International Journal of Women's Health

Dovepress

open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

Sleep Health and Anxiety Symptoms in Midlife Women: The Study of Women's Health Across the Nation (SWAN)

Howard M Kravitz[1], Kristine Ruppert[2], Pam Lian[2], Genevieve Neal-Perry[3], Leslie M Swanson[4]

[1]Department of Psychiatry and Behavioral Sciences, and Department of Family and Preventive Medicine, Rush University Medical Center, Chicago, IL, USA; [2]Department of Epidemiology, University of Pittsburgh, Pittsburgh, PA, USA; [3]Department of Obstetrics and Gynecology, University of North Carolina, Chapel Hill, NC, USA; [4]Department of Psychiatry, University of Michigan, Ann Arbor, MI, USA

Correspondence: Howard M Kravitz, Rush University Medical Center, Department of Psychiatry and Behavioral Sciences, Rush West Campus, 2150 West Harrison Street, Room 278, Chicago, IL, 60612, USA, Tel +1 312 942 4161, Email hkravitz@rush.edu

Purpose: To investigate the associations between anxiety symptoms in midlife women and sleep features later in life, the aim is to test the hypothesis that poor sleep, as measured by each of six individual dimensions (4 objective actigraphy measures, 2 self-reports) of sleep health, is associated with higher levels of anxiety symptoms in midlife women.

Participants and Methods: The participants in this longitudinal analysis included women from the SWAN Sleep I Study, a subcohort of the community-dwelling midlife women participating in the core Study of Women's Health Across the Nation (SWAN), which was initiated in 1996. Of the 370 participants enrolled in the Sleep Study, 270 were included in the analytic sample, and 100 who did not meet the inclusion criteria were excluded. Baseline measures of six dimensions of multidimensional sleep health (actigraphy measures: efficiency, duration, mid-sleep timing, regularity; self-report measures: alertness, satisfaction) were obtained between 2003 and 2005, corresponding to SWAN core annual/biennial assessments 5–8. Associations of each dimension with self-reported anxiety symptoms (Generalized Anxiety Disorder – 7-item scale; GAD-7), collected during visits 12 (2009–2011), 13 (2011–2013), and 15 (2015–2017), were examined using mixed models. The GAD-7 outcome was measured both continuously and as a categorical variable due to its skewed distribution.

Results: No statistically significant associations were found between any of the six baseline sleep health dimensions and the GAD-7 score after adjustment for covariates.

Conclusion: The reasons for the lack of support for our hypothesis, despite previous evidence supporting an association between sleep and anxiety, are unclear. There is considerable overlap between anxiety and sleep symptoms, which may complicate the interpretation of our the findings. Thus, the failure to identify associations is likely multifactorial, and more studies with shorter follow-up intervals are warranted to better understand these relationships.

Keywords: generalized anxiety disorder 7-item scale, GAD-7, longitudinal, mixed model analysis, actigraphy, community study, observational study

Introduction

Sleep and mental health problems are commonly reported health concerns.[1,2] Anxiety disorders are the most common mental health problem in the United States, and insufficient sleep is known to have sweeping negative implications for overall health.[3] Moreover, anxiety and sleep symptoms, particularly those of insomnia, overlap (eg, worrying, hyperarousal, feeling tense or stressed) and are inter-connected, closely linked, and highly comorbid.[4–9]

Nevertheless, relative to depression, investigation concerning sleep and anxiety "has played a kind of a stepchild role".[10] Despite the prevalence of anxiety and its impact on health, both physical and emotional, it is an understudied aspect of psychological health. A growing body of work highlights the role of disturbed sleep in anxiety symptoms and disorders. Several studies have found associations between sleep disturbance and anxiety symptoms.[11–13] Recent meta-analytic work

Received: 20 December 2023
Accepted: 23 May 2024
Published: 10 June 2024

has found that both subjective and objective sleep disturbances are evident across anxiety disorders,[14] and underlying brain mechanisms that contribute to an emerging biological framework for elucidating the interrelationship between sleep and anxiety have been reviewed.[15]

Previous studies have found prospective associations between poor sleep and subsequent anxiety in the transition from childhood to young adulthood,[16] as well as across adulthood.[17] A study in China of nearly 4000 people aged 60 and older found that those with poor sleep quality and shorter duration, compared with those with good sleep quality and who regularly slept at least 7 hours, were at higher risk for anxiety.[18]

However, the links between sleep and anxiety among midlife women have not been well delineated. This is an important gap in the literature, as risk for anxiety increases during and after the menopause transition.[19] Further, the transition through menopause is associated with increased difficulty sleeping,[20–22] and up to 60% of post-menopausal women report insomnia symptoms,[23] which may be associated with anxiety symptoms.[24] There is also preliminary evidence to suggest that reduced insomnia symptoms following cognitive behavioral therapy for insomnia are associated with reduced anxiety symptoms in postmenopausal women.[25] Together, these findings suggest that midlife may be an important period for understanding the associations between sleep disturbance and anxiety symptoms in women.

"Sleep health" and its multidimensional nature, and associated health conditions, were well elucidated in Buysse's review of this concept almost a decade ago.[26] In a recent cross-sectional analysis of data from the Study of Women's Health Across the Nation (SWAN), Swanson et al examined cross-sectional associations between two of these dimensions (sleep regularity and timing) and psychological health, including anxiety symptoms.[27] They found that irregular sleep but not sleep timing (sleep midpoint) was associated with higher anxiety levels.[27] Although the literature on multidimensional sleep health since Buysse's review has grown, the longitudinal association of these individual sleep-related components with anxiety symptoms in a cohort of community-dwelling middle-age women has not been addressed.

Theoretical models suggest a bidirectional relationship between anxiety symptoms and difficulty sleeping, with the sleep problem being both a cause and consequence of anxiety.[14] The detrimental effects associated with sleep disturbance exacerbate anxiety symptoms, leading to more sleep problems,[28] and difficulty sleeping is associated with increased anxiety symptoms.[29,30] Whereas prior research on anxiety-associated insomnia suggests that sleep problems are prevalent across anxiety disorders, relatively less research has examined the association between sleep problems and anxiety outcomes.[6] Therefore, we chose to examine only unidirectional associations from sleep to anxiety because this is consistent with our theoretical conceptualization of the detrimental effects of poor sleep health.

In this report, we will examine which dimension(s) of sleep health are associated prospectively with anxiety symptoms. Our hypothesis is that poorer sleep as measured by each of six individual dimensions (4 objective actigraphy measures, 2 self-reports) of sleep health is associated with higher levels of anxiety symptoms in midlife women.

Materials and Methods

Study Design and Participants

SWAN is a multi-ethnic/multi-racial, community-based, cohort study of midlife women's health during the menopausal transition. The core SWAN cohort comprised 3302 women who were enrolled at seven sites, and study assessments were initiated in 1996. Study design and cohort recruitment have been described in detail.[31] Briefly, each site recruited White women and a racial/ethnic minority group. Eligible women were 42–52 years, premenopausal or early perimenopausal, had an intact uterus and at least one ovary, and in the three months preceding enrollment had at least one menstrual period and were not pregnant/lactating or using any sex steroid hormones. At baseline, extensive data on psychosocial and health parameters were collected, and follow-up visits were conducted annually or biennially. Institutional review board approval was obtained at each SWAN study site, and written informed consent was obtained from participants. The following IRBs approved the study at their respective sites: University of Michigan, Massachusetts General Hospital, Rush University Medical Center, University of California Davis/Kaiser and Kaiser Permanente Northern California, University of California Los Angeles, Albert Einstein College of Medicine, and University of Pittsburgh.

The SWAN Sleep Study (Sleep Study I) was a cross-sectional study of sleep patterns conducted at 4 of the 7 study sites (Chicago, southeast Michigan, Pittsburgh, Oakland, CA) between 2003 and 2005 (core SWAN visits 5–8), and enrolled 370 women from the SWAN cohort (White women at all sites, Black women in Chicago, southeast Michigan, and Pittsburgh, and Chinese women in Oakland); at Sleep Study enrollment these women were 48–59 years. Each participating site's institutional review board approved the Sleep Study protocols. All women gave written informed consent and were paid for participating. Further details on recruitment, eligibility, and inclusions/exclusions can be found elsewhere.[24] Briefly, Sleep Study participants did not differ from Core SWAN participants at visit 05 (beginning of Sleep Study enrollment) with regard to age, self-assessed sleep quality, race/ethnicity, self-reported health status, or depressive symptoms, and Sleep Study participants had a slightly higher mean body mass index (BMI). Hot flashes were reported slightly less frequently over the 2-weeks preceding Sleep Study participation by the Sleep Study participants than by Study non-participants ($p < 0.02$).[24]

Procedure and Measures

Participant selection for inclusion in the analytic sample is shown in Figure 1 flow chart. Of the 370 women enrolled in the SWAN Sleep Study, 270 were included in the analytic sample. Table 1 displays the baseline comparisons between the women in the analytic sample (n = 270) and excluded women (n = 100). The analytic sample included a smaller percentage of Black women, due to the larger number who were excluded from the Chicago site due to missing data. Although similar in age at baseline, education, and financial strain, the included sample had a larger percentage with unknown menopausal status (ie, pre-/peri-menopausal women who were receiving menopausal hormone therapy); vasomotor symptoms (VMS) reporting was similar between included and excluded groups. Included women reported higher percentages of upsetting life events and antianxiety but similar antidepressant medication use, and lower sedative/hypnotic medication use; depression and anxiety symptom scale scores were similar. Apnea hypopnea index (AHI) and BMI were also similar between the two groups. The six sleep health dimensions were also similar between the included and excluded groups (Table 2).

Dependent Variable

The outcome measure was the anxiety symptoms score measured at visits 12 (2009–2011), 13 (2011–2013), and 15 (2015–2017) with the 7-item generalized anxiety disorder (GAD-7) scale.[32] Each participant needed at least one GAD-7 score at any of the time points: 86% of the participants had GAD-7 scores at all 3 visits, 10% had only 2, and 4% had only 1. Participants were asked to indicate how much they were bothered by each of these symptoms during the previous

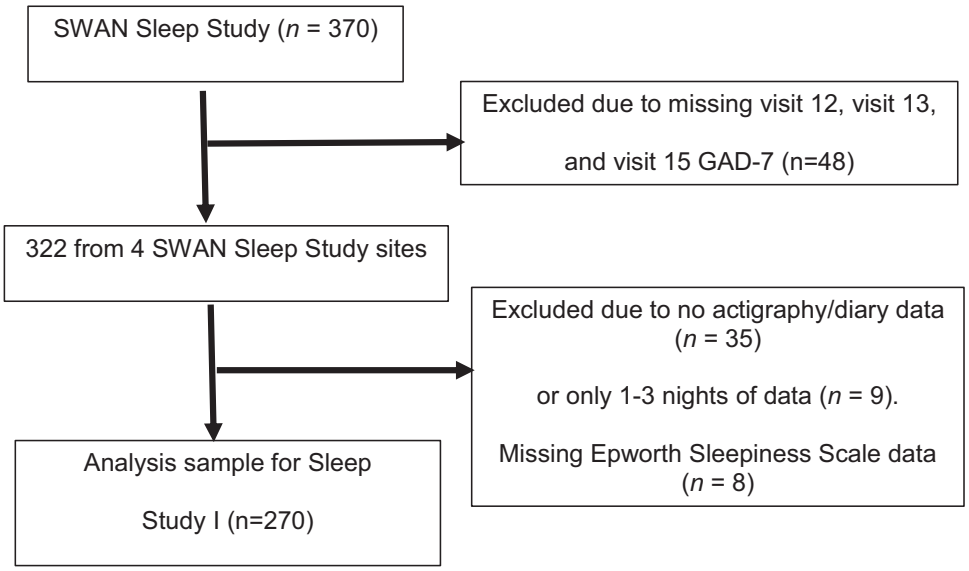

Figure 1 Participant flow chart for Sleep Study I.

Table 1 Comparisons Between Included (n=270) and Excluded (n=100[a]) Participants at SWAN Sleep Study Baseline

	Included in the Sample (n = 270)	Excluded from the Sample (n = 91)[a]
	N (%)	N (%)
Race/ethnicity		
White	130 (48.15)	38 (41.76)
Black	90 (33.33)	44 (48.35)
Chinese	50 (18.52)	9 (9.89)
Study site		
Michigan	57 (21.11)	14 (15.38)
Chicago	41 (15.19)	40 (43.96)
UC Davis	95 (35.19)	15 (16.48)
Pittsburgh	77 (28.52)	22 (24.18)
Menopausal status		
Postmenopausal	31 (11.48)	12 (13.19)
Late perimenopausal	50 (18.52)	20 (21.98)
Early perimenopausal	149 (55.19)	52 (57.14)
Pre perimenopausal	16 (5.93)	5 (5.49)
Unknown	24 (8.89)	2 (2.20)
Menopausal hormone use	29 (10.74)	3 (3.30)
Antidepressant use	85 (31.48)	22 (24.18)
Antianxiety use	27 (10.00)	5 (5.49)
Sedative/hypnotics use	8 (2.96)	4 (4.40)
Education		
High school or less	50 (18.52)	14 (15.38)
More than high school	220 (81.48)	73 (80.22)
Missing	–	4 (4.40)
Financial strain (how hard to pay for basics)		
Very hard/somewhat hard	64 (23.70)	19 (20.88)
Not hard	193 (71.48)	53 (58.24)
Missing	13 (4.81)	19 (20.88)
Vasomotor symptoms		
None	106 (39.26)	35 (38.46)
1–5 days/2 weeks	90 (33.33)	31 (34.07)
6–14 days/2 weeks	71 (26.30)	23 (25.27)
Missing	3 (1.11)	2 (2.20)
Upsetting Life Events		
None	133 (49.26)	46 (50.55)
1	58 (21.48)	19 (20.88)
2+	74 (27.41)	17 (18.68)
Missing	5 (1.85)	9 (9.89)
	Mean (SD), (n missing)	Mean (SD), (n missing)
Age	51.84 (2.16)	51.66 (2.15)
Body mass index	29.52 (7.91), (6)	30.69 (6.06), (7)
CES-D	7.69 (8.11), (6)	7.16 (7.81), (5)
Apnea-hypopnea index	10.82 (16.38), (14)	9.16 (10.92), (6)
STAI-State	15.11 (4.13)	16.08 (5.47)

Notes: [a]Percentages for excluded group based on N = 91; 9 women excluded from table due to missing data for Sleep Health and Generalized Anxiety Disorder-7 (GAD-7) variables.
Abbreviations: CES-D, Center for Epidemiologic Studies Depression Scale; STAI State, State-Trait Anxiety Inventory-State version (10-item version).

Table 2 Sleep Health Dimension Comparisons, Binary and Continuous, for Included (n=270) and Excluded (n=100 [a]) Participants at SWAN Sleep Study Baseline

	Included in the Sample (n = 270)	Excluded from the Sample (n = 91)[a]
	N (%)	N (%)
Binary sleep dimensions:		
Efficiency		
0: ≥ 85%, Optimal	71 (26.30)	13 (14.29)
1: < 85%	199 (73.70)	42 (46.15)
Missing	–	36 (39.56)
Timing		
0: 2 am - 4 am, Optimal	238 (88.15)	50 (54.95)
1: < 2 am or > 4 am	32 (11.85)	5 (5.49)
Missing	-	36 (39.56)
Regularity		
0: < 60 minutes, Optimal	220 (81.48)	41 (45.05)
1: ≥ 60 minutes	50 (18.52)	11 (12.09)
Missing	-	39 (42.86)
Duration		
0: 6–8 hours, Optimal	132 (48.89)	28 (30.77)
1: < 6 hours or > 8 hours	138 (51.11)	27 (29.67)
Missing	-	36 (39.56)
Satisfaction		
0: 2–4, Moderately to extremely rested, Optimal	149 (55.19)	48 (52.75)
1: 0–1, Not rested	121 (44.81)	38 (41.76)
Missing	-	5 (5.49)
Alertness		
0: ≤ 10 (Alert), Optimal	204 (75.56)	59 (64.84)
1: > 10	66 (24.44)	18 (19.78)
Missing	-	14 (15.38)
Continuous sleep dimensions:		
	Mean (SD)	Mean (SD), (n missing)
Efficiency, percent, actigraphy	77.60 (10.36)	76.90 (12.64), (36)
Timing, sleep midpoint (hours [am]), actigraphy	3.36 (0.56)	3.34 (0.57), (36)
Regularity, standard deviation (SD) of midpoint (hours), actigraphy	0.75 (0.33)	0.71 (0.37), (39)
Duration, minutes, actigraphy	357.29 (56.36)	355.15 (65.46), (36)
Satisfaction, restedness on awakening, morning diary	2.04 (0.63)	2.06 (0.60), (5)
Alertness, Epworth Sleepiness Scale	7.75 (4.37)	7.22 (4.11), (14)

Notes: [a]Percentages for excluded group comparisons based on N = 91; 9 women excluded due to missing data for all 6 Sleep Health variables.

2 weeks (0 = not at all, 1 = several days, 2 = more than half of the days, 3 = nearly every day). The GAD-7 scale score ranges from 0 to 21.

Independent Variables

The six sleep health dimensions obtained during the SWAN Sleep Study were sleep efficiency, timing, regularity, duration (measured by actigraphy),[26,33] sleep satisfaction (self-report sleep diary), and alertness (Epworth Sleepiness Scale, ESS).[34,35] The wrist actigraph (Actiwatch-64 [AW-64]; Philips Respironics, MiniMitter, Bend, OR) was worn for an entire menstrual cycle or 35 days, whichever was shorter, to account for night-to-night variability across one cycle in a sample that was largely pre-/peri-menopausal. The data were collected in 1-minute sampling epochs, and sleep-wake variables were calculated using the Actiware version 5.04 software program time above threshold mode at medium sensitivity. Bedtimes and wake-up times recorded in participants' diaries were used to set the parameters for total time in

bed in the actigraphy software. Sleep duration was defined as the total minutes of sleep, and sleep efficiency was defined as sleep duration divided by total minutes of time in bed, multiplied by 100. Timing and regularity were calculated according to Swanson et al.[27] Sleep timing is the midpoint from sleep onset to wake-up. The sleep midpoint is determined by converting sleep onset and wake-up times to decimals and then centering around midnight (negative values indicate times before midnight) and is calculated as sleep onset time + ((wake-up time – sleep onset time)/2). Sleep regularity was defined as the standard deviation (in hours) of the sleep midpoint from sleep onset to wake-up across all nights of actigraphy; higher values indicate more irregularity in sleep timing. Satisfaction was defined as the average "restedness" after a night of sleep as reported first thing in the morning in a daily sleep diary, which was completed concurrently with the actigraph recordings (0–4 scale: 0 = not at all, 1 = a little, 2 = moderately, 3 = quite a bit, 4 = extremely; in analytic models this variable was dichotomized as 0–1 versus 2–4).[33] Alertness was assessed once at the Sleep Study baseline. The ESS includes 8 items rated 0–3, and the total score ranges from 0 to 24, with higher scores indicating greater sleepiness; a score of 10 or less is considered optimal sleep health.

Covariates

The primary covariates were selected based on previously identified associations with anxiety symptoms. Covariates from core SWAN were obtained from the closest available core SWAN assessment preceding the Sleep Study.[24] Baseline non-time varying variables included the 10-item version of the self-report State-Trait Anxiety Inventory–State scale (STAI; each item was scored 1–4 and total scores could range from 10 to 40,[36–38] race/ethnicity, education, study site, age at Sleep Study assessment, and sleep apnea (AHI was assessed with in-home polysomnography on Sleep Study night 1). Core SWAN time-varying variables included financial strain (how hard to pay for basics: very/somewhat versus not hard),[39] the Center for Epidemiologic Studies-Depression (CES-D) scale;[40] Stressful Life Events (SLE, modified from Dohrenwend et al;[41] categorized as 0, 1, 2+ upsetting events); VMS (categorized as none, 1–5 days/2 weeks, 6–14 days/2 weeks); psychotropic medications, including the following binary yes/no drug classes: (1) antidepressants, (2) antianxiety, and (3) sedative/hypnotics; menopausal status;[42] menopausal hormone therapy use (HT); and BMI (calculated as weight (kg)/height $(m)^2$). The longitudinal model also included time since baseline (rather than age at each study visit).

Data Analysis

Baseline demographics (Table 1) and sleep health dimensions (Table 2) of those who were included/excluded from the Sleep Study I cohort were constructed using descriptive statistics. To examine whether any of the sleep baseline sleep dimensions predict GAD-7 scores at visits 12, 13, and 15, mixed model regression was used.[43,44] There were 3 models for each of the six dimensions:

Model 1: GAD-7 score = time, sleep dimension.

Model 2: Model 1 + age at sleep assessment, STAI score, race/ethnicity, and site.

Model 3: Model 2 + medication use (sedative/hypnotics, antianxiety, antidepressant), VMS categories, menopausal status, HT, AHI, CES-D, BMI, education, financial strain, and SLE.

Secondary Analyses

Additional sets of analyses were conducted using Sleep Study data collected from women (n=281) who also participated in a second wave of assessments in 2006–2008, corresponding to core SWAN visits 8–10 (Table 3, Sleep Study II). The time line for Sleep Study I and II relative to core SWAN calendar years and follow-up visits is shown in Figure 2. This time point was used as the analytic baseline instead of the initial sleep data point to determine whether sleep measurements that were more proximal to the three GAD-7 assessments (visits 12, 13, and 15; 2009–2017) would show the hypothesized associations (Table 3, Sleep II with STAI). Also, baseline STAI was significantly correlated with the GAD-7 scores (initial Sleep Study: r = 0.31–0.38; follow-up Sleep Study: r = 0.36–0.40; all P values <0.0001) for the Sleep I and Sleep II analytic samples, so we reanalyzed the data without including the baseline STAI as a covariate (Table 3, without STAI). Due to the non-normal distribution of the GAD-7 scores (all skewness values were greater than 1, indicating a highly skewed distribution) the data were reanalyzed using a GAD-7 cut-point of ≤4 (low) versus >4 (high). This cut-point was chosen because GAD-7 scores ranging from 0 to 4 indicate a minimal level of anxiety

Table 3 Parameter Estimates (Standard Error) for Sleep Health Dimension Associations with Generalized Anxiety Disorder – 7-Item Scale (GAD-7) Score, with and without State-Trait Anxiety Inventory – State Version (STAI) Score as Baseline Covariate

Sleep Health Dimension	Sleep I		Sleep II	
	With STAI	Without STAI	With STAI	Without STAI
Sleep Duration				
Model 1	0.001 (0.003)	0.001 (0.003)	-0.0005 (0.0027)	−0.0005 (0.0027)
Model 2	0.001 (0.003)	0.001 (0.003)	−0.0006 (0.0026)	−9.16E-6 (0.0029)
Model 3	< 0.001 (0.002)	<0.001 (0.002)	−0.001(0.002)	−0.001 (0.002)
Sleep Efficiency				
Model 1	−0.017 (0.015)	−0.017 (0.015)	−0.031(0.015)*	−0.031 (0.015)*
Model 2	−0.010 (0.016)	−0.015 (0.018)	−0.028 (0.014)	−0.032 (0.016)
Model 3	0.012 (0.013)	0.011 (0.013)	−0.005 (0.012)	−0.005 (0.012)
Sleep Timing (sleep time midpoint)				
Model 1	0.349 (0.289)	0.349 (0.289)	0.287 (0.159)	0.287 (0.159)
Model 2	0.123 (0.271)	0.322 (0.299)	0.175 (0.144)	0.280 (0.162)
Model 3	−0.258 (0.205)	−0.209 (0.208)	−0.120 (0.114)	−0.098 (0.116)
Sleep regularity				
Model 1	0.865 (0.481)	0.865 (0.481)	0.392 (0.188)*	0.392 (0.188)*
Model 2	1.037 (0.451)*	0.822 (0.501)	0.244 (0.174)	0.398 (0.196)*
Model 3	0.615 (0.396)	0.549 (0.403)	0.110 (0.135)	0.134 (0.137)
Sleep satisfaction				
Model 1	−1.015 (0.245)***	−1.015 (0.245)***	−1.134 (0.230)***	−1.134 (0.230)***
Model 2	−0.431 (0.245)	−1.006 (0.249)***	−0.577 (0.223)*	−1.095 (0.234)***
Model 3	−0.021 (0.188)	−0.155 (0.185)	−0.151 (0.176)	−0.268 (0.174)
Alertness (Epworth Sleepiness Scale score)				
Model 1	0.084 (0.036)*	0.084 (0.036)*	0.110 (0.036)**	0.110 (0.036)**
Model 2	0.025 (0.035)	0.084 (0.037)*	0.038 (0.034)	0.115 (0.037)**
Model 3	0.010 (0.026)	0.025 (0.026)	0.029 (0.027)	0.047 (0.026)

Notes: ***p<0.001, **p<0.01, *p<0.05 Sleep Health dimension estimates. Covariates for Model 1: time. Covariates for Model 2: model 1 + age at sleep assessment, State-Trait Anxiety Inventory – State (STAI) score, race/ethnicity, site. Covariates for Model 3: model 2 + medication use (sedative/hypnotics, antianxiety, antidepressants), vasomotor symptoms, menopausal status, hormone therapy use, Apnea-Hypopnea Index, Center for Epidemiologic Studies-Depression score, body mass index, stressful life events, education, financial strain.
Abbreviation: STAI State, State-Trait Anxiety Inventory-State version (10-item version).

severity.[32] Again, mixed model regression was used. The same models using both the continuous and dichotomous outcomes as mentioned above (without STAI) were examined. Parameter estimates and standard errors (SE) are presented for all models. Finally, we removed participants who used antianxiety, sedative/hypnotic, and antidepressant medications to see if this changed any of the interpretations in the models.

All analyses were conducted using SAS 9.3 (SAS, Cary, NC), and two-tailed P values <0.05 were considered statistically significant.

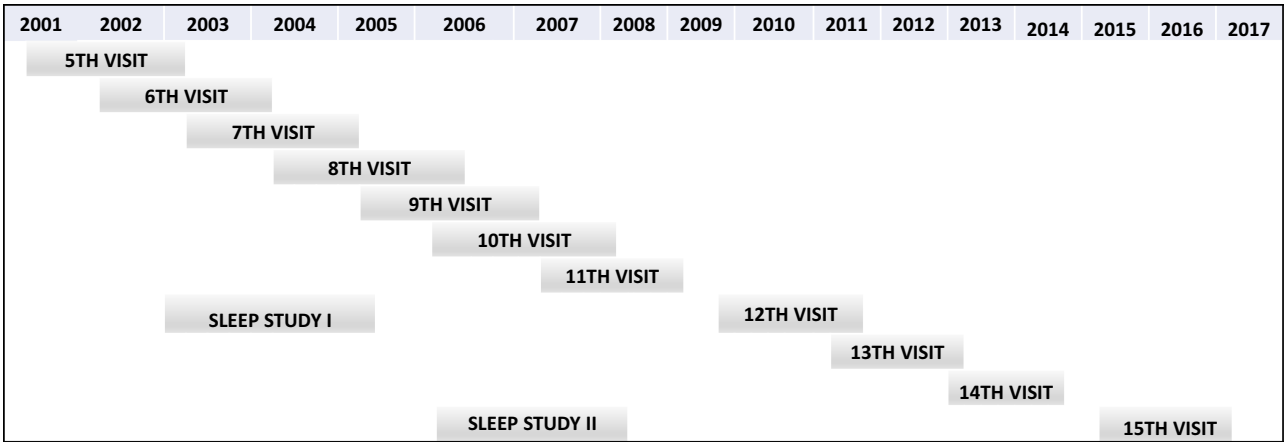

Figure 2 Time line for SWAN visits and Sleep Study I and II.
Notes: SWAN Sleep Study I was conducted between 2003 and 2005, corresponding to core SWAN visits 5–8. Sleep Study II was conducted between 2006 and 2008, corresponding to core SWAN visits 8–10. The three Generalized Anxiety Disorder (GAD-7) scale assessments were administered at core SWAN visits 12 (2009–2011), 13 (2011–2013), and 15 (2015–2017).

Results

Baseline Characteristics

The mean age of the Sleep Study I sample was 51.8 ± 2.2 years. Women attended an average of 13 study visits (range = 2–15 visits). Table 1 displays baseline characteristics for the analytic sample. Racial/ethnic distribution was almost 50% White by design. Most women had more than a high school education and did not have difficulty paying for basics. At Sleep Study I baseline, 61% were early peri- or premenopausal, and 9% were unknown due to HT use prior to menopause, and about 60% were experiencing VMS. Almost half of the women reported no upsetting life events. Antidepressant medication use was reported by 31%, antianxiety medication use by 10%, sedative/hypnotic medication use by 3%. Baseline mean (SD) CES-D and STAI scores were 7.7 (8.1) and 15.1 (4.1), respectively. GAD-7 assessments were not obtained until SWAN follow-up 12 and were completed by 265 (98%) women at visit 12, 259 (96%) at visit 13, and 238 (88%) at visit 15.

Table 2 shows the baseline actigraphy, sleep satisfaction (restedness) and ESS data that were collected for the 270 women for a mean (SD) of 27.27 (7.91) days and a median (interquartile range, the difference between upper quartile and lower quartile) of 30.00 (12.00) days for each woman. Mean (SD) values for the sleep health dimensions were as follows:[33,45] mean sleep duration was just under 6 hours (optimal: 6–8 hours) and sleep efficiency was 78% (optimal: greater than or equal to 85%). The mean sleep midpoint was 3.36 (3:22 am; optimal: 2–4 am), and the regularity was 0.75 hours (ie, 45 minutes) (optimal: less than 60 minutes). Average sleep satisfaction score was 2.0 (moderately; optimal: at least moderately), and ESS was 7.75 (optimal: 10 or less).

Primary Analyses

Table 3 (Sleep Study I, with STAI) shows the results of the mixed model analyses for each of the 6 sleep health dimensions. The final adjusted analyses (model 3) showed non-statistically significant results for all six dimensions when STAI, the baseline anxiety covariate, was included in these models. Removing STAI from the models did not substantively change the outcomes (Table 3, Sleep Study I, without STAI).

Secondary Analyses

Using a GAD-7 cut-point of 4, only 24%, 20%, and 16% of women reported mild or more severe anxiety (GAD-7 scores ≥5) at visits 12, 13, and 15, respectively. All of the secondary analyses using Sleep Study II data yielded non-significant results, whether or not the baseline STAI score was included as a covariate. Similarly, for the GAD-7 cut-point analyses neither the final models nor their interpretations changed substantially from the continuous score models (data not

presented). After removing the participants who were using antianxiety, sedative/hypnotic, and antidepressant medications, there were no major changes in any interpretations of the models (data not presented).

Discussion

In this longitudinal analysis of sleep health dimensions and anxiety symptom self-reports, our findings were consistent in showing no significant associations. Given the considerable overlap between anxiety and sleep symptoms, and their interconnectedness and highly comorbid nature, we wondered how this could be?

Our analyses revealed no evidence to support the primary (or secondary) hypothesis that any of the six sleep health dimensions are associated longitudinally with anxiety symptoms. Note that the GAD-7 does not include a sleep item so this would not confound the measurement of the sleep health dimension exposures with the anxiety outcome. Failure to find associations is likely to be multifactorial. First, this may be due to the interval between the actigraphy recordings and self-report measures and the anxiety outcome. Our outcome measure, the GAD-7, was not introduced into SWAN data collection until the twelfth follow-up assessment. Thus, Sleep I sleep measures were obtained, on average, 5.4 (SD 0.7) years, 6.4 (SD 0.7) years, and 8.4 (SD 0.7) years before visit 12, 13, and 15 GAD-7 scale data collections, respectively (for Sleep II, the intervals were 2.1 (SD 0.2), 3.1 (0.2), and 5.0 (0.2) years between baseline sleep measures and GAD-7 scores). A second possibility is that the lack of a relationship between anxiety symptoms and sleep variables could be related to the low levels of anxiety symptoms, and thus low base rates of clinically significant anxiety, in our community sample of middle-aged women, which was not selected for the presence of anxiety or other mental health concerns. The mean (SD) STAI State score at Sleep I baseline was 15.11 (4.13) (Sleep II baseline mean 14.95 (4.72)) in our sample of middle-aged women, consistent with the mean score reported by Bergua et al[38] in population-based cohorts of French older adults (15.6, SD 6.5). Moreover, using Spitzer et al's[32] cut-points, only 13%, 10%, and 8% of women reported mild or more severe anxiety (GAD-7 scores ≥5) at visits 12, 13, and 15, respectively. Perhaps, the findings may have differed if the range of symptoms of anxiety was broader. Third, some participants were taking medications to treat their anxiety or other mental health conditions, but because SWAN is an observational study, we had no control over their use. Although reported use of antianxiety and sedative/hypnotic medication was relatively low, more than 30% of the women reported taking antidepressants, which are known to affect both sleep and anxiety; this may have both confounded and suppressed the association. However, after removing participants who used antianxiety, sedative/hypnotic, and antidepressant medications, there were no major changes in interpretation. Fourth, anxiety is also a symptom of and strongly associated with VMS, particularly hot flashes.[46] Although a strength of this study is the adjustment for VMS, in our analyses VMS were not significantly associated with GAD-7 scores either; however, it should be noted that these symptoms too can be alleviated with antidepressant use.[47] Moreover, GAD-7 scores were significantly associated with sleep regularity, daytime alertness and satisfaction with sleep in unadjusted and minimally adjusted models, but these associations did not survive adjustment for covariates. It is possible that these specific sleep - anxiety pathways are closely influenced by covariates (vasomotor symptoms, depression symptoms, stressful life events, financial strain, etc.). Fifth, in regard to whether socioeconomic status could have affected our observations, neither education nor financial strain made any notable difference in the sleep health – anxiety final models. We should mention that the Sleep Study cohort was relatively well educated and financially stable.[48] Although the time frame of the study (2003–2017) could limit the current relevance, the methods and measurements are still applicable. This issue can be explored as more recent data become available in this ongoing cohort study. We also suggest that other investigators examine these associations in cohorts with shorter follow-up intervals, as the length of follow-up and follow-up intervals could also explain the lack of associations.

Strengths of the SWAN cohort and our longitudinal analyses include a long follow-up in a large community sample of women unselected for anxiety or depressive symptoms, which enhances the generalizability of our sample and decreases the risk of selection bias. Objective sleep measures were obtained from actigraph recordings over the period of one menstrual cycle to account for night-to-night variability associated with hormonal fluctuations in menstruating women and was conducted in a large sample of women from three racial/ethnic groups. Our sample included only 50 Chinese women so we compared only Black and White women and in this exploratory analysis found no significant racial/ethnic differences in the final models. Although the GAD-7 was designed as a screening tool for generalized anxiety, it also

performs well as a screening tool for three other common anxiety disorders – panic disorder, social anxiety disorder, and posttraumatic stress disorder.[49] The large sample and number of observations provided sufficient statistical power to control for the effects of a number of covariates. Mixed model analyses are generally valid for handling missing at random data and are commonly used for modeling repeated outcome measures such as those in our report.

Several limitations of these data should be considered. In particular, among the excluded women, their missing observations may not meet the missing at random criterion. Also, in regard to generalizability, our results may be limited to women who are relatively healthy. Actually, the included women reported higher percentages of upsetting life events and would be expected to report higher levels of anxiety. Use of a self-report measure of anxiety symptoms may be considered a limitation because it carries a risk of information bias, but it is a clinical criterion standard for clinical management of anxiety symptoms, particularly generalized anxiety disorder. Women were not screened for anxiety disorders. Although SWAN has collected a substantial number of variables related to anxiety, it was not designed to assess all potential correlates of anxiety symptoms in this community sample designed to study sleep patterns and symptoms of women during the menopausal transition. Moreover, we have no information on the previous number, duration, type or severity of personal and family history of anxiety disorders. Nevertheless, the US Preventive Services Task Force has recently recommended screening for anxiety disorders in adults and included the GAD scale among available screening tools that may be used.[50] Clinicians should consider the likelihood that women who are less healthy, exposed to greater stress, etc., when premenopausal and early perimenopausal may be at greater risk for developing anxiety symptoms when they are postmenopausal and should be assessed for both anxiety and depression, as these two symptoms are commonly comorbid.

Conclusion

None of the six dimensions of multidimensional sleep health were associated with anxiety symptoms as measured by the GAD-7 in this longitudinal analysis. It is unclear why we did not prove our hypothesis given previous studies suggest an association between sleep and anxiety. Nevertheless, considering the prevalence of both of these health conditions among midlife women, clinicians encountering women with sleep problems should consider screening for the presence of anxiety as well as other conditions associated with this ubiquitous symptom, as well as the presence of depression.

Abbreviations

SWAN, Study of Women's Health Across the Nation; AW-64, Actiwatch-64; VMS, vasomotor symptoms; AHI, apnea hypopnea index; BMI, body mass index; GAD-7, 7-item generalized anxiety disorder scale; ESS, Epworth Sleepiness Scale; CES-D, Center for Epidemiologic Studies-Depression scale; SLE, Stressful Life Events; HT, menopausal hormone therapy; STAI, State-Trait Anxiety Inventory–State scale; SE, standard error; SD, standard deviation.

Acknowledgments

The Study of Women's Health Across the Nation (SWAN) has grant support from the National Institutes of Health (NIH), DHHS, through the National Institute on Aging (NIA), the National Institute of Nursing Research (NINR) and the NIH Office of Research on Women's Health (ORWH) (Grants U01NR004061; U01AG012505, U01AG012535, U01AG012531, U01AG012539, U01AG012546, U01AG012553, U01AG012554, U01AG012495, and U19AG063720). Funding for the Study of Women's Health Across the Nation Sleep Study was provided by the National Institute on Aging (grants R01AG019360, R01AG019361, R01AG019362, and R01AG019363). Sleep data were processed with the support of grant RR024153. The content of this article is solely the responsibility of the authors and does not necessarily represent the official views of the NIA, NINR, ORWH or the NIH.

Clinical Centers: University of Michigan, Ann Arbor – Carrie Karvonen-Gutierrez, PI 2021–present, Siobán Harlow, PI 2011–2021, MaryFran Sowers, PI 1994–2011; Massachusetts General Hospital, Boston, MA – Sherri-Ann Burnett-Bowie, PI 2020–Present; Joel Finkelstein, PI 1999–2020; Robert Neer, PI 1994–1999; Rush University, Rush University Medical Center, Chicago, IL – Imke Janssen, PI 2020–Present; Howard Kravitz, PI 2009–2020; Lynda Powell, PI 1994–2009; University of California, Davis/Kaiser – Elaine Waetjen and Monique Hedderson, PIs 2020–Present; Ellen Gold, PI 1994–2020; University of California, Los Angeles – Arun Karlamangla, PI 2020 – Present; Gail Greendale, PI 1994–

2020; Albert Einstein College of Medicine, Bronx, NY – Carol Derby, PI 2011–present, Rachel Wildman, PI 2010–2011; Nanette Santoro, PI 2004–2010; University of Medicine and Dentistry – New Jersey Medical School, Newark – Gerson Weiss, PI 1994–2004; and the University of Pittsburgh, Pittsburgh, PA – Rebecca Thurston, PI 2020–Present; Karen Matthews, PI 1994–2020.

NIH Program Office: National Institute on Aging, Bethesda, MD – Rosaly Correa-de-Araujo 2020–present; Chhanda Dutta 2016–present; Winifred Rossi 2012–2016; Sherry Sherman 1994–2012; Marcia Ory 1994–2001; National Institute of Nursing Research, Bethesda, MD – Program Officers.

Central Laboratory: University of Michigan, Ann Arbor – Daniel McConnell (Central Ligand Assay Satellite Services).

Coordinating Center: University of Pittsburgh, Pittsburgh, PA – Maria Mori Brooks, PI 2012–present; Kim Sutton-Tyrrell, PI 2001–2012; New England Research Institutes, Watertown, MA – Sonja McKinlay, PI 1995–2001.

Steering Committee: Susan Johnson, Current Chair; Chris Gallagher, Former Chair.

We thank the study staff at each site and all the women who participated in SWAN.

Disclosure

Dr. Kravitz reported grants from the National Institutes of Health (NIH). Drs. Ruppert and Lian declared no conflicts of interest or financial involvement (including employment, fees, share ownership) or affiliation with any organization whose financial interests may be affected by material in the manuscript, or any other conflicts of interest which might potentially bias it. Dr. Neal-Perry reported grants from NIH & Merck, scientific advisor for Astellas and Natera. Dr. Swanson reported grants from the National Institutes of Health (NIH) during the conduct of the study. The authors report no other conflicts of interest in this work.

References

1. COVID-19 Mental Disorders Collaborators. Global prevalence and burden of depressive and anxiety disorders in 204 countries and territories in 2020 due to the COVID-19 pandemic. *Lancet*. 2021;398(10312):1700–1712.
2. Seng EK, Cervoni C, Lawson JL, et al. The burden of sleep problems: a pilot observational study in an ethnically diverse urban primary care setting. *J Prim Care Community Health*. 2016;7(4):276–280.
3. Suni E, Dimitriu A. Anxiety and sleep. Sleep Foundation. Available from: https://www.sleepfoundation.org/mental-health/anxiety-and-sleep. Accessed June 19, 2023.
4. Babson KA, Feldner MT. Temporal relations between sleep problems and both traumatic event exposure and PTSD: a critical review of the empirical literature. *J Anxiety Disord*. 2010;24(1):1–15.
5. Cox RC, Olatunji BO. A systematic review of sleep disturbance in anxiety and related disorders. *J Anxiety Disord*. 2016;37:104–129.
6. Kaczkurkin AN, Tyler J, Turk-Karan E, Belli E, Asnaanic A. The association between insomnia and anxiety symptoms in a naturalistic anxiety treatment setting. *Behav Sleep Med*. 2021;19(1):110–125.
7. Ramsawh HJ, Stein MB, Belik SL, Jacobi F, Sareen J. Relationship of anxiety disorders, sleep quality, and functional impairment in a community sample. *J Psychiatr Res*. 2009;43(10):926–933.
8. Roth T, Jaeger S, Jin R, Kalsekar A, Stang PE, Kessler RC. Sleep problems, comorbid mental disorders, and role functioning in the National Comorbidity Survey Replication. *Biol Psychiatry*. 2006;60(12):1364–1371.
9. Soehner AM, Harvey AG. Prevalence and functional consequences of severe insomnia symptoms in mood and anxiety disorders: results from a nationally representative sample. *Sleep*. 2012;35(10):1367–1375.
10. Riemann D. Sleep, insomnia and anxiety – bidirectional mechanisms and chances for intervention. *Sleep Med Rev*. 2022;61:101584.
11. Cox RC, Ebesutani C, Olatunji BO. Linking sleep disturbance and maladaptive repetitive thought: the role of executive function. *Cognit Ther Res*. 2016;40(1):107–117.
12. Nota JA, Coles ME. Shorter sleep duration and longer sleep onset latency are related to difficulty disengaging attention from negative emotional images in individuals with elevated transdiagnostic repetitive negative thinking. *J Behav Ther Exp Psychiatry*. 2018;58:114–122.
13. Timpano KR, Carbonella JY, Bernert RA, Schmidt NB. Obsessive compulsive symptoms and sleep difficulties: exploring the unique relationship between insomnia and obsessions. *J Psychiatr Res*. 2014;57:101–107.
14. Cox RC, Olatunji BO. Sleep in the anxiety-related disorders: a meta-analysis of subjective and objective research. *Sleep Med Rev*. 2020;51:101282.
15. Chellappa SL, Aeschbach D. Sleep and anxiety: from mechanisms to interventions. *Sleep Med Rev*. 2022;61:101583.
16. Gregory AM, Caspi A, Eley TC, Moffitt TE, Oconnor TG, Poulton R. Prospective longitudinal associations between persistent sleep problems in childhood and anxiety and depression disorders in adulthood. *J Abnorm Child Psychol*. 2005;33(2):157–163.
17. Neckelmann D, Mykletun A, Dahl AA. Chronic insomnia as a risk factor for developing anxiety and depression. *Sleep*. 2007;30(7):873–880.
18. Shi WY, Guo MH, Du P, et al. Association of sleep with anxiety in the elderly aged 60 years and older in China. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2020;41(1):13–19.
19. Bromberger JT, Kravitz HM, Chang Y, et al. Does risk for anxiety increase during the menopausal transition? Study of Women's Health Across the Nation (SWAN). *Menopause*. 2013;20(5):488–495.

20. Kravitz HM, Zhao X, Bromberger JT, et al. Sleep disturbance during the menopausal transition in a multi-ethnic community sample of women. *Sleep*. 2008;31(7):979–990.
21. Kravitz HM, Janssen I, Bromberger JT, et al. Sleep trajectories before and after the final menstrual period in the Study of Women's Health Across the Nation (SWAN). *Curr Sleep Med Rep*. 2017;3(3):235–250.
22. Kravitz HM, Matthews KA, Joffe H, et al. Trajectory analysis of sleep maintenance problems in midlife women before and after surgical menopause: the Study of Women's Health Across the Nation (SWAN). *Menopause*. 2020;27(3):278–288.
23. National Institutes of Health. National Institutes of Health state of the science conference statement: manifestations and management of chronic insomnia in adults, June 13–15, 2005. *Sleep*. 2005;28(9):1049–1057.
24. Kravitz HM, Avery E, Sowers MF, et al. Relationships between menopausal and mood symptoms and EEG sleep measures in a multi-ethnic sample of middle-aged women: the SWAN Sleep Study. *Sleep*. 2011;34(9):1221–1232.
25. Kalmbach DA, Cheng P, Arnedt JT, et al. Treating insomnia improves depression, maladaptive thinking, and hyperarousal in postmenopausal women: comparing cognitive-behavioral therapy for insomnia (CBTI), sleep restriction therapy, and sleep hygiene education. *Sleep Med*. 2019;55:124–134.
26. Buysse DJ. Sleep Health: can We Define It? Does It Matter? *Sleep*. 2014;37(1):9–17.
27. Swanson LM, Hood MM, Hall MH, et al. Sleep timing, sleep regularity, and psychological health in early late life women: findings from the Study of Women's Health Across the Nation (SWAN). *Sleep Health*. 2023;9(2):203–210.
28. Harvey AG. A cognitive model of insomnia. *Behav Res Ther*. 2002;40:869–893.
29. LeBlanc M, Beaulieu-Bonneau S, Mérette C, Savard J, Ivers H, Morin CM. Psychological and health-related quality of life factors associated with insomnia in a population-based sample. *J Psychosom Res*. 2007;63(2):157–166.
30. Belleville G, Cousineau H, Levrier K, St-Pierre-Delorme ME. Meta-analytic review of the impact of cognitive-behavior therapy for insomnia on concomitant anxiety. *Clin Psychol Rev*. 2011;31(4):638–652.
31. Sowers MF, Crawford SL, Sternfeld B, et al. SWAN: a multicenter, multiethnic, community-based cohort study of women and the menopausal transition. In: Lobo RA, Kelsey J, Marcus R, editors. *Menopause: Biology and Pathobiology*. San Diego, CA: Academic Press; 2000:175–188.
32. Spitzer RL, Kroenke K, Williams JBW, Löwe B. A brief measure for assessing generalized anxiety disorder: the GAD-7. *Arch Intern Med*. 2006;166(10):1092–1097.
33. Bowman MA, Kline CE, Buysse DJ, et al. Longitudinal association between depressive symptoms and multidimensional sleep health: the Study of Women's Health Across the Nation Sleep Study. *Ann Behav Med*. 2021;55(7):641–652.
34. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. *Sleep*. 1991;14(6):540–545.
35. Johns MW. Sleepiness in different situations measured by the Epworth Sleepiness Scale. *Sleep*. 1994;17(8):703–710.
36. Spielberger CD. *Preliminary Manual for the State-Trait Personality Inventory (STPI)*. Tampa, FL: University of South Tampa; 1979.
37. Spielberger CD, Reheiser EC. Measuring anxiety, anger, depression, and curiosity as emotional states and personality traits with the STAI, STAXI, and STPI. In: Hersen M, Hilsenroth MJ, Segal DL, editors. *Comprehensive Handbook of Psychological Assessment, Volume 2: Personality Assessment*. Hoboken, NJ: John Wiley & Sons, Inc.; 2003:70–86.
38. Bergua V, Meillon C, Potvin O, et al. Short STAI-Y anxiety scales: validation and normative data for elderly subjects. *Aging Mental Health*. 2016;20(9):987–995.
39. Kahn JR, Pearlin LI. Financial strain over the life course and health among older adults. *J Health Soc Behav*. 2006;47:17–31.
40. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. *Appl Psychol Meas*. 1977;1:385–401.
41. Dohrenwend BS, Krasnoff L, Askenasy AR, Dohrenwend BP. Exemplification of a method for scaling life events: the PERI life events scale. *J Health Soc Behav*. 1978;19:205–229.
42. WHO Scientific Group on Research on the Menopause in the 1990s. Research on the menopause in the 1990s: report of a WHO scientific group. *World Health Organ Tech Rep Ser*. 1996;866:1–107.
43. Brown H, Prescott R. *Applied Mixed Models in Medicine, 2nd Ed*. West Sussex: John Wiley & Sons Ltd; 2006.
44. Littell RC, Milliken GA, Stroup WW, Wolfinger RD, Schabenberger O. *SAS for Mixed Models*. *2nd* ed. Cary, NC: SAS Institute Inc; 2006.
45. Furihata R, Hall MH, Stone KL, et al. An aggregate measure of sleep health is associated with prevalent and incident clinically significant depression symptoms among community-dwelling older women. *Sleep*. 2017;40(3):zsw075.
46. Freeman EW, Sammel MD, Lin H, Gracia CR, Kapoor S, Ferdousi T. The role of anxiety and hormonal changes in menopausal hot flashes. *Menopause*. 2005;12(3):258–266.
47. Juang K-D, Wang S-J, Lu S-R, Lee S-J, Fuh J-L. Hot flashes are associated with psychological symptoms of anxiety and depression in peri- and post- but not premenopausal women. *Maturitas*. 2005;52:119–126.
48. Hall MH, Matthews KA, Kravitz HM, et al. Race and financial strain are independent correlates of sleep in midlife women: the Swan Sleep Study. *Sleep*. 2009;32(1):73–82.
49. Kroenke K, Spitzer RL, Williams JB, Monahan PO, Löwe B. Anxiety disorders in primary care: prevalence, impairment, comorbidity, and detection. *Ann Intern Med*. 2007;146(5):317–325.
50. US Preventive Services Task Force. Screening for anxiety disorders in adults: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2023;329(24):2163–2170.