who picked symptoms other than VMS as their top symptom to alleviate ($n = 145$), women who picked VMS ($n = 210$) were significantly more likely to be African-American ($p = 0.02$), had significantly greater VMS frequency

Table 1 Priorities for menopausal symptoms women would most like to alleviate ($n = 354$)

	Priority symptom							
	First		*Second*		*Third*		*Overall*	
	n	%	*n*	%	*n*	%	*n*	%
Hot flushes/night sweats	210	59.2	75	21.1	37	10.4	322	90.7
Disturbed sleep	48	13.5	100	28.2	43	12.1	191	53.8
Remembering/concentrating	27	7.6	40	11.3	73	20.6	140	39.4
Fatigue	27	7.6	40	11.3	49	13.8	116	32.7
Loss of interest in sex	14	3.9	25	7.0	29	8.2	68	19.2
Vaginal dryness or pain with sexual intercourse	9	2.5	17	4.8	39	11.0	65	18.3
Uncontrollable loss of urine	5	1.4	14	3.9	10	2.8	29	8.2
Mood swings	4	1.1	14	3.9	15	4.2	33	9.3
Feeling irritable	4	1.1	12	3.4	22	6.2	38	10.7
Aches and pains	3	0.9	8	2.3	19	5.4	30	8.5
Headaches	2	0.6	5	1.4	4	1.1	11	3.1
Heart palpitations	1	0.3	4	1.1	8	2.3	13	3.7

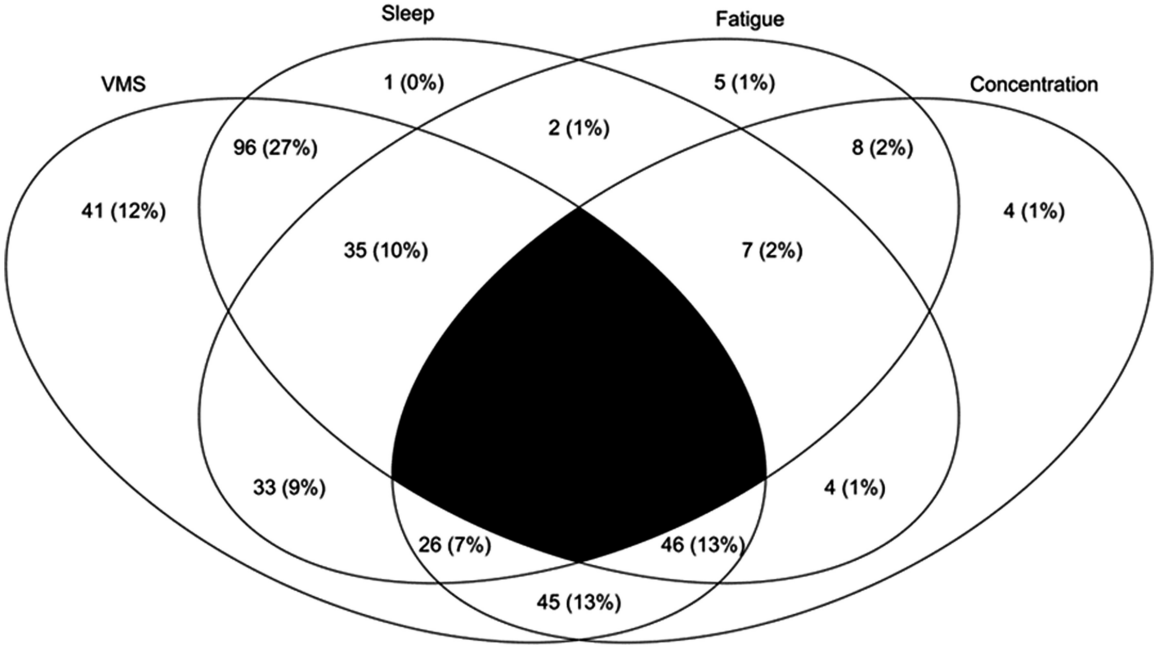

Figure 1 Co-occurrence of menopausal symptoms prioritized as those that women would most like to alleviate. Venn diagram depicts the overlap among symptom priorities. Numbers are *n* (%). VMS are vasomotor symptoms. Sleep indicates disturbed sleep. Fatigue refers to feeling tired or worn out. Concentration refers to trouble remembering or concentrating. The four symptoms appeared most often as one of the top three symptoms women would most want to alleviate. There was one (0.28%) participant who did not pick any of the top four symptoms, thus this figure reflects $n = 353$. The black center reflects the area of overlap not assessed since women rated their top three and not four symptoms

($p = 0.019$), severity ($p = 0.005$), bother ($p < 0.001$), and tended to report greater VMS interference ($p = 0.052$) (Table 3).

Table 4 shows results of an adjusted logistic regression model identifying factors associated with selecting VMS as the top-priority symptom to alleviate. Those who picked VMS reported greater VMS severity (odds ratio (OR) 2.55, $p = 0.004$) and were more likely to have never smoked (OR 1.90, $p = 0.012$) after adjusting for the other variables. The AUC based on HFRDIS score was 0.56 ($n = 328$, 95% confidence interval (CI) 0.50–0.63), indicating a level of predictive accuracy that was no better than chance.

Disturbed sleep as top symptom priority

Tables 2 and 3 show unadjusted differences between women who selected disturbed sleep as their top-priority symptom to alleviate and those that did not. Compared to women who picked symptoms other than sleep as their top symptom to

Table 2 Demographic differences between women based on first priority symptom chosen to alleviate

	Chose VMS		*Chose other*			*Chose disturbed sleep*		*Chose other*		
	n	%	*n*	%	*p*	*n*	%	*n*	%	*p*
Age group					0.390					0.482
42–49 years	8	3.8	11	7.6		3	6.3	16	5.2	
50–54 years	101	48.1	61	42.4		19	39.6	143	46.7	
55–59 years	76	36.2	54	37.5		22	45.8	108	35.3	
60–62 years	25	11.9	18	12.5		4	8.3	39	12.7	
Ethnicity					0.019					0.654
White	130	61.9	97	67.4		33	68.8	194	63.4	
African-American	65	31.0	28	19.4		10	20.8	83	27.1	
Other/unknown	15	7.1	19	13.2		5	10.4	29	9.5	
Education					0.273					0.044
≤ High school diploma or GED	16	7.6	5	3.5		0	0.0	21	6.9	
Some post high school	62	29.5	50	34.7		10	20.8	102	33.3	
College graduate	131	62.4	89	61.8		38	79.2	182	59.5	
Marital status					0.544					0.093
Never married	18	8.6	16	11.1		9	18.8	25	8.2	
Divorced or separated	40	19.0	36	25		10	20.8	66	21.6	
Widowed	4	1.9	3	2.1		1	2.1	6	2	
Married/partnered	147	70.0	88	61.1		27	56.3	208	68	
Smoking					0.097					0.079
Never	147	70.0	84	58.3		30	62.5	201	65.7	
Past	43	20.5	46	31.9		16	33.3	73	23.9	
Current	19	9.0	13	9		1	2.1	31	10.1	
Alcoholic drinks/week					0.489					0.106
0	81	38.6	55	38.2		16	33.3	120	39.2	
1 to <7	95	45.2	61	42.4		18	37.5	138	45.1	
7+	32	15.2	28	19.4		14	29.2	46	15	
Body mass index (kg/m^2)					0.990					0.535
<25	73	34.8	49	34		14	29.2	108	35.3	
25 to <30	85	40.5	59	41		23	47.9	121	39.5	
≥30	52	24.8	36	25		11	22.9	77	25.2	
Menopausal status					0.443					0.486
Postmenopausal	167	79.5	122	84.7		42	87.5	247	80.7	
Late transition	38	18.1	20	13.9		5	10.4	53	17.3	
Early transition	5	2.4	2	1.4		1	2.1	6	2	
Health rating					0.314					0.600
Excellent	39	18.6	19	13.2		8	16.7	50	16.3	
Very good	97	46.2	64	44.4		18	37.5	143	46.7	
Good/fair	73		61	42.4		22		112	36.6	
ISI										<0.001
≤15	165	78.6	95	66.0	0.008	21	43.8	239	78.1	
>15 (insomnia)	45	21.4	49	34.0		27	56.3	67	21.9	
PSQI										<0.001
<8	106	50.5	57	39.6	0.021	11	22.9	152	49.7	
≥8 (poor sleep)	95	45.2	85	59.0		37	77.1	143	46.7	

GED, general equivalency diploma; VMS, vasomotor symptoms; HFRDIS, Hot Flash Related Daily Interference Scale; ISI, Insomnia Severity Index; PSQI, Pittsburgh Sleep Quality Index

Table 3 Differences in frequency, severity and bother of vasomotor symptoms (VMS) as reported in daily diaries between women based on first priority symptom chosen to alleviate. Data are given as mean ± standard deviation

	Chose VMS	*Chose other*	*p*	*Chose disturbed sleep*	*Chose other*	*p*
VMS diary frequency	4.7 ± 2.5	4.0 ± 2.5	0.005	3.8 ± 1.9	4.5 ± 2.6	0.079
VMS diary severity	1.1 ± 0.4	0.9 ± 0.4	<0.001	0.8 ± 0.4	1.0 ± 0.4	0.005
VMS diary bother	2.0 ± 0.5	1.8 ± 0.5	<0.001	1.8 ± 0.5	2.0 ± 0.5	0.004
HFRDIS	34.3 ± 21.9	29.7 ± 21.1	0.052	30.8 ± 18.3	32.7 ± 22.2	0.594

VMS, vasomotor symptoms; HFRDIS, Hot Flash Related Daily Interference Scale

alleviate ($n = 306$), women who picked disturbed sleep as their top symptom ($n = 48$) were significantly more likely to have ISI scores >15 ($p < 0.001$) and PSQI scores >8 ($p < 0.001$). They also tended to have more education ($p = 0.044$).

Table 5 shows the results of adjusted logistic regression models predicting disturbed sleep as a top-priority symptom. Both ISI (OR 1.22, $p < 0.001$) and PSQI (OR 1.26, $p < 0.001$) remained significant after adjusting for education, marital status, and smoking and drinking habits. Education also remained significant in both models and had similar effect sizes in each (OR = 1.54 for PSQI and 1.50 for ISI).

The AUC was 0.76 for ISI ($n = 350$, 95% CI 0.70–0.83) and 0.71 for PSQI ($n = 344$, 95% CI 0.64–0.78), indicating that both provided a fair level of accuracy for predicting whether or not a participant would pick disturbed sleep as most bothersome.

If sensitivity and specificity were treated as equally important, then a PSQI score of 9 was optimal to indicate a participant picked disturbed sleep as a top-priority symptom to alleviate (sensitivity 66.7, specificity 63.9). This cut-off had a Youden's index of 0.31 and would correctly classify 32 out of 48 women who picked sleep as most bothersome, and 189 out of 296 who picked other symptoms as most bothersome. Similarly, an ISI score of 11 was optimal (sensitivity 89.6, specificity 44.7). This cut-off had the highest Youden's index, 0.34, and would correctly classify 43 of the 48 women who picked sleep as most bothersome, but would only correctly classify 135 of the 302 women who picked other symptoms as most bothersome.

Table 4 Multivariate logistic regression identifying factors associated with women who chose hot flushes as priority symptom to alleviate

Factor	*Odds ratio (95% confidence interval)*	*p Value*
HFRDIS	1.00 (0.99–1.02)	0.410
VMS frequency	1.07 (0.96–1.19)	0.204
VMS severity	2.55 (1.35–4.82)	0.004
Ethnicity		
White	reference	0.136
African-American	1.56 (0.88–2.77)	
Other/unknown	0.68 (0.31–1.48)	
Smoking		
Never	1.90 (0.82–4.38)	0.012
Past	0.87 (0.35–2.14)	
Current	reference	

HFRDIS, Hot Flash Related Daily Interference Scale; VMS, vasomotor symptoms

DISCUSSION

There were three principal findings from this study. First, VMS and disturbed sleep, followed by feeling tired (fatigue) and trouble remembering or concentrating, were overall the most highly prioritized symptoms that women presenting for a VMS treatment trial wanted to alleviate. Only slightly more than half of women enrolled in a trial for VMS treatment chose VMS as the top symptom they would most like to eliminate. Second, race/ethnicity and VMS severity but not HFRDIS scores were associated with women's ranking of VMS as their top-priority symptom to alleviate. Third, educational level, ISI and PSQI scores were associated with ranking disturbed sleep as a top-priority symptom to alleviate.

Strengths and weaknesses of this study include the following. This was a large and relatively diverse sample from a multi-site study. Data were carefully annotated using daily diaries, the card sort and questionnaires that were administered during a clinic visit. VMS are the most common symptom associated with the menopausal transition associated with decreased health-related quality of life and we focused on those with two or more bothersome VMS per day. The sample

Table 5 Multivariate logistic regression models identifying factors associated with women who chose disturbed sleep as a priority symptom to alleviate

	PSQI model		*ISI model*	
Factor	*Odds ratio (95% confidence interval)*	*p Value*	*Odds ratio (95% confidence interval)*	*p Value*
Education	1.54 (1.19–1.97)	<0.001	1.50 (1.16–1.93)	0.002
Marital status				
Never married	3.05 (1.15–8.13)	0.167	3.70 (1.16–1.94)	0.079
Divorced or separated	1.40 (0.59–3.33)		1.83 (0.75–4.50)	
Widowed	1.56 (0.16–15.22)		1.59 (0.15–17.28)	
Married/partnered	reference		reference	
Smoking				
Never	reference	0.341	reference	0.356
Past	1.36 (0.62–2.95)		1.35 (0.62–2.93)	
Current	0.30 (0.04–2.40)		0.30 (0.04–2.43)	
Alcoholic drinks/week				
None	reference	0.273	reference	0.232
1 to <7	1.06 (0.48–2.35)		1.13 (0.49–2.59)	
7+	2.02 (0.80–5.13)		2.20 (0.84–5.75)	
PSQI	1.26 (1.13–1.40)	<0.001		
ISI			1.22 (1.13–1.31)	<0.001

PSQI, Pittsburgh Sleep Quality Index; ISI, Insomnia Severity Index

was limited to women who participated in a treatment trial for VMS and therefore results may not be generalizable to midlife women who are already receiving VMS treatment or who choose not to seek VMS treatment. However, it is important to note that, even though these women were participating in a VMS treatment study, for 41% of them, VMS was *not* their priority symptom. In addition, women using selective serotonin reuptake inhibitors for VMS were excluded, which may have disproportionately eliminated women with mood problems, an important menopausal symptom documented in other studies[2]. This may at least partially account for the low ranking of mood and irritability in the card sort. The great majority of midlife women experience frequent and bothersome VMS during the menopausal transition, and understanding the priorities for symptom relief among this large population group has a high degree of clinical relevance.

The emergence of disturbed sleep as a top-priority symptom among this sample of women seeking treatment for VMS was not surprising. Numerous large, population-based studies have documented the co-occurrence of VMS and disturbed sleep[2,5,28]. In addition, our study participants from this analysis were similar to participants in our other trials, nearly one-third of whom had moderate to severe insomnia on the ISI and 40% of whom had poor subjective sleep quality on the PSQI[29].

The emergence of low energy and problems with memory/concentration difficulties as top symptom priorities serves as an important reminder for assessing these symptoms in clinical practice and research. These symptoms were not assessed in our network trials except with these card sort data. Changes in concentration and memory were part of the symptom cluster documented in women participating in the Seattle Midlife Women's Health Study[2]. Similarly, verbal memory performance was related to the objectively recorded hot flush frequency in a study of 29 midlife women with moderate to severe hot flushes[30]. Fatigue and memory/concentration problems may be part of a cascade of symptoms resulting from disturbed sleep.

Pain did not appear as a top-priority symptom despite other studies showing it to be commonly experienced during menopause. In the Seattle Midlife Women's Health Study, mood and pain also emerged as important symptoms[2], which differs from our results showing these were, respectively, the 8th and 10th most prioritized symptoms. Similarly, in the Penn Ovarian Aging Study, aches and joint pain were among a handful of symptoms most commonly reported in the late transitional stage[10].

When evaluating VMS as a top symptom to alleviate, VMS severity but not frequency or interference emerged as significant correlates. VMS frequency and severity were moderately correlated ($r = 0.36$) and, when the model was run without severity (not shown), frequency was significant (OR 1.13, $p = 0.02$). However, severity with an odds ratio of 2.66 seems more salient. HFRDIS findings may reflect the importance of VMS severity in a woman's life and/or limitations of the HFRDIS. In particular, the HFRDIS includes items related to VMS interference with sleep, concentration and sexuality[21], which may have resulted in it being a less than ideal measure for differentiating women who selected VMS as the top symptom to alleviate and women who picked other symptoms such as disturbed sleep, concentration problems, or sexual concerns.

Importantly, associations between symptom priorities and diary VMS severity or standardized sleep measures indicate the card sort may be a valid and efficient method for quickly assessing symptom priorities in clinical practice or research. Because VMS often co-occur with other menopausal symptoms, not all of which can be addressed at once or may not be fully controlled, the card sort could help clinicians identify women's priorities for which symptoms to target first so treatment can be tailored accordingly. The card sort could be used as the first step of an assessment algorithm to guide more detailed symptom assessments tailored only to the subset of symptoms women would most like to alleviate. This could result in greater efficiency and speed of symptom assessments in clinical practice and research, while retaining a focus on those symptoms women are most concerned about managing. Ultimately, the card sort assessment method with a tailored treatment approach could improve symptom management by reducing the burden and impact of these symptoms.

Future research directions include repeating the card sort study in a more broadly selected sample of midlife women with bothersome menopause symptoms that may or may not include VMS to determine the replicability of our findings. Understanding the prioritization of symptoms in women not presenting for VMS trials might result in different findings. We also recommend studying the implementation of the card sort in clinical practice to assess feasibility in busy practice settings and potential impact on the clinical care of midlife women. In theory, a computerized version of the card sort could be directly linked to the electronic medical record to facilitate tracking and provide efficiency in clinical practice.

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