Symptoms of Depressed Mood, Disturbed Sleep, and Sexual Problems in Midlife Women: Cross-Sectional Data from the Study of Women's Health Across the Nation

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Abstract

Background: Women report many nonvasomotor symptoms across the menopausal transition, including sleep disturbances, depressed mood, and sexual problems. The co-occurrence of these three symptoms may represent a specific menopausal symptom triad. We sought to evaluate the interrelatedness of disturbed sleep, depressed mood, and sexual problems in the Study of Women's Health Across the Nation (SWAN) and determine the characteristics of women exhibiting this symptom triad.

Methods: SWAN is a multisite, multiethnic observational cohort study of the menopausal transition in the United States. Sleep disturbance, sexual problems, and depressed mood were determined based on self-report. Women who reported all three symptoms simultaneously were compared to those who did not. Logistic regression models estimated the association of demographic, psychosocial, and clinical characteristics with the symptom triad.

Results: Study participants ($n = 1716$) were 49.8 years old on average and primarily in very good or excellent health. Sixteen and a half percent had depressed mood, 36.6% had a sleep problem, and 42.2% had any sexual problem. Five percent of women ($n = 90$) experienced all three symptoms. Women with the symptom triad compared with those without had lower household incomes, less education, were surgically postmenopausal or late perimenopausal, rated their general health as fair or poor, and had more stressful life events and lower social support.

Conclusions: The symptom triad of sleep disturbance, depressed mood, and sexual problems occurred in only 5% of women, and occurred most often among women with lower socioeconomic status, greater psychosocial distress, and who were surgically menopausal or in the late perimenopause.

Introduction

WOMEN IN THE UNITED STATES and other countries report a wide range of symptoms during the menopausal transition (MT) and early postmenopause (STRAW [Study of Women's Health Across the Nation] + 10 stages −2 to +1b, which are early MT through 2 years after the final menstrual period or early postmenopause).[1] Vasomotor symptoms (hot flashes/flushes and night sweats) have been clearly attributed to hormonal fluctuations during the MT, while many other common symptoms, including sleep disturbance, depressed mood, and sexual problems, have less clear etiologies during the transition, particularly during the latter part of the transition (late perimenopause). Researchers have been studying these symptoms for decades,[2–5] but clear elucidation of etiology remains an area of ongoing investigation. Whether the myriad symptoms reported by women during the MT and early postmenopause are caused by hormonal changes, by

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underlying psychiatric distress including undiagnosed depression and dysthymia, or are unrelated to the transition itself and merely co-occur in time remains to be examined. Furthermore, determining whether certain symptoms occur together within women is an area of active investigation.[6–8] Improving our understanding of how symptoms cluster will lead to better understanding of underlying mechanisms and improved, targeted therapies for specific symptom clusters.

Sleep disturbances are commonly reported by women going through the MT.[9,10] Studies of women in the MT have shown that sleep disruption is a major contributor to decreased quality of life[6] and are an important reason women seek care for menopausal symptoms.[11,12] Large cohort studies, including SWAN, The Penn Ovarian Aging Study, and the Harvard Study of Moods and Cycles, have reported an increased risk for depressed mood in women going through the MT,[13–15] although the mechanism underlying this association is unclear. For both women and men, sexual activity decreases as a function of age. For women, postmenopausal status is related to increasing complaints of vaginal dryness and dyspareunia, which may also worsen with increasing time from the final menstrual period. Studies have shown repeatedly that relationship factors (availability of sexual partner and quality of relationship) and psychological factors including mood, anxiety, and depression outweigh hormonal contribution to overall sexual function in menopausal-aged women.[16–19]

During the MT, the symptom triad of disturbed sleep, depressed mood, and sexual problems may be more likely to co-occur in women with psychosocial risk factors. In our clinical population of midlife women aged 40–60 years seeking care from menopause specialists, 20% of women surveyed complained of the symptom triad of disturbed sleep, depressed mood, and sexual problems.[20] These symptoms are commonly reported, but there are minimal data to examine whether they co-vary in individual women. While symptoms of clinical depression include sleep disturbance and decreased libido, depressed symptoms may co-occur with sleep disturbance and sexual problems as a particular symptom triad during midlife distinct from clinical depression. However, women seeking care from specialist clinics are not representative of the overall population, including reporting higher symptom burden.[21,22]

We aimed to evaluate the interrelatedness of symptoms of depressed mood, disturbed sleep, and sexual problems in a large, population-based cohort (SWAN) and to characterize women exhibiting this symptom triad with respect to demographic, psychosocial, and clinical characteristics. We hypothesized that women with more stressful life events, with lower social support, and in the late perimenopausal stage of the MT would be more likely to have this complex of symptoms than women with fewer stressful life events, greater social support, and pre-, early peri- or post-menopausal stage.

Materials and Methods

Sample

SWAN is a multisite, multiethnic observational cohort study of the MT in women across the United States. SWAN is approved by the institutional review boards at each of its seven participating sites. Written informed consent was obtained at the beginning of assessments. Detailed description

of the SWAN study design has been previously published.[23] Briefly, each site recruited white women and women identifying as belonging to one specified minority (African American in Pittsburgh, Boston, Chicago, and the Detroit area; Japanese in Los Angeles; Chinese in the Oakland, CA region; and Hispanic in Newark, NJ). Eligible women were aged 42–52 years at baseline and had an intact uterus, at least one menstrual period, and no use of reproductive hormones in the previous 3 months. A total of 3302 women were enrolled in the longitudinal cohort.

For these analyses, we used data from a single follow-up assessment (study year 4). Year 4 was chosen for this study because it contained sufficient numbers both pre- and perimenopausal women. Baseline visit data was also used for some sociodemographic data as described below. In order to investigate the sexual function items, women without partnered sexual activity at study-year 4 were excluded from the analysis, leaving 1716 for this analysis.

Measures

Demographic information was acquired at baseline, and menopausal status was assessed at the time of the study visit. Menopausal status classification was based on menstrual bleeding patterns in the previous 12 months and was categorized as premenopausal if menses in the past 3 months with no change in regularity in the previous 12 months; early perimenopausal if menses in the past 3 months with change in regularity; late perimenopausal if no menses within the past 3 months, but some menstrual bleeding within the past 12 months; and postmenopausal if no menses within the past 12 months; hormone therapy use was defined as currently using hormone therapy or hormone use at a previous follow-up visit. Indeterminate status was assigned for women who were pre- or perimenopausal and using hormone therapy. The classifications are, with the exception of "hormone therapy group," similar to those recommended by the World Health Organization.[24] All women were pre- or early perimenopausal at baseline.

Depression was assessed using the Center for Epidemiological Studies Depression Scale (CES-D) with a total score ≥ 16 indicating elevated levels of depressive symptoms.[25,26] Variables assessing sleep problems and sexuality have been previously described.[27–29] Briefly, sleep was assessed by self-report on a three-question scale. Frequency of trouble falling asleep (difficulty with sleep initiation), several nighttime awakenings (difficulty with sleep maintenance), and waking earlier than planned with inability to fall asleep again (early morning awakening) in each of the last 2 weeks was measured as none, < 1 time per week, 1–2 times per week, 3–4 times per week; or ≥ 5 times per week. Consistent with measures used in sleep research, a sleep problem was defined as frequency of ≥ 3 times a week for any one of the three questions.[29]

Sexual function outcomes were assessed by self-report on the 20-item SWAN sexuality questionnaire.[27] The questionnaire was derived from several sources: The Massachusetts Women's' Health Study, The National Health and Social Life Survey, the National Survey of Family Growth, and the Women's Health Initiative Daily Life Form.[27,28] Items of interest for this study were five questions comprising a sexual function subset asking about desire, arousal, satisfaction, orgasm, and vaginal dryness. The remaining items from the questionnaire, assessing sexual practices and

importance of sex, were not evaluated. Women were identified as having a sexual problem if they had a problem in any one of these five sexual function domains. Sexual problems included any vaginal dryness, complete lack of desire, almost never or never feeling aroused, almost never or never having an orgasm, and almost never or never feeling satisfaction with sexual activity.

Social support was assessed using four items from the Medical Outcomes Study Social Support Survey,[30] with a higher score indicating better social support. Stressful life events were scored continuously based on answers to 18 questions [Likert scale 1 (not upsetting) to 5 (very upsetting and still upsetting] with a range of 18 (no stressful life events) to 90 (18 very stressful life events). Overall self-rated health status was asked as a single question with a scale of five possible responses from poor to excellent taken from the Medical Outcomes Study 36-item short-form health survey (SF- 36).[31]

Analysis

Descriptive statistics, means, and standard deviations for continuous characteristics and percentages for discrete characteristics were performed. Spearman correlations were used to assess the pairwise association among depression, sleep, and sexual problems. Ordered logistic regression models were used to estimate the association of the demographic, psychosocial, and clinical characteristics with the number of symptoms present, while logistic regression was used to estimate the association with the presence of the symptom triad; p values ≤ 0.05 were considered statistically significant. Consistent with SWAN analyses, study site was included in all analytic models. We therefore refer to all models as multivariable.

Results

The 1716 women who engaged in partnered sexual activities in study-year 4 were 49.8 years old on average, and 49.7% White, 24.2% African American, 10.1% Japanese, 9.3% Chinese and 6.7% Hispanic. The relatively young mean age in this sample resulted in a relatively low percent of women who were early or late postmenopausal (22.6%). The majority (55%) of women were early or premenopausal, married/cohabitating (90.5%), not using hormone therapy (80.2%), and rated their overall health as excellent or very good (56.9%) (Table 1). Table 2 shows the individual subscale scores in sexual function and sleep questions for the sample. The number of women who had valid responses for each score is indicated; the range for each index as well as the mean and standard deviation for each index is also included. Sixteen and one-half percent had CES-D scores ≥ 16 (indicating high depressive symptom burden), 36.6% had a sleep problem, and 42.2% had a sexual problem. Figure 1 presents a Venn diagram showing how many women experienced each of the three main symptoms (elevated CES-D, sexual problems, or sleep disturbance) and overlap between each of the possible groups. Because a single year early in the SWAN study was analyzed and the women were relatively young, they could be expected to have a lower prevalence of sexual problems than older women. Only 5% of the women ($n = 90$) experienced all three symptoms.

TABLE 1. SAMPLE CHARACTERISTICS ($N = 1716$)

Characteristic	n (%)
Age, years (mean: 49.8 ± 2.6)	1716
Ethnicity	
White	853 (49.7)
African American	415 (24.2)
Chinese	160 (9.3)
Japanese	173 (10.1)
Hispanic	115 (6.7)
Education	
≤ High school	362 (21.3)
> High school	1337 (78.7)
Annual income	
≤ $50,000	487 (30.0)
> $50,000	1138 (70.0)
Marital status	
Married/cohabitating	1548 (90.5)
Single	163 (9.5)
Menopausal status	
Pre-/early menopausal	943 (55.0)
Late perimenopausal	177 (10.3)
Naturally postmenopausal	318 (18.5)
Surgically postmenopausal	71 (4.1)
Undeterminable	206 (12.0)
Hormone therapy	
Yes	340 (19.8)
No	1376 (80.2)
Self-rated health status	
Excellent/very good	965 (56.9)
Good	519 (30.6)
Fair/poor	213 (12.6)

An elevated CES-D score, poor sleep, and sexual problems were weakly correlated in this sample. Spearman's R for two-way correlation for CES-D and sleep was $r = 0.33$, $p < 0.001$; CES-D and sexual problem $r = 0.187$, $p < 0.001$; sexual problem and sleep was $r = 0.095$, $p < 0.001$. Table 3 shows the results of separate analyses for each baseline characteristic adjusted for site for having 1, 2, or 3 symptoms compared with no symptoms (reference group). Because the CES-D includes a question about sleep, analyses were performed inclusive and exclusive of this question, with no significant difference in results. Results are presented using the entire CES-D inclusive of the sleep question. When women with no problems in the outcomes of interest (sleep, depressed mood, sexual function) were compared with women reporting one, two, or three problems (the symptom triad), higher number of stressful life events, less social support, lower household income, late peri- or surgically postmenopausal status, and poorer overall health were associated with an increased likelihood of having more problems (overall $p < 0.001$ for all) (Table 3). ORs presented indicate the odds of moving from one symptom class to the next class for any single unit increase in the variable in question (i.e. for moving from 1 to 2 symptoms). For example, for the continuous value of stressful life events, every one point increase in stress would increase your odds of shifting from, for example, two to three symptoms, by 1.1 (95% confidence interval [95% CI]: 1.1–1.11). No association was noted for hormone therapy use, ethnicity, age, or education.

In multivariable models comparing women with the symptom triad with those without symptoms in all three

TABLE 2. SCALE SCORE RESULTS ($N = 1716$)

Domain	n (%)[a]	Mean (SD)
CES-D (score range: 0–50)	11716	8.5 (8.5)
< 16	1433 (84%)	
≥ 16	283 (16%)	
Sexual function (range: 5–25)	1716	11.4 (3.3)
Vaginal dryness in the past 2 weeks	1715	
Never	1159 (68%)	
1–5 days	367 (21%)	
6–8 days	70 (4%)	
9–13	47 (3%)	
Every day	72 (4%)	
Desire	1716	
Not at all	70 (4%)	
Monthly	609 (35%)	
Weekly	556 (32%)	
More than weekly	443 (26%)	
Daily	38 (2%)	
Climax	1711	
Always	358 (21%)	
Mostly	637 (37%)	
Sometimes	510 (30%)	
Rarely	128 (7%)	
Never	78 (5%)	
Arousal	1712	
Always	466 (27%)	
Mostly	685 (40%)	
Sometimes	445 (26%)	
Rarely	91 (5%)	
Never	25 (2%)	
Satisfaction	1712	
Always	407 (24%)	
Mostly	728 (43%)	
Sometimes	454 (27%)	
Rarely	85 (5%)	
Never	38 (2%)	
Sleep disturbance (range: 3–15)[b]	1716	6.6 (3.2)
Initiation	1716	
Never	954 (56%)	
< 1	302 (18%)	
1–2	235 (14%)	
3–4	133 (8%)	
5+	92 (5%)	
Maintenance	1715	
Never	538 (31%)	
< 1	303 (18%)	
1–2	314 (18%)	
3–4	284 (17%)	
5+	276 (16%)	
Early awakening	1715	
Never	830 (48%)	
< 1	340 (20%)	
1–2	274 (16%)	
3–4	172 (10%)	
5+	99 (6%)	

[a]Percents may not equal 100 due to rounding.
[b]Sleep questions ask frequency in the last 2 weeks of difficulty falling asleep (sleep initiation), waking in the night (sleep maintenance), and early morning awakening.
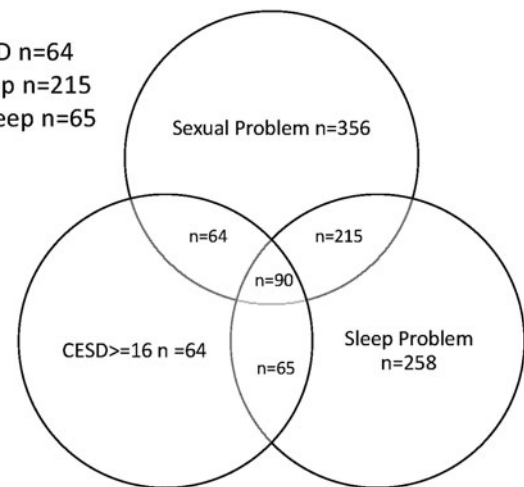CES-D, Center for Epidemiological Studies Depression Scale; SD, standard deviation.

FIG. 1. Participants in each symptom category with over-laps, $N = 1716$. Total with at least 1 problem in the 3 domains, $n = 1112$.

domains (i.e., compared with women having < 3 symptoms), women with the symptom triad were more likely to have lower household incomes, to have less education, to be surgically postmenopausal or late perimenopausal, to rate their general health as fair or poor, to have a higher number of stressful life events, and to have lower social support (Table 4). The presence of the symptom triad did not differ by race/ethnicity or use of hormone therapy, with 19.8% of women reporting hormone use. Additionally, correlations between individual items comprising each of the three indices (total CES-D score, three sleep questions and five sexual function questions) are weakly correlated across index (individual sleep questions are weakly correlated with sexual function, sexual function questions are weakly correlated with CES-D, and CES-D is weakly correlated with sleep items excluding the overlapping question).

Discussion

In this cross-sectional analysis of the SWAN cohort, only 5% of women were affected by the symptom triad of depressed mood, disturbed sleep, and sexual problems. This is lower than we have noted in our clinical population seeking care from menopause specialists, where 20% of women reported this symptom triad. Sleep disturbances, elevated CES-D score, and sexual problems were weakly correlated in this study. Psychosocial stressors including stressful life events, poor social support, and lower household income were associated with having one or more problems in each of the three areas investigated (sleep, depressed mood, and sexual problems). However, only a small percentage of women in this large sample were affected by all three symptoms simultaneously. Women with the symptom triad were more likely to have psychosocial stressors and were also more likely to have poorer overall health status and be surgically postmenopausal or late perimenopausal. There were no significant differences in having the symptom complex based on ethnicity or the use of hormone therapy. Among women with the symptom triad, scores on individual components comprising the indices were not highly correlated. This suggests that, rather than the triad representing different aspects of a

TABLE 3. MULTIVARIABLE RESULTS COMPARING WOMEN WITH NO SYMPTOMS
AND THOSE WITH ONE, TWO, AND ALL THREE SYMPTOMS

	Number of symptoms				Analyses	
Characteristic	0 (n = 604)	1 (n = 678)	2 (n = 344)	3 (n = 90)	OR (95% CI)	p
Age (years), mean ± SD	49.5 ± 2.6	50.0 ± 2.7	50.0 ± 2.6	49.2 ± 2.6	1.0 (1.0, 1.1)	0.07
Ethnicity, n (%)						0.1
White	299 (35.1)	335 (39.3)	179 (21.0)	40 (4.7)	REF	
African American	141 (34.0)	167 (40.2)	80 (19.3)	27 (6.5)	1.0 (0.8, 1.3)	
Chinese	65 (40.6)	61 (38.1)	29 (18.1)	5 (3.1)	0.7 (0.4, 1.1)	
Japanese	65 (37.6)	73 (42.2)	27 (15.6)	8 (4.6)	0.8 (0.5, 1.1)	
Hispanic	34 (29.6)	42 (36.5)	29 (25.2)	10 (8.7)	1.7 (0.9, 3.2)	
Education level, n (%)						0.07
≤High school	113 (31.2)	145 (40.1)	72 (19.9)	32 (8.8)	1.2 (1.0, 1.5)	
>High school	483 (36.1)	526 (39.3)	270 (20.2)	58 (4.3)	REF	
Annual family income, n (%)						0.006
≤$50,000	157 (32.2)	180 (37.0)	106 (21.8)	44 (9.0)	1.3 (1.1, 1.7)	
>$50,000	422 (37.1)	455 (40.0)	220 (19.3)	41 (3.6)	REF	
Marital status, n (%)						0.4
Married/cohabitating	549 (35.5)	614 (39.7)	309 (20.0)	76 (4.9)	0.9 (0.7, 1.2)	
Single	55 (33.7)	60 (36.8)	34 (20.9)	14 (8.6)	REF	
Menopausal status, n (%)						<0.0001
Pre-/early perimenopausal	383 (40.6)	345 (36.6)	176 (18.7)	39 (4.1)	REF	
Late perimenopausal	55 (31.1)	70 (39.5)	38 (21.5)	14 (7.9)	1.5 (1.1, 2.0)	0.006
Naturally postmenopausal	92 (28.9)	141 (44.3)	68 (21.4)	17 (5.3)	1.5 (1.2, 1.8)	0.001
Surgically postmenopausal	17 (23.9)	32 (45.1)	13 (18.3)	9 (12.7)	1.8 (1.2, 2.9)	0.007
Undeterminable	57 (27.7)	89 (43.2)	49 (23.8)	11 (5.3)	1.6 (1.2, 2.1)	<0.001
Hormone therapy, n (%)						0.02
Yes	97 (28.5)	151 (44.4)	74 (21.8)	18 (5.3)	1.3 (1.1, 1.6)	
No	507 (36.8)	527 (38.3)	270 (19.6)	72 (5.2)	REF	
Self-rated health status, n (%)						<0.0001
Excellent/very good	409 (42.4)	379 (39.3)	153 (15.9)	24 (2.5)	REF	
Good	148 (28.5)	221 (42.6)	121 (23.3)	29 (5.6)	1.8 (1.5, 2.2)	<0.0001
Fair/poor	40 (18.8)	68 (31.9)	68 (31.9)	37 (17.4)	4.3 (3.8, 5.7)	<0.0001
Stressful life events, mean ± SD	5.4 ± 5.1	6.7 ± 5.9	8.3 ± 7.9	11.6 ± 8.5	1.1 (1.05, 1.1)	<0.0001
Social support, mean ± SD	13.9 ± 2.5	13.3 ± 2.9	12.7 ± 3.2	10.8 ± 3.8	0.9 (0.85, 0.9)	<0.0001

Each model adjusted for clinical site.
95% CI, 95% confidence interval; OR, odds ratio.

single underlying problem, we have identified a menopausally related symptom triad.

Across the MT, women report myriad symptoms that we have thus far been unable to attribute to a single etiology. It remains unknown whether common symptoms reported by transitioning midlife women derive from a single etiology. Treatment of such symptoms individually is somewhat random and not always efficacious. Furthermore, a group of symptoms may have greater impact on health and well-being than individual symptoms. Thus, increasing interest has been generated in looking at subsets of symptoms that may form distinct clusters[32] and may respond better to treatment designed to address the cluster as a whole rather than individual symptoms.

In an analysis of cohort data from the Herbal Alternatives for Menopause Trial,[33] Reed et al. found that both depression and poor sleep quality were highly associated with diminished libido but had a weaker association with other menopausal symptoms (i.e., hot flushes). The Study of Decisions at Menopause—a mixed-methods cross-cultural study—compared somatic and psychological symptoms and symptom clusters among community women aged 45 to 55 years in the United States (central Massachusetts) and three other countries.[7] Results showed a high prevalence of somatic and psychological symptoms in the four countries. Among the women in the U.S., fatigue clustered with anxiety, depression, and nervousness, and dizziness clustered with anxiety, stress, and nervousness on both quantitative and qualitative analyses. Clusters that appeared in the quantitative analysis—such as the association of gastrointestinal complaints with psychological symptoms were not all consistent with the qualitative analyses. Methods to best examine symptom clusters are still in development, and a mixed methodology may prove to be the most useful. Greenblum et al. investigated the relationship between symptom clusters and quality of life in a cross-sectional study of 112 women aged 45–60 years.[6] They found three symptom clusters: psychological factors (anxiety, irritability, fatigue); weight gain and stress urinary incontinence; and vaginal dryness and sleep disturbance. Of these clusters, the vaginal dryness and sleep disturbance cluster had the greatest impact on quality of life. Vasomotor symptoms were not significantly associated with any other symptoms included in their analysis.

The association of this symptom triad with menopausal stage supports the hypothesis that this complex is related to the MT, with late perimenopausal and surgically postmenopausal women (i.e., hysterectomy with bilateral oophorectomy) at particularly high risk for having this complex.

TABLE 4. MULTIVARIABLE RESULTS COMPARING WOMEN WITH SYMPTOM
TRIAD TO WOMEN WITH FEWER THAN THREE SYMPTOMS

Characteristic	Symptom triad present (n = 90)	Symptom triad absent (n = 1626)	Analysis OR (95% CI)	p
Age (years)				
Mean + SD	49.2 + 2.6	49.8 + 2.6	0.9 (0.8, 1.0)	0.02
Median (min, max)	49 (46, 55)	50 (45, 57)		
Ethnicity, n (%)				0.4
White	40 (4.7)	813 (95.3)	REF	
African American	27 (6.5)	388 (93.5)	1.1 (0.7, 2.0)	
Chinese	5 (3.1)	155 (96.1)	0.5 (0.2, 1.7)	
Japanese	8 (4.6)	165 (95.4)	1.7 (0.5, 5.9)	
Hispanic	10 (8.7)	105 (91.3)	4.7 (0.593, 38.23)	
Education, n (%)				0.004
≤ High school	32 (8.8)	330 (91.2)	2.0 (1.3, 3.2)	
> High school	58 (4.3)	1279 (95.7)	REF	
Annual income, n (%)				0.0001
≤ $50,000	44 (9.0)	443 (91.0)	2.5 (1.6, 4.0)	
> $50,000	41 (3.6)	1097 (96.4)	REF	
Marital status				0.2
Married/cohabitating	76 (90.5)	1472 (95.1)	0.6 (0.4, 1.2)	
Single	14 (8.6)	149 (91.4)		
Menopausal status, n (%)				0.03
Pre-/early menopausal	39 (4.1)	904 (95.9)	REF	
Late perimenopausal	14 (7.9)	163 (92.1)	2.0 (1.1, 3.8)	0.03
Naturally postmenopausal	17 (5.3)	301 (94.7)	1.3 (0.7, 2.3)	0.4
Surgically postmenopausal	9 (12.7)	62 (87.3)	3.1 (1.4, 6.7)	0.005
Undeterminable	11 (5.3)	195 (94.7)	1.4 (0.7, 2.7)	0.4
Hormone therapy, n (%)				0.8
Yes	18 (5.3)	322 (94.7)	1.1 (0.6, 1.8)	
No	72 (5.2)	1304 (94.8)	REF	
Self-rated health status, n (%)				< 0.0001
Excellent/very good	24 (2.5)	941 (97.5)	REF	
Good	29 (5.6)	490 (94.4)	2.2 (1.3, 3.9)	0.005
Fair/poor	37 (17.4)	176 (82.6)	8.3 (4.8, 14.5)	< 0.0001
Stressful life events, mean ± SD	11.6 + 8.5	6.6 + 6.2	1.1 (1.10, 1.11)	< 0.0001
Social support, mean ± SD	10.8 + 3.8	13.4 + 2.8	0.8 (0.8, 0.9)	< 0.0001

Each model adjusted for clinical site.

Surgically menopausal women have been found to be at higher risk of depressive symptoms and anxiety than women undergoing natural menopause, which may be due to the rapid cessation of ovarian sex steroid hormone production, underlying social, psychological, or medical factors related to the need for surgery, or a combination of the two.[34] Findings from the SWAN study have shown a correlation between the perimenopause and increased risk of depressed mood when compared with women who are premenopausal.[35] Women in perimenopause, who have the greatest fluctuations in sex steroid hormones, are particularly likely to report menopausal symptoms including sleep disturbance, psychological symptoms, and vasomotor symptoms.[36]

It can be difficult to tease out separate effects of age versus menopausal status. Given the cross-sectional nature of this study (in the context of our longitudinal cohort), our next step will be to examine these outcomes over time to facilitate the differentiation of aging versus menopausal status. In addition to concerns about differentiating age from menopausal status, whether symptoms are incidental to or caused by the MT is another area of research. O'Bryant et al.[37] carefully reviewed

studies of pre-, peri-, and postmenopausal women to establish baseline rates of common symptoms reported during the MT, concluding that attributing symptoms other than the cessation of menstruation to the MT may be inaccurate due to the overlap between multiple medical and psychological diseases. This study has multiple strengths. The SWAN sample is a large and well-characterized, ethnically diverse sample. Additionally, measures used to assess outcomes are well validated. While this analysis is hypothesis generating, we believe it represents a novel approach to thinking about how symptoms may covary.

Limitations of this study include the cross-sectional design, limiting our ability to examine the timing of symptom onset relative to the MT or to link them to prior history or across the MT. There were small numbers of women who had undergone surgical menopause, limiting the interpretation of findings in that group. This study had limited power to detect risk factors for the symptoms due to small numbers, and results need to be interpreted in light of this. The generally healthy sample may exhibit comparatively lower levels of symptom clusters as compared with a specialized clinic

population, who may most benefit from interventions targeted at multiple symptoms.

The symptom triad of sleep disturbance, depressed mood, and sexual problems occurred in only 5% of women and occurred most often among women with lower socioeconomic status, greater psychosocial distress, and who were surgically menopausal or in late perimenopause. Future studies would benefit from including the timing of symptom onset in relation to each other and menopausal stage, and qualitative data to evaluate symptom experiences. The 5% of women identified in this cross-sectional study can be further evaluated for prior history of depression and to examine their symptom course longitudinally. The symptom triad of disturbed sleep, depressed mood, and sexual problems in the menopausal tradition can be investigated as an outcome for targeted interventions.

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