Objective and Subjective Sleep Quality in Premenopausal, Perimenopausal, and Postmenopausal Women in the Wisconsin Sleep Cohort Study

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Study Objective: Assess objectively measured sleep quality in premenopausal, perimenopausal, and postmenopausal women.
Design: Observational epidemiology study.
Setting: Community-based.
Participants: Probability sample of 589 premenopausal, perimenopausal, and postmenopausal women recruited from state employee records.
Interventions: None.
Measurements and Results: Menopausal status was determined by menstrual history, surgical history, and use of hormone replacement therapy. Sleep quality was objectively measured by full in-laboratory polysomnography and by self-reported sleep problems. Linear and logistic regression were used to estimate associations adjusted for potential confounding factors.
Objective: Sleep quality was not worse in perimenopausal or postmenopausal women, compared with premenopausal women. To the contrary, postmenopausal woman had more deep sleep (16% vs 13% stages 3/4, P<0.001) and significantly longer total sleep time (388 minutes vs 374 minutes, P=0.05). Menopausal status was moderately related to self-reported dissatisfaction with sleep but was not consistently associated with symptoms of insomnia or sleepiness.
Conclusions: Menopause is not associated with diminished sleep quality measured by polysomnography. Although perimenopausal and postmenopausal women, relative to premenopausal women, were less satisfied with their sleep, menopause was not a strong predictor of specific sleep-disorder symptoms. Symptoms and signs of sleep abnormalities in midlife women should not be attributed primarily to menopause before ruling out underlying sleep disorders.
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INTRODUCTION

THE PREVALENCE OF SLEEP PROBLEMS IN WOMEN APPEARS TO INCREASE MOST DRAMATICALLY DURING MIDDLE AGE, AND THIS INCREASE IS WIDELY ATTRIBUTED TO MENOPAUSE. However, results from studies of menopause and sleep, including population-based surveys of general menopausal symptoms,[1-7] cross-sectional studies with objective indicators of disturbed sleep,[8,9] and hormone-replacement trials,[10-14] are inconsistent.

Most, but not all, findings from the population-based surveys provide some evidence for a link between menopause and self-reported sleep problems. In a survey of 47-year-old British women, Kuh et al[1] reported statistically significant associations of menopause and sleep problems: odds ratios for *trouble sleeping* were 3.4 for postmenopausal versus premenopausal women, and 1.5 for perimenopausal versus premenopausal women. Owen and Mathews[5] investigated several parameters of self-reported insomnia in a longitudinal study of women transitioning through menopause. At a 48-month follow-up, women who had become menopausal were significantly more likely to report incident sleep problems. Sleep quality and menopause was investigated in the multicenter multiethnic Survey of Women's Health Across the Nation (SWAN) study, using data from a single question on difficulty sleeping over the past 2 weeks (*yes, no* response).[7] This study reported that perimenopausal and postmenopausal women, compared with premenopausal women, were significantly more likely to report difficulty sleeping (adjusted odds ratios=1.3-1.6). However, findings from other studies suggest that correlations of sleep problems and menopausal status may be confounded by age-related problems, including depression, chronic pain, and increased morbidity from conditions that negatively affect sleep.[6,15,16]

Data from the few studies of objectively measured sleep quality and menopause are based on very small samples of patients and volunteers and, thus, are difficult to interpret. Baker et al,[8] in a study of 28 patients and a convenience sample of 13 controls, reported that, compared with premenopausal women, perimenopausal but not postmenopausal women had more movement-related arousals from sleep as measured by wrist actigraphy. However, in the only observational study with polysomnography measures, Shaver et al[9] studied a convenience sample of 20 premenopausal, 32 perimenopausal, and 24 postmenopausal women and found no statistically significant differences across menopausal groups on sleep quality indicated by polysomnographic parameters.

Synthesizing results from past studies of menopause and sleep problems is hampered by serious methodologic shortcomings that vary from study to study, including low study power, measurement error, unknown sample bias, and lack of control for confounding factors. Data on menopause and polysomnographically measured sleep quality are particularly sparse, and none are available from a large population-based sample of midlife women. The aim of our study was to determine if polysomnographic indicators of sleep quality differed according to the menopausal status of middle-aged women enrolled in the Wisconsin Sleep Cohort Study.

METHODS

Sample and Data Collection

The sample for this study comprised middle-aged women participating in the Wisconsin Sleep Cohort Study, an ongoing population-based longitudinal study of sleep disorders. Full details of the 2-phase sample construction are given elsewhere.[17] In brief, in the first phase, a sample of all employees of 5 Wisconsin state agencies (with a full range of job categories from unskilled to professional) in Dane County, aged 30 to 60

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years, were surveyed regarding sleep characteristics and other factors to provide a defined sampling frame (n=5091) for recruiting a subgroup for polysomnography and other tests at baseline and at 4-year intervals thereafter. To increase variability in sleep-disordered breathing (SDB), snorers were oversampled by approximately 1.4 to 1.0, but the cohort sample is reweighted to the original sampling frame as needed. From the total probability sample of 2884 survey participants selected for recruitment into the cohort, 1531 have been successfully studied to date. The response rate for women was 52% for the baseline study, 87% for 4-year follow-up, and 92% for 8-year follow-up. Comparison of participants with nonparticipants using extensive data from payroll records and the survey has shown few differences. There were no differences between participants and nonparticipants regarding age, hourly salary, and most sleep characteristics, but a lower proportion of participants compared with nonparticipants were smokers (21% vs 26%) and reported having excessive daytime sleepiness 5 or more days per month (32% vs 25%). Of the 616 women who completed a baseline study, 402 have completed at least 1 follow-up study. After exclusions due to unknown menopausal status (described below), data from 589 women, for a total of 1024 observations, were available for analysis. The sample size was inadequate for exclusively longitudinal analyses, so statistical techniques for repeated measures were used to make full use of the data.

Data were obtained from an overnight sleep protocol conducted at a dedicated sleep laboratory with rooms furnished to resemble typical bedrooms. Participants arrived in the early evening, and informed consent was obtained. Before bedtime, data on menstrual history, occurrence of hot flashes or flushes associated with sleep or with other activities, gynecologic surgery, satisfaction with the usual night's sleep, and self-perceived sleep problems were collected by interview and questionnaire. Questions on insomnia and hot flashes were added to the protocol later in the study, so these data were not available on the entire sample (n= 412). Weight, height, and other parameters were measured, and polysomnography leads were applied. Participants were encouraged to follow their usual bedtime routine and choose their wake time. In the morning, participants had a blood sample drawn.

Table 1—Selected baseline values for the study sample

Variable	Value
Mean age, y (SD)	46.3 (8.1)
Median body mass index, kg/m^2 (range)	28.5 (17.9-62.0)
Excessive daytime sleepiness, %	24
Trouble maintaining sleep*, %	30
Trouble initiating sleep*, %	12
Wake too early*, %	12
Wake and cannot return to sleep*, %	15
Hormone replacement therapy, %	15
Caucasian, %	98
Mean systolic blood pressure, mmHg (SD)	121.3 (14.7)
Mean diastolic blood pressure, mmHg (SD)	78.9 (9.7)
Blood-pressure medication use, %	12
Evaluation of health, %	
Excellent	19
Very good	49
Good, fair, or poor	32
Education, %	
High school or less	31
Some college	32
Bachelors degree or higher	37
Depressed†, %	11
Diabetes, %	3
Reproductive surgery, %	19
Current contraceptive use, %	6
Some or most of the time satisfied with the usual night's sleep, %	83
Time since last menstrual period‡, %	
3-12 mo	5.6
1-3 y	17.2
3-10 y	42.2
> 10 y	35.0

*often or almost always
† Zung score > 60 or use of antidepressant medication
‡premenopausal women excluded

Menopausal Status

Menopausal status was assessed by self-reported menstrual history (date of last menstrual period, cycle characteristics, change in cycle characteristics), history of hysterectomy and oophorectomy (details and date of operation), and use of hormone replacement therapy (HRT).

The following operational definitions were used to categorize women regarding menopausal status: *premenopause*, occurrence of menstrual period within the previous 3 months; *perimenopause*, amenorrhea for at least 3 months but less than 12 months or onset of irregular menstrual periods or cycle changes in women who were previously regular in their cycles; *postmenopause,* amenorrhea for at least 12 months or complete hysterectomy (uterus plus both ovaries) or bilateral oophorectomy performed 6 or more months previously.

Menopausal status for some women could not be classified by the above definitions and required individual consideration. Longitudinal data were useful in ascertaining status for some women. Those who could not be clearly categorized (n=13) and women with hysterectomies and unknown ovarian status were excluded from the analysis (n=37).

Objective Sleep Quality

Measurements of sleep architecture and other parameters reflecting sleep quality and fragmentation were determined by a single overnight polysomnography using an 18-channel polysomnographic recording system (Model 78, Grass Instruments, Quincy Mass). Electroencephalography, electromyography, and electrooculography were used to identify sleep stages. Oxyhemoglobin saturation was continuously recorded with a pulse oximeter (Model 3740, Ohmeda, Englewood, Colo). Thermocouples (Pro-Tec Hendersonville, Tenn) detected oral and nasal airflow. Respiratory inductance plethysmography (Respitrace, Ambulatory Monitoring, Ardsley, NY) recorded ribcage and abdominal excursion. The polysomnograms were scored by trained technicians using conventional criteria to identify the sleep stage of each 30-second epoch[18] and document abnormal breathing events (apnea and hypopnea).[17]

Sleep-stage data were used to calculate the percentage of total sleep time spent in stage 1, stage 2, stages 3 and 4, and rapid eye movement (REM) stage sleep. Sleep fragmentation was described by the mean time between shifts from stages 2, 3, or 4 to stage 1 or to wake. Sleep latency was defined as the elapsed time from lights out until the first of 3 consecutive epochs of stage 1 sleep or the first epoch of any other stage of sleep, and REM latency was defined as the elapsed time from the end of the epoch in which sleep onset occurred to the first epoch of REM sleep. Sleep efficiency was expressed as the percentage of total time in bed spent in polysomnographically confirmed sleep. An episode of apnea was defined as cessation of airflow for at least 10 seconds, and hypopnea by a discernable reduction on calibrated respiratory inductance plethysmography lasting at least 10 seconds that was associated with a reduction in the oxyhemoglobin saturation of at least 4%.

Subjective Sleep Quality

Subjective sleep quality was based on responses to questions of how often sleep was satisfactory (*most of the time*, *some of the time*, *not usually*, *never*), and the frequency of difficulty initiating and maintaining sleep (*never*, *rarely*, *sometimes*, *often*, and *always or almost always*). Women reporting *not usually* or *never* have satisfactory sleep or *often* or *almost always* to the insomnia questions were considered positive for these problems. Excessive daytime sleepiness that interfered with life was indicated by a positive response to the question of having uncontrollable sleepiness that negatively affected at least 1 item from of a list of major aspects of daily living, including personal relationships, work, and recreation.

Statistical Analysis

Analyses were based on a total of 1024 observations from 589

women. Each woman could contribute from 1 to 3 data points to the analysis, depending on her number of follow-up exams. Within each woman, menopausal status and sleep-quality measures varied from visit to visit. Specialized statistical techniques (mixed modeling for continuous data[19] and generalized estimating equations[20] for binary data were used to estimate the relationship between menopausal status and sleep quality. These techniques combine cross-sectional (between women) and longitudinal (within women) estimates of association and correct the estimates for the correlation due to multiple measures within women. Additionally, these techniques specify the variance and covariance of measures within and among women, such that standard errors used in testing the significance of the associations are robust. In our analyses, an unstructured variance-covariance matrix was used for mixed modeling (SAS Procedure Mixed[21]), and an independence working correlation matrix was used for generalized estimating equations modeling (SAS Procedure Genmod[21]).

All models used menopausal status categories and examined the following potential confounding factors as independent variables: (1) age—in years; (2) body mass index (BMI)—kilogram per meter squared; (3) smoking—current, past, or never; (4) alcohol—self reported number of drinks consumed per week; (5) exercise—self reported number of hours of planned exercise per week; (6) caffeine—self reported number of drinks containing caffeine consumed per day; (7) education—high school or less, some college, bachelor's degree, or beyond bachelor's degree; (8) health status—self reported as excellent, very good, good, fair, or poor; and (9) depression—Zung Depression scale score of 60 or greater or antidepressant use. Covariates were retained in the models if their inclusion changed the β-coefficient for menopausal status by 10% or more.

As in ordinary regression, the adjusted means for sleep-quality parameters for each menopausal category were calculated from the mixed-model results by summing the intercept and the products of the β-coefficients of the independent variables multiplied by the mean value of that covariate plus the β-coefficient for the particular menopausal category. Odds ratios for self-reported sleep problems were calculated using the coefficients obtained from the generalized estimating equation models. Robust standard errors were used to construct confidence intervals for both mean values and odds ratios.

Table 2—Sleep-quality parameters* stratified by menopausal status and hormone replacement therapy use

Parameter	Premenopause n=493	Perimenopause n=116	Total n=415	Postmenopause With HRT n=189	Postmenopause Without HRT n=226
Sleep stage†, %					
Stage 1	8.9 (8.2, 9.5)	7.6 (6.9, 8.4) $p_1 = 0.004$	8.6 (7.9, 9.3) $p_1 = 0.67$	9.2 (8.2, 10.1) $p_1 = 0.63$	8.1 (7.3, 8.9) $p_1 = 0.17$ $p_2 = 0.06$
Stage 2	59.9 (58.7, 61.1)	59.4 (56.6, 60.2) $p_1 = 0.14$	56.2 (54.9, 57.4) $p_1 = 0.0003$	56.4 (54.9, 57.9) $p_1 = 0.002$	55.9 (54.3, 57.5) $p_1 = 0.0005$ $p_2 = 0.59$
Stages 3 + 4	12.9 (11.8, 14.0)	16.0 (14.4, 17.6) $p_1 = 0.0005$	16.4 (15.2, 17.6) $p_1 < 0.0001$	15.4 (13.9, 16.8) $p_1 = 0.011$	17.4 (15.9, 18.9) $p_1 < 0.0001$ $p_2 = 0.03$
REM sleep	17.9 (17.1, 18.7)	18.1 (16.9, 19.2) $p_1 = 0.82$	18.6 (17.7, 19.5) $p_1 = 0.29$	18.8 (17.6, 20.0) $p_1 = 0.26$	18.5 (17.4, 19.5) $p_1 = 0.46$ $p_2 = 0.64$
Sleep latency, min	13.7 (11.9, 15.5)	12.7 (9.9, 15.4) $p_1 = 0.48$	11.8 (10.0, 13.6) $p_1 = 0.19$	12.7 (10.6, 14.9) $p_1 = 0.52$	10.9 (8.8, 13.0) $p_1 = 0.07$ $p_2 = 0.12$
REM latency, min	125.4 (116.6, 134.1)	127.6 (114.3, 140.9) $p_1 = 0.75$	131.9 (121.9, 142.0) $p_1 = 0.39$	134.7 (120.5, 148.9) $p_1 = 0.33$	129.4 (118.7, 140.0) $p_1 = 0.61$ $p_2 = 0.49$
Sleep efficiency, %‡	84.0 (82.8, 85.2)	85.1 (83.6, 86.7) $p_1 = 0.17$	86.3 (85.2, 87.4) $p_1 = 0.01$	86.0 (84.5, 87.4) $p_1 = 0.05$	86.5 (85.2, 87.9) $p_1 = 0.01$ $p_2 = 0.53$
Total sleep time, min	374.2 (366.1, 382.2)	380.1 (370.4, 390.3) $p_1 = 0.33$	387.6 (378.7, 396.5) $p_1 = 0.05$	391.6 (381.4, 401.9) $p_1 = 0.018$	383.8 (373.0, 394.6) $p_1 = 0.22$ $p_2 = 0.18$
Sleep fragmentation, mean time in minutes before shift to stage 1 sleep or wake	13.7 (12.9, 14.5)	14.6 (13.3, 15.9) $p_1 = 0.27$	14.6 (13.6, 15.7) $p_1 = 0.26$	13.9 (12.7, 15.0) $p_1 = 0.87$	15.3 (13.9, 16.7) $p_1 = 0.08$ $p_2 = 0.05$

*Data, presented as means (95% confidence interval), are from 1024 observations on 589 women and are estimated using generalized estimating equations adjusted for age, body mass index, alcohol consumption, hours of planned exercise, smoking and caffeine intake at the mean values of these covariates in this population
†Percentage of total sleep time
‡Percentage of time in bed with lights out spent as time asleep
p_1: compared to premenopause
p_2: compared to postmenopause with hormone replacement therapy (HRT)
REM indicates rapid eye movement

RESULTS

Characteristics of the sample are given in Table 1. The average age in years of the 589 women in the sample at baseline was 46.3 (SD = 8.1), and 98% were Caucasian. The mean BMI was 30.1 kg/m^2, but the distribution was skewed to the right; 3 women with very high BMIs (54 kg/m^2, 58 kg/m^2, and 62 kg/m^2) caused an extreme right tail of the distribution. Thus, the median is lower (28.5 kg/m^2; range 17.9-62.0 kg/m^2) and better reflects this characteristic in the sample. The distribution of menopausal status and age range for each category were 59% premenopause (mean age = 41.6 years, range= 31-53 years), 8% perimenopause (mean age =48.3 years, range = 36-56 years), and 31% postmenopause (mean age = 55.2 years, range=37-68 years). Fifteen percent of the sample used HRT. On average, women slept 374 minutes (range = 240-581 minutes). Compared with the typical distribution of sleep time by sleep stage in adults, the women had slightly more stage 1 sleep and slightly less REM sleep, but all values were within normal ranges.[22]

A comparison of polysomnographically determined sleep-quality parameters by menopausal status, adjusted for confounding factors of BMI, age, alcohol use, smoking, caffeine use, and exercise is given in Table 2. Other factors investigated for confounding (self-reported health evaluation, Zung Depression Scale, use of antidepressants, apnea-hypopnea index [AHI]) did not alter the associations of menopause and sleep quality and were not included in the final models. The proportions of time spent in the various sleep stages showed no indication of a less-favorable sleep architecture for perimenopausal or postmenopausal women, compared with premenopausal women. To the contrary, postmenopausal compared with premenopausal women had significantly better sleep quality, including 3.4% more in the proportion of total sleep time spent in slow-wave sleep (stages 3/4), 13.4 more minutes of sleep overall, and a lower proportion of their time in bed spent awake; perimenopausal compared with premenopausal women had significantly less light sleep (1.3 % less in the

proportion of total sleep time spent in stage 1) and more deep sleep (3.1% higher proportion of total sleep time spent in stages 3/4).

We found no indication that HRT use was associated with better sleep quality. Postmenopausal women without HRT compared to those with HRT had better sleep architecture, including less light sleep ($P = 0.02$) and more deep sleep ($P = 0.07$), fell asleep faster ($P = 0.002$), had better sleep efficiency ($P = 0.06$), and slept longer ($P = 0.04$).

Based on subjective measures of sleep quality, both perimenopausal and postmenopausal women were significantly more dissatisfied with their sleep than were premenopausal women (Table 3). Compared with premenopausal women, perimenopausal and postmenopausal women had twice the odds ($P < 0.05$) of reporting they were *never* or *not usually* satisfied with their sleep. However, the odds ratios for other sleep problems and menopause were not consistent. In comparing perimenopausal and premenopausal women with regard to 4 insomnia symptoms, only the association with *difficulty initiating sleep* was statistically significant; postmenopause was not significantly associated with any insomnia symptom but was weakly associated with daytime sleepiness. We investigated whether increased sleep apnea, a potential cause of daytime sleepiness, was an explanatory factor, but adding a variable for AHI did not affect the findings. None of the associations were significantly modified by further categorization of menopausal status by HRT use.

Menopausal women who reported hot flashes, regardless of whether or not they were associated with sleep, did not differ from those who reported no hot flashes on any of the polysomnography sleep parameters. The odds of reporting some subjective sleep problems were greater for women who experienced flashes or flushes, compared with menopausal women without these symptoms, but only the association of dissatisfaction with sleep and sleep-related hot flashes was statistically significant (Table 4).

To investigate how SDB, an established cause of sleep disruption, might influence the association of menopause and objective sleep quality, we compared mean values for sleep-stage distribution—adjusted for BMI and age—by AHI categories after stratification on menopausal status. As shown in Table 5, as SDB severity—indicated by AHI categories—increased, sleep architecture was less favorable (more stage 1, less stage 3/4, and less REM sleep) for both premenopausal and menopausal (perimenopausal and postmenopausal) women. Furthermore, at any AHI level, postmenopausal women still had less stage 1 sleep and more stage 3/4 sleep than did premenopausal women.

Table 3—Odds ratios* for self-reported sleep problems and menopausal status

Sleep problem	Odds ratios (95% confidence intervals)	
	Perimenopause vs Premenopause	Postmenopause vs Premenopause
Waking up repeatedly during night	0.59 (0.25, 1.43)	1.58 (0.70, 3.54)
Difficulty initiating sleep	4.18 (1.37, 12.77)	2.77 (0.79, 9.72)
Waking up during night and can not sleep	1.93 (0.70, 5.36)	1.57 (0.54, 4.52)
Awakening too early in the morning	1.43 (0.53, 3.89)	0.80 (0.31, 2.10)
Always or almost always dissatisfied with sleep	2.01 (1.14, 3.54)	2.23 (1.24, 4.01)
Excessive daytime sleepiness	0.91 (0.55, 1.52)	1.70 (1.04, 2.77)

* Adjusted for age and body mass index

Table 4— Odds ratios* for self-reported sleep problems in menopausal women with vasomotor symptoms

Sleep problem	Odds ratios (95% confidence intervals)	
	Hot flashes associated with other activities vs no hot flashes	Hot flashes associated with sleep vs no hot flashes
Waking up repeatedly during night	1.10 (0.63, 1.93)	1.09 (0.60, 1.98)
Difficulty initiating sleep	1.46 (0.69, 3.08)	0.87 (0.33, 2.30)
Waking up during night and can not sleep	1.69 (0.86, 3.31)	1.42 (0.68, 2.99)
Awakening too early in the morning	0.82 (0.38, 1.74)	1.00 (0.46, 2.15)
Always or almost always dissatisfied with sleep	1.56 (0.93, 4.55)	1.88 (1.05, 3.37)
Excessive daytime sleepiness	1.00 (0.63, 1.58)	0.83 (0.49, 1.42)

*Adjusted for age and body mass index

Table 5—Sleep-stage distribution by apnea-hypopnea index, stratified on menopausal status*

Sleep Stage, %	AHI < 5		AHI 5-15		AHI > 15	
	Premenopause	Menopause†	Premenopause	Menopause†	Premenopause	Menopause†
1	8.1 (0.2)	8.2 (0.3)	8.8 (0.7)	7.9 (0.4)	12.3 (1.9)‡	10.8 (1.3)‡
2	59.2 (0.5)	56.7 (0.5)	59.4 (1.7)	57.1 (0.9)	62.5 (2.4)	60.1 (1.5)‡
3/4	13.5 (0.4)	16.1 (0.5)	14.4 (1.5)	16.3 (1.0)	10.9 (2.3)	14.7 (1.5)
REM	18.7 (0.3)	18.8 (0.3)	16.9 (1.3)	18.5 (0.6)	13.4 (1.8)§	14.6 (1.2)§

*Data are presented as mean (SD), adjusted for age and body mass index
†Combined Perimenopause and Postmenopause groups
‡ $P < 0.05$ for AHI > 15 vs AHI < 5
§ $P < 0.005$ for AHI > 15 vs AHI < 5
AHI indicates apnea-hypopnea index

DISCUSSION

In this population-based sample of midlife women, objectively measured sleep quality was not less favorable in perimenopausal or postmenopausal women, relative to premenopausal women. To the contrary, postmenopausal women had the best overall sleep architecture, while premenopausal women had the worst. The importance of the comparison lies not in the small increment in better sleep quality for menopausal women, but in finding statistical significance *against* the hypothesis that menopause diminishes sleep quality.

Our major finding that menopause was not related to diminished sleep quality, as indicated by polysomnography, is consistent with the limited previously published data. Shaver et al[9] found no statistically significant associations of menopausal status with any of 17 sleep-quality parameters derived from polysomnography. However, small sample size, unknown participation bias, and lack of control for age and other potential confounding factors in that study limits confidence in the true concordance of our results with those of Shaver et al's study. Confirmation of our findings with data from another large community-based sample is needed.

Both perimenopausal and postmenopausal women, compared with premenopausal women, were twice as likely to be dissatisfied with their sleep. The odds ratios for dissatisfaction with sleep and perimenopausal and postmenopausal status (2.0 and 2.2, respectively) do not seem high enough to confidently implicate menopause per se as the primary explanation for sleep difficulties in midlife women. Previous work is in concordance with our interpretation. Dennerstein and colleagues, in prospective data from 172 Australian women, found only a small gradual increase in trouble sleeping over the menopausal transition.[6] The investigators contrasted this change with the large incremental increase seen over the menopausal transition in vaginal dryness, night sweats, and hot flashes and concluded that trouble sleeping is not a direct effect of hormone changes in menopause.

We did not find that objective sleep quality in menopausal women differed by whether or not they reported hot flashes or flushes. It is likely that women may underestimate flashes during sleep that may slightly disrupt sleep but not result in wakefulness. Unfortunately, we have no data on objective measurement of flashes during sleep to better investigate the role of hot flashes in sleep quality. Few data are available for comparison, but in a study of 19 menopausal women, more intermittent wake time and sleep-stage shifts were seen in women with

reported flashes or flushes compared to women without these symptoms.[23] However, similar to our findings, flashing or flushing was actually associated with more deep sleep and longer total sleep time.

Although a stronger role for vasomotor symptoms in sleep quality would be expected, it is possible that other predictors of sleep problems in midlife, not specific to menopause, overshadow the role of vasomotor symptoms in both objective and subjective sleep quality. Results from other studies indicate that psychologic distress and somatic symptoms such as musculoskeletal pain, independent of menopause, may explain perceived sleep problems. In comparing attributes of women with reported *poor* and *good* sleep, Shaver et al found vasomotor symptoms to be only 1 of several contributors to self-reported poor sleep and concluded that sleep problems in midlife cannot be attributed solely to menopause.[24] Our data on subjective sleep quality showing only a slight increase in dissatisfaction with sleep among menopausal women with versus without vasomotor symptoms during sleep are in accordance with this conclusion. Furthermore, investigators of the Survey of Women's Health Across the Nation study of menopause and sleep dissatisfaction found that associations of menopausal status and sleep difficulty were not substantially weaker in the subgroup of women without vasomotor symptoms.[7] In the total sample, odds ratios (95% confidence intervals) for sleep difficulty with late perimenopausal, natural postmenopausal, and surgical postmenopausal status (versus premenopausal status) were 1.33 (1.07-1.65), 1.21 (1.03-1.43), and 1.55 (1.25-1.92), respectively; in the subsample without vasomotor symptoms, the corresponding odds ratios were 1.4 (1.01-1.92), 1.26 (1.01-1.58), and 1.19 (0.87 1.62).

We did not find HRT use to be associated with better objectively measured sleep quality. Our data are similar to those from a study of women aged 55 years and older enrolled in the Sleep Heart Health Study.[25] Compared with HRT users, women who did not use HRT had significantly less stage 1 sleep ($P = 0.05$), and more slow-wave sleep ($P < 0.0001$). While results from these 2 large population samples are intriguing, interpretation is limited by the cross-sectional observational nature of both studies: women with poor sleep in menopause, regardless of the cause, may be more likely to seek HRT. Unfortunately, we were not able to stratify the HRT use on type (estrogen alone or with progesterone) or dose.

Data from blinded randomized trials of HRT outcomes are mixed with respect to objectively and subjectively measured sleep quality. Polo et al[10] found that the use of HRT improved subjective sleep quality; there was no improvement in objectively measured sleep quality, including sleep latency, total sleep time, or other parameters. Interestingly, the use of HRT was associated with increased arousals detected by electroencephalography but with decreased arousals detected by body movement. Only a small improvement in subjective sleep quality with HRT use versus placebo was reported from the Women's Health Initiative.[26] Although statistically significant, the authors noted that the effect size was too small to be considered clinically significant. Furthermore, the positive effect was seen at 1-year follow-up but not at 3-year follow-up.

In our study, the association of menopause and sleep quality differed for objective and subjective measures of sleep. Several reports have noted that with aging, women, compared to men, have a higher prevalence of self-reported sleep problems, but evaluation with polysomnography suggests their sleep architecture is better, with better preservation of slow-wave sleep with age.[27-30] Interestingly, in this sample of middle-aged women, we saw no decline in percentage of slow-wave sleep with age; the correlation of age with percentage of slow-wave sleep was very slightly positive ($r = .06$, $P = 0.03$). It is possible that menopause negatively affects components of sleep not reflected by polysomnography; the contradictory associations of menopause with objective and subjective sleep quality emphasize the complexity of the perception of diminished sleep quality and the need to better understand the aspects of sleep reflected by different measures. Alternatively, subjected to lay media reports that emphasize sleep problems in menopause, menopausal women may expect to have sleep problems and consequently underestimate their sleep quality.

Menopause is believed to be a risk factor for SDB. Because the apnea and hypopnea events of SDB can result in sleep fragmentation and less-favorable sleep architecture, understanding the role of SDB in the relationship of menopause and sleep quality is important. We have previously reported a statistically significant positive association of menopause with SDB indicated by AHI.[31] The odds ratio, adjusted for age, BMI, and other factors for an AHI of 5 or greater versus an AHI less than 5 was 2.6 (1.4, 4.8) for postmenopausal versus premenopausal women. When we investigated sleep-stage distribution by AHI categories, we did find that higher AHI was associated with worse sleep architecture (more stage 1, less stages 3/4, and less REM sleep), and this was true for both the premenopausal and the combined perimenopausal and postmenopausal groups. However, the differences are not large; it is clear that SDB does not explain a great deal of the overall variability in polysomnographic sleep stage variables. Most important in relation to this study, at any AHI level, postmenopausal women still had more favorable objectively measured sleep quality than did premenopausal women.

Our findings must be considered in light of study limitations. Our objective measures of sleep quality are based on a single-night polysomnography. If premenopausal, compared with perimenopausal and postmenopausal women, had more trouble sleeping in the laboratory, their sleep quality could be underestimated. However, women were asked to compare their night's sleep during the polysomnography night with their usual night's sleep (*much worse, worse, about the same, better, much better*), and we found no difference by menopausal status.

Although we were able to investigate confounding with many variables, some of the variables may be inadequate surrogates for the latent variables of importance. For example, using education level for socioeconomic status or the Zung Depression scale and use of antidepressant medications for mental health may have resulted in residual confounding. However, to spuriously cause a significant positive association of menopause and objective sleep quality if a true negative association existed, the omitted confounding factors would have to be very influential in order to reverse the direction of the association.

Our self-report data are limited by the cross-sectional design and cannot address causality of associations. Prospective data are needed to more validly measure any changes in sleep quality as women pass through the menopausal transition. The findings may also be influenced by a birth cohort effect: the way menopause is viewed both personally and clinically differs for women who are currently experiencing menopause, who became menopausal in the past, or who will become menopausal in the future. Women currently experiencing menopause are exposed to reports in the popular media stating that sleep problems should be expected with menopause, and this may lead them to overreport poor sleep quality.

Finally, our findings are based on a probability sample of middle-aged women from south central Wisconsin with no oversampling of minority groups. Consequently, the sample consists almost entirely of Caucasian women of European heritage. To the extent that the effect of menopause on sleep varies by race, our findings may not be generalizable to all racial or ethnic groups.

CONCLUSIONS

Our study, unique in comparing sleep quality determined by polysomnography in a large, well-characterized, population-based, probability sample of premenopausal, perimenopausal, and postmenopausal women, demonstrates that menopause is not independently associated with objectively measured diminished sleep quality. We saw no evidence that the use of HRT was associated with better sleep quality, but interpretation is limited by the cross-sectional nature of our data. Although menopause was associated with nonspecific dissatisfaction with sleep, specific insomnia or sleepiness complaints were not consistently reported more frequently in menopausal women.

Of particular clinical significance, our findings indicate that abnormal sleep in midlife women should not be routinely treated as simply a

menopausal symptom, and polysomnography irregularities should not be attributed to menopause. General literature and primary care guidelines on the menopausal transition often convey the view that sleep disorders, like hot flashes and effects of vaginal atrophy, are hallmarks of menopause that can be treated with HRT.[12,32,33] However, as the first or sole approach to sleep problems in menopausal women, this view may lead to unwarranted exposure to the health risks of HRT,[34] and underlying sleep disorders may be missed. Signs and symptoms that would normally trigger a full sleep evaluation in premenopausal women should be taken as seriously in menopausal women.

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