

# Effects of menopause on sleep quality and sleep disorders: Canadian Longitudinal Study on Aging

Sheida Zolfaghari, MD,<sup>1,2</sup> Chun Yao, MSc,<sup>1,2</sup> Cynthia Thompson, PhD,<sup>3</sup> Nadia Gosselin, PhD,<sup>3,4,8</sup>  
Alex Desautels, MD, PhD,<sup>3,5,8</sup> Thien Thanh Dang-Vu, MD, PhD,<sup>6,7,8</sup>  
Ronald B. Postuma, MD, MSc,<sup>2,3,8</sup> and Julie Carrier, PhD<sup>3,4,7,8</sup>

## Abstract

**Objectives:** Sleep complaints are common during the menopause transition. However, it is difficult to disentangle changes in sleep related to aging from those directly due to menopause. We compared sleep disorders in 45 to 60-year-old women in a large population-based study, according to menopausal status.

**Methods:** Women aged between 45 and 60 years who self-reported menopausal status were selected from the Canadian Longitudinal Study of Aging, excluding those with prior hysterectomy. Participants completed assessments for overall sleep satisfaction, hours of daily sleep, sleep-onset insomnia, sleep-maintenance insomnia, daytime somnolence, rapid eye movement sleep behavior disorder (RBD), restless leg syndrome (RLS), and obstructive sleep apnea (OSA). Each sleep variable was compared between postmenopausal and pre/perimenopausal women using multivariate regression, adjusting for potential confounders.

**Results:** Among 6,179 women included, 3,713 (60.1%; age  $55.7 \pm 3.3$  years) were postmenopausal and 2,466 (39.9%) were pre/perimenopausal (age  $49.80 \pm 3.1$  years). Compared with pre/perimenopausal women, postmenopausal women were more often reported requiring  $\geq 30$  minutes to fall asleep (20.4% vs 15.5%; adjusted odds ratio [AOR] 1.24, 95% confidence interval [CI] 1.00-1.53) and were more likely to meet criteria for possible sleep-onset insomnia disorder (10.8% vs 7.3%; AOR 1.51, 95% CI 1.07-2.12). Postmenopausal women were also more likely to screen positive for OSA (14.6% vs 10.4%; AOR 1.48, 95% CI 1.14-1.92). The two groups did not differ on sleep dissatisfaction (32.4% vs 29%), daytime somnolence disorder (1.6% vs 1.3%), sleep-maintenance insomnia disorder (17% vs 14.5%), RLS (23.5% vs 20.9%), or RBD (3.9% vs 4.0%).

**Conclusions:** Menopause is associated with increased sleep-onset insomnia. Postmenopausal women also are more likely to screen positive for OSA. However, menopausal status is not associated with sleep maintenance, somnolence, or RLS, and RBD.

**Key Words:** CLSA – Obstructive sleep apnea – Rapid eye movement sleep behavior disorder – Restless legs syndrome – Sleep initiation and maintenance disorders – Somnolence disorder.

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From the <sup>1</sup>Integrated Program in Neuroscience, McGill University, Montréal, Québec, Canada; <sup>2</sup>Department of Neurology, McGill University, Montreal General Hospital, Montréal, Québec, Canada; <sup>3</sup>Center for Advanced Research in Sleep Medicine, Hôpital du Sacré-Coeur de Montréal, Montréal, Québec, Canada; <sup>4</sup>Department of Psychology, Université de Montréal, Montréal, Québec, Canada; <sup>5</sup>Department of Neuroscience, Université de Montréal, Montréal, Canada; <sup>6</sup>Center for Studies in Behavioral Neurobiology, PERFORM Center, Department of Health, Kinesiology and Applied Physiology, Concordia University, Montréal, Québec, Canada; <sup>7</sup>Institut Universitaire de Gériatrie de Montréal and CRIUGM, CIUSSS du Centre-Sud-de-l'Île-de-Montréal, Montréal, Québec, Canada; and <sup>8</sup>Canadian Sleep and Circadian Network (CSCN).

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**Address correspondence to:** Dr Julie Carrier, Center for Advanced Research in Sleep Medicine, Hôpital du Sacré-Coeur de Montréal, 5400 Boulevard Gouin Ouest, Montréal, Québec H4J 1C5, Canada. E-mail: [julie.carrier.1@umontreal.ca](mailto:julie.carrier.1@umontreal.ca); Dr Ronald B. Postuma, Department of Neurology, L7-305 Montreal General Hospital, 1650 Cedar Ave, Montreal H3G1A4, Canada. E-mail: [ron.postuma@mcgill.ca](mailto:ron.postuma@mcgill.ca)

Sleep disorders are reported to occur frequently in 40% to 60% of peri and postmenopausal women, and often persist during the rest of their life.<sup>1-8</sup> These sleep problems can be major sources of impaired quality of life and can lead to physical and psychological conditions such as cardiovascular diseases, diabetes, depression, anxiety, and overuse/abuse of hypnotic medications.<sup>9-11</sup> As average life span increases, women are expected to live nearly half of their lives in the postmenopausal state, implying that menopause-related problems represent an increasingly high priority.<sup>12,13</sup>

There has been controversy about the relationship between menopause and sleep, with several studies finding more difficulties falling asleep, fragmented sleep, night-time wakefulness, and inability to resume sleep during the menopause transition,<sup>5,6,14-26</sup> whereas others found no differences.<sup>27-30</sup> Moreover, beyond menopause itself, changes in sleep organization are also a hallmark of the normal aging process.<sup>31-34</sup> Multiple specific sleep disorders are age-related, including obstructive sleep apneas (OSA), periodic leg movements during sleep (PLMS), rapid eye movement sleep behavior disorder (RBD), and changes in the normal sleep cycle.<sup>35-37</sup> Because most studies linking sleep to aging did not enquire about menopausal status, it was difficult to disentangle changes in sleep due to aging from those caused by menopause itself. Finally, during the perimenopausal period, prevalence of anxiety and major depressive disorders increases,<sup>38</sup>

which might induce poorer perception of one's sleep. Therefore, age and psychological issues can confound observed relationships between menopause and sleep disorders, and require further study.

The objective of this study was to compare sleep quality, sleep duration, and symptoms of sleep disorders between postmenopausal and pre/perimenopausal women, of similar age (45-60 years) in the Canadian Longitudinal Study of Aging (CLSA), adjusting for age and numerous potential confounding factors.

## METHODS

### Study population

The study was approved by the CIHR Advisory Committee on Ethical, Legal and Social Issues (ELSI), and all participants signed informed consent to participate. Baseline data were collected from participants of the CLSA, a population-based research study cohort, recruiting 51,338 participants, aged 45 to 85 years randomly sampled from 10 Canadian provinces from 2011 to 2015. For this study, we used data from the 30,097-participant comprehensive cohort. This included participants living within 25 to 50 km from collection sites in which data were collected by face-to-face interviews, as described elsewhere.<sup>39</sup> Of these 30,097 participants, we studied 6,179 women between 45 and 60 years of age, whose menopausal status was specified, excluding those with prior hysterectomy (Fig. 1).

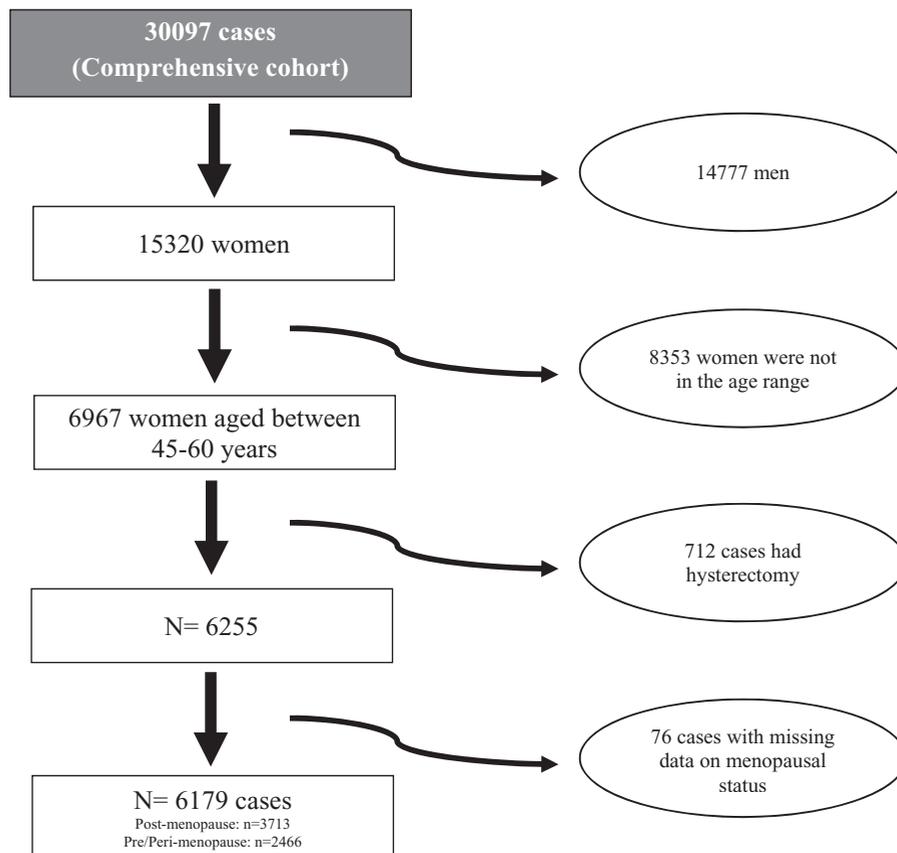


FIG. 1. Flowchart of inclusion and exclusion of participants in the study.

Women who responded ‘yes’ to the question “Have you gone through menopause, meaning that your menstrual periods stopped for at least one year and did not restart?” were classified as postmenopausal and women who responded ‘no’ were classified as pre/perimenopausal. Moreover, for those who underwent menopause, the onset age of menopause was questioned.

### Sleep questionnaire

The full sleep questionnaire is provided in Supplementary Table 1 (<http://links.lww.com/MENO/A518>). The following variables were derived from the questionnaire:

- 1) Overall sleep satisfaction was assessed in a 5-point Likert scale. Responses were categorized into two groups: dissatisfied (‘very dissatisfied’ or ‘dissatisfied’) or satisfied (‘neutral’, ‘satisfied’ or ‘very satisfied’).
- 2) Total hours of sleep per day (numerical variable).
- 3) Difficulty falling asleep was queried as the number of times per week in which it would take 30 minutes or more to fall asleep. We defined possible sleep-onset insomnia disorder according to Diagnostic and Statistical Manual of Mental Disorders version 5 (DSM-V) criteria, as dissatisfaction with sleep pattern (ie, question 1), with difficulty initiating sleep at least 3 nights per week for a duration of at least 3 months, and significant interference with daily functioning.<sup>11</sup>
- 4) Difficulty maintaining sleep was defined as ‘waking-up in the middle of the night or too early in the morning and finding it difficult to fall asleep again’ at least three times per week. Possible sleep-maintenance insomnia disorder was defined based on DSM-V criteria, as dissatisfaction with sleep pattern, difficulty maintaining sleep at least three nights per week for a duration of at least 3 months, and significant interference with daily functioning.<sup>11</sup>
- 5) Daytime somnolence was defined as difficulty to stay awake during normal waking hours at least three times per week. Possible daytime somnolence disorder was defined based on DSM-V criteria as difficulty staying awake, despite having a minimum 7 hours of night-time sleep, for at least three times per week for a duration of at least 3 months, which moderately or severely interferes with daily functioning.<sup>11</sup>
- 6) Possible idiopathic RBD was defined as positive screening on RBD Single-Question Screen (RBD1Q), excluding those with onset before age 20 (possible non-REM parasomnia), self-reported Parkinson’s disease or Alzheimer disease (not idiopathic), and with a positive screen for obstructive sleep apnea, as previously described.<sup>40</sup>
- 7) Symptoms of restless leg syndrome (RLS) were screened using four questions adapted from the Hopkins Telephone interview,<sup>41,42</sup> including two screening questions (uncomfortable feeling in the legs, urge to move the legs while sitting or lying down), and follow-up questions for those answering “yes” to the screening questions (worsening during the evening or night, and disappearance when active). To be considered as positive for possible RLS based on essential diagnostic criteria of International Restless Legs Syndrome Study Group (IRLSSG),

participants had to endorse all four questions.<sup>43,44</sup> It should be noted that the fifth criteria which is “the occurrence of these symptoms should not be due to other medical or behavioral condition” was not available in this study.

For those participants who had any of the sleep disorders above, duration of having that difficulty was also questioned.

- 8) Finally, for assessment of possible OSA, questions from the Snoring, Tiredness, Observed apnea, blood Pressure (STOP) questionnaire were used, namely the presence of snoring, daytime somnolence, being observed to stop breathing and hypertension (neck circumference was not assessed in the CLSA). Those who had two or more factors were considered as high risk for obstructive sleep apnea.<sup>45</sup>

### Sociodemographic, life style data, and past medical history

Data on age, marital status, number of biological children, use and type of hormone therapy (HT), education, income, satisfaction with income, physical activity, smoking habits, alcohol consumption, and diet were assessed on a self-report basis, and were included in our analyses. Height and weight were measured at the time of interview, and body mass index (BMI) was calculated as:  $\frac{\text{weight(kg)}}{\text{height(m)}^2}$ .

Participants self-reported physician-diagnosed history of breast or ovarian cancer or any other types of cancer, thyroid dysfunction, and anxiety.

Hypertension was described as systolic blood pressure  $\geq 140$ , or diastolic blood pressure  $\geq 90$  measured at the time of interview (mean of four measures), or self-reported history of being diagnosed with hypertension/taking antihypertensive medications.

Standard questionnaires were also used to evaluate depression (by Center for Epidemiologic Studies Depression Scale Revised [CESD-R-10]), post-traumatic stress disorder (by Primary Care PTSD Screen [PC-PTSD]), and psychological distress (by Kessler Psychological Distress Scale [K10 questionnaire]).<sup>46-49</sup>

See Supplementary Methods and Supplementary Table 2 (<http://links.lww.com/MENO/A518>) for classification and distribution of these variables.

### Statistical analysis

We classified participants according to their menopausal status into postmenopausal versus pre/perimenopausal group and compared demographic, lifestyle, and health variables in these groups using independent-samples *t* test for continuous variables and chi-square test for categorical variables. We calculated odds ratio (OR) to compare sleep satisfaction and sleep disorders of postmenopausal with pre/perimenopausal group using binary logistic regression analysis. To calculate the mean difference of total hours of sleep between these groups we used linear regression analysis. Both regression models were adjusted for age, marital status, number of biological children, use and type of HT, BMI, education,

income, satisfaction with income, physical activity, smoking, alcohol, diet, history of cancer, anxiety, depression, post-traumatic stress disorder, psychological distress, thyroid dysfunction, and hypertension. There is an exception for the OSA, in which hypertension was not considered in the adjustment model, because it was included in the STOP questionnaire.

To assess potential time course of symptoms, we generated a histogram comparing the timing of sleep disorders and menopause onset age by plotting the difference between menopause onset and the self-reported duration of sleep disorders. This therefore assessed the relative duration between menopause onset (time zero) and when the sleep disorder started (ie, duration of menopause – duration of the sleep disorder); positive values indicated that the sleep disorder started after menopause and vice versa. Moreover, it should be mentioned that the recalled self-reported time of menopause onset refers to menopause transition time.

Statistical analysis was performed using SPSS version 24, and significance level was considered 0.05 for all the tests.

### Secondary and sensitivity analysis

To further evaluate the most important confounders like age and HT, we added some sensitivity and secondary analyses. First, we conducted a sensitivity analysis in a more restricted age group consisting of the middle three quintiles (age 48-56 years), using similar statistical methods as the main analysis. Then, to better understand the impact of age among women with the same menopausal status, we evaluated the association between age and each sleep disorder, within each menopausal group. We used binary logistic and linear regression, considering age as the predictor, and each of sleep variables as the dependent variable. Finally, we excluded HT users and re-evaluated the association of menopause and sleep disorders only in HT nonusers.

## RESULTS

### Demographic, medical, and lifestyle variables

Among 6,179 women included, 2,466 (39.9%) were pre/perimenopausal (mean age  $49.8 \pm 3.1$  years) and 3,713 (60.1%) were postmenopausal (mean age  $55.7 \pm 3.3$  years, mean age of menopause  $50.2 \pm 3.6$  years). Age was significantly different between these groups ( $P < 0.001$ ). Compared with pre/perimenopausal women, higher proportions of postmenopausal women used HT, had higher BMI, were living with no partner, had lower education, smoked, and had lower income. Further characteristics of these groups are shown in Table 1.

### Sleep variables

Comparison of sleep satisfaction, hours of sleep, sleep symptoms, and disorders between postmenopausal and pre/perimenopausal women is shown in Table 2. There was no difference after adjustment in overall sleep satisfaction between the two menopausal status groups with 29% of pre/perimenopausal women and 32.4% of postmenopausal

women expressing poor sleep satisfaction. Similarly, the number of sleep hours was not significantly different between menopausal status groups ( $6.72 \pm 1.2$  vs  $6.79 \pm 1.2$  hours).

As compared with pre/perimenopausal women, postmenopausal women were more likely to report requiring  $\geq 30$  minutes to fall asleep (20.4% vs 15.5% endorsed a frequency of 3/wk or more; adjusted OR [AOR] 1.24, 95% confidence interval [CI] 1.00-1.53). In addition, postmenopausal women were more likely to meet criteria for possible sleep-onset insomnia disorder (10.8% vs 7.3%; AOR 1.51, 95% CI 1.07-2.12). When insomnia symptom onset was compared with menopause onset, there was a clear peak in insomnia onset in the 2 years before to 6 years after menopause onset (Fig. 2).

Postmenopausal status was associated with higher risk of possible OSA (14.6% vs 10.4%; AOR 1.48, 95% CI 1.14-1.92). However, there was no significant difference in individual symptoms of snoring (23.0% vs 18.7%; AOR 1.08, 95% CI 0.88-1.33) or stopping of breathing (9.6% vs 7.5%; AOR 1.27, 95% CI 0.94-1.71) between post and pre/perimenopausal women.

Among other sleep disorders, we found no difference between postmenopausal and pre/perimenopausal women on symptoms of sleep-maintenance difficulties (28.4% vs 27%; AOR 0.99, 95% CI 0.83-1.18), possible maintenance insomnia disorder (17% vs 14.5%; AOR 1.07, 95% CI 0.81-1.42), difficulty staying awake during the day (7.4% vs 6.7%; AOR 1.28, 95% CI 0.93-1.75), and possible daytime somnolence disorder (1.6% vs 1.3%; AOR 1.14, 95% CI 0.52-2.50).

Finally, there was no significant difference between pre/perimenopausal and postmenopausal women regarding their acting out dreams (10.1% vs 11.3%; AOR 1.02, 95% CI 0.80-1.31), possible RBD (3.9% vs 4.0%; AOR 1.10, 95% CI 0.69-1.74), and possible RLS (24.7% vs 22%; AOR 1.06, 95% CI 0.86-1.31) (Table 2).

### Secondary and sensitivity analysis

We investigated the association of menopause and sleep disorders, only including 48 to 56-year-old women, to decrease residual effects of age. Similar to the main results, we found statistically significant differences between sleep-onset insomnia (10.9% vs 7.1%; AOR 1.52, 95% CI 1.04-2.21), and OSA (14.2% vs 10.3%; AOR 1.60, 95% CI 1.19-2.15), between pre/perimenopausal and postmenopausal women (Supplementary Table 3, <http://links.lww.com/MENO/A518>). Then, to investigate the role of age itself, within this 15-year age group, we evaluated the association between age and sleep disorders, stratified by menopausal status. We could not detect a significant effect of age on sleep disorders in any of the menopausal groups (except for sleep hours in the postmenopausal group), suggesting that our results were not confounded by age; and the role of age itself among women in this restricted age group is unclear (Supplementary Table 4, <http://links.lww.com/MENO/A518>). Then, to further control potential effects of HT, we excluded HT users from the sample, with similar effects of menopause on possible sleep-onset insomnia disorder (10.5% vs 7.0%;

**TABLE 1.** Demographic, lifestyle, and health variables in postmenopausal and pre/perimenopausal women

		Postmenopause (n = 3,713)	Pre/perimenopause (n = 2,466)	P <sup>a</sup>
Demographic and socioeconomic status	Age, Mean ± SD	55.72 ± 3.3	49.80 ± 3.1	<0.001
	Marital status, % (n)			
	Single/never married	11.9 (419)	10.0 (234)	<0.001
	Married/living with partner	68.1 (2399)	74.6 (1744)	
	Widowed, divorced, or separated	20.0 (704)	15.4 (360)	
	Education, % (n)			
	Without secondary diploma	2.6 (97)	1.4 (34)	<0.001
	With secondary diploma	51.8 (1923)	45.7 (1127)	
	College degree and above	45.6 (1692)	52.9 (1303)	
	Annual income, % (n)			
\$100,000 or more	45.1 (1585)	55.7 (1316)	<0.001	
\$50,000-100,000	34.0 (1197)	30.8 (728)		
Less than \$50,000	20.9 (734)	13.5 (320)		
Income satisfies daily needs, % (n)				
Inadequate or difficult	10.6 (376)	11.8 (276)	0.175	
Lifestyle	Alcohol, % (n)			
	At least once a week	54.2 (2013)	55.1 (1358)	0.498
	Smoke, % (n)			
	Never smoker	52.8 (1952)	63.8 (1564)	<0.001
	Previous smoker	37.0 (1369)	29.1 (714)	
	Currently daily smoker	10.2 (377)	7.1 (175)	
	Physical activity, % (n)			
	At least once a week	57.9 (2148)	60.2 (1484)	0.077
BMI, Mean ± SD	26.93 ± 5.0	26.56 ± 5.1	0.006	
Hormonal status	Use and type of HT, % (n)			
	No HT	75.4 (2795)	91.0 (2242)	<0.001
	Both estrogen and progesterone	11.8 (439)	3.1 (76)	
	Estrogen	7.8 (288)	1.5 (36)	
	Progesterone	2.8 (105)	3.5 (87)	
	HT-positive (unknown type)	2.2 (81)	1.0 (24)	
Age of starting HT, Mean ± SD	49.44 ± 5.1	47.93 ± 4.9	<0.001	
Number of living biological children, Mean ± SD	1.65 ± 1.2	1.76 ± 1.2	<0.001	
Psychological status	Anxiety disorder, % (n)	11.7 (435)	10.9 (269)	0.347
	Depression, % (n)	18.7 (695)	18.5 (455)	0.815
	Post-traumatic stress disorder, % (n)	5.3 (196)	4.8 (118)	0.408
	Moderate or severe psychological distress, % (n)	5.3 (187)	6.0 (140)	0.27
Physical problems	Thyroid dysfunction, % (n)	14.2 (520)	15.1 (368)	0.335
	Hypertension, % (n)	28.1 (1032)	19.8 (484)	<0.001
	Cancer, % (n)			
	No cancer	89.3 (3311)	94.4 (2326)	<0.001
	Breast or ovarian cancer	4.2 (156)	1.3 (33)	
Other cancer types	6.5 (240)	4.2 (104)		

The above table shows some baseline characteristics of postmenopausal and pre/perimenopausal 45 to 60-year-old women.

BMI, body mass index; HT, hormone therapy.

<sup>a</sup>Independent-samples *t* test for continuous variables and chi-square test for categorical variables were used. Results are not adjusted for age or other covariates.

AOR 1.49, 95% CI 1.01-2.18) and OSA (14.5% vs 10.1%; AOR 1.39, 95% CI 1.04-1.87) (Table 3). Finally, we found overall changes in the STOP questionnaire for OSA screening, but did not find a significant difference for the individual components of snoring, stopped breathing, and daytime somnolence (although it should be noted that the OR point estimates for each of these components was >1). This could suggest that the observed difference comes from hypertension rather than OSA itself. Therefore, in a sensitivity analysis, we excluded hypertension from the definition of STOP questionnaire, such that women with 2 of 3 components were considered as possible OSA. Based on this secondary definition, 7.2% (n = 247) of postmenopausal and 5.8% (n = 135) of pre/perimenopausal women were labeled as possible OSA which remains a significant difference (AOR 1.44, 95% CI 1.02-2.03).

## DISCUSSION

In this large population-based study, postmenopausal status was associated with a higher occurrence of sleep-onset insomnia. Moreover, insomnia symptoms tended to begin in the years soon before and after menopause, indicating a temporal link between menopause and insomnia. We also observed increased possible OSA in the postmenopausal women. Overall sleep satisfaction and other sleep disorders including sleep-maintenance insomnia, possible RBD, and possible RLS did not differ between menopausal status groups.

The degree of sleep dysfunction seen with menopause remains controversial. Several studies have indicated that women report more difficulties falling asleep, fragmented sleep, night-time wakefulness, and inability to resume sleep during the menopause transition.<sup>5,6,14-26</sup> However, other

**TABLE 2.** Sleep dissatisfaction, sleep hours, and sleep disorders in postmenopausal and pre/perimenopausal groups

		Postmenopause (n = 3,713)	Pre/perimenopause (n = 2,466)	Crude odds ratio [95% CI]	Adjusted odds ratio <sup>a</sup> [95% CI]
Sleep satisfaction	Dissatisfaction with current sleep pattern, % (n)	32.4 (1203)	29.0 (715)	<b>1.17 [1.05 to 1.31]</b>	1.13 [0.95 to 1.34]
Sleep hours	Number of sleep hours during past month (mean ± SD)	6.72 ± 1.2	6.79 ± 1.2	<b>-0.07 [-0.13 to -0.01]<sup>b</sup></b>	-0.08 [-0.17 to 0.00] <sup>b</sup>
Insomnia (onset)	Requiring more than 30 min to fall asleep for at least 3/wk, % (n)	20.4 (758)	15.5 (382)	<b>1.40 [1.22 to 1.60]</b>	<b>1.24 [1.00 to 1.53]</b>
Insomnia (maintenance)	Possible sleep-onset insomnia disorder, % (n)	10.8 (292)	7.3 (142)	<b>1.54 [1.25 to 1.90]</b>	<b>1.51 [1.07 to 2.12]</b>
	Waking up and having difficulty falling asleep again for at least 3/wk, % (n)	28.4 (1056)	27.0 (666)	1.07 [0.96 to 1.20]	0.99 [0.83 to 1.18]
	Possible sleep-maintenance insomnia disorder, % (n)	17.0 (414)	14.5 (230)	<b>1.21 [1.01 to 1.44]</b>	1.07 [0.81 to 1.42]
Daytime somnolence	Finding difficulty to stay awake during normal hours for at least 3/wk, % (n)	7.4 (274)	6.7 (165)	1.11 [0.91 to 1.36]	1.28 [0.93 to 1.75]
	Possible daytime somnolence disorder, % (n)	1.6 (50)	1.3 (26)	1.29 [0.80 to 2.07]	1.14 [0.52 to 2.50]
OSA	Snoring loudly, % (n)	23.0 (751)	18.7 (418)	<b>1.29 [1.13 to 1.48]</b>	1.081 [0.88 to 1.33]
	Stopped breathing in sleep, % (n)	9.6 (334)	7.5 (174)	<b>1.30 [1.08 to 1.58]</b>	1.27 [0.94 to 1.71]
	Possible obstructive sleep apnea, % (n)	14.6 (504)	10.4 (240)	<b>1.48 [1.26 to 1.74]</b>	<b>1.48 [1.14 to 1.92]</b>
RBD	Acting out on dreams while asleep, % (n)	10.1 (372)	11.3 (278)	0.88 [0.75 to 1.04]	1.02 [0.80 to 1.31]
	Possible RBD (excluding confounds), % (n)	3.9 (102)	4.0 (74)	0.96 [0.70 to 1.297]	1.10 [0.69 to 1.74]
RLS	Experiencing uncomfortable feeling in legs while sitting or lying down, % (n)	35.5 (1317)	31.7 (782)	<b>1.18 [1.06 to 1.32]</b>	1.17 [0.90 to 1.38]
	Experiencing urge to move legs while sitting or lying down, % (n)	36.7 (1360)	32.6 (803)	<b>1.20 [1.08 to 1.34]</b>	1.15 [0.97 to 1.35]
	Possible restless leg syndrome, % (n)	24.7 (694)	22.0 (429)	<b>1.17 [1.02 to 1.34]</b>	1.06 [0.86 to 1.31]

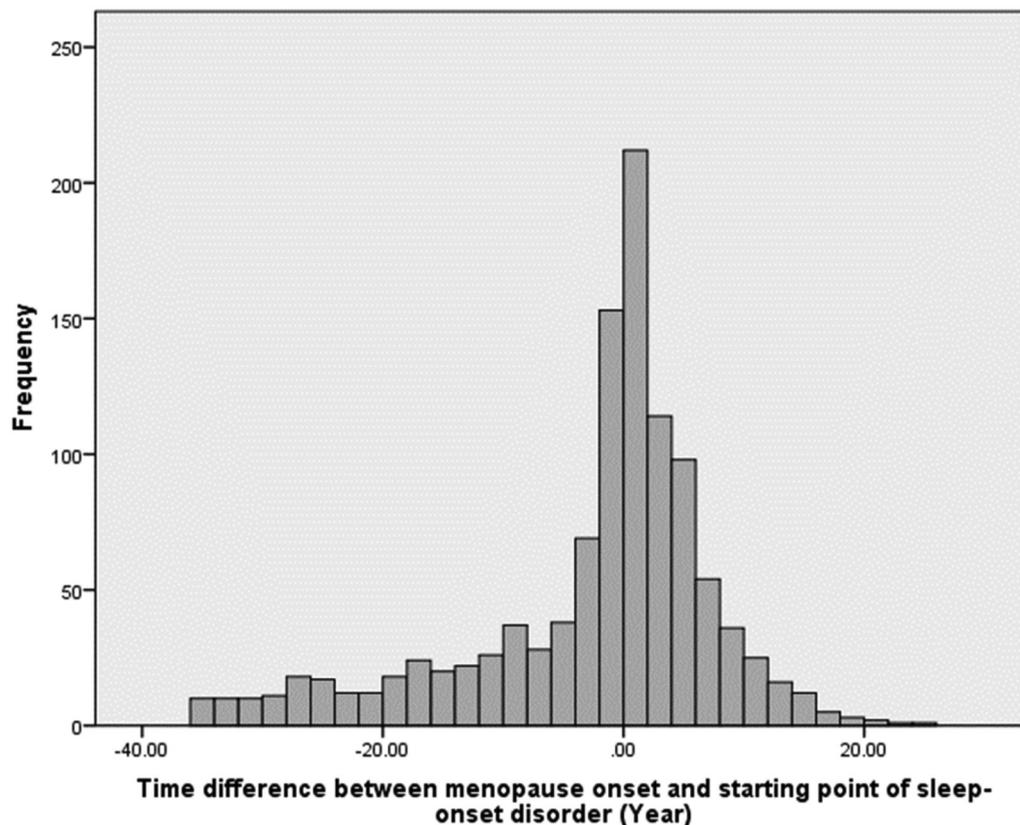
The above table compares distribution of sleep dissatisfaction, sleep hours, and each of the sleep disorders in 45 to 60-year-old postmenopausal and pre/perimenopausal women.

Items in bold font have 95% confidence interval (CI) that do not cross 1.

OSA, obstructive sleep apnea; RBD, rapid eye movement sleep behavior disorder; RLS, restless leg syndrome.

<sup>a</sup>Odds ratio adjusted for age, marital status, child numbers, education, income, satisfaction with income, use of hormone therapy, BMI, physical activity, smoke, alcohol, diet, anxiety, depression, PTSD, psychological distress, physician-diagnosed thyroid dysfunction, cancer, and hypertension.

<sup>b</sup>For this cell, mean difference (B-coefficient and 95% CI) is presented, instead of odds ratio, because “sleep hours” is a continuous variable.



**FIG. 2.** Time difference between menopause onset and starting point of sleep-onset disorder. (0 = menopause onset point). If sleep disorders started before menopause, the value is negative; if afterwards, they are positive. Note the bell-shaped distribution, demonstrating that the large majority of women reported that insomnia symptoms started within 2 years before and 6 years after menopause onset.

**TABLE 3.** Sleep dissatisfaction, sleep hours, and sleep disorders in postmenopausal and pre/perimenopausal groups, excluding HT users

		Postmenopause (n = 2,795)	Pre/perimenopause (n = 2,242)	Crude odds ratio [95% CI]	Adjusted odds ratio <sup>a</sup> [95% CI]
Sleep satisfaction	Dissatisfaction with current sleep pattern, % (n)	31.9 (891)	28.5 (639)	<b>1.17 [1.04 to 1.33]</b>	1.12 [0.93 to 1.36]
Sleep hours	Number of sleep hours during past month (mean ± SD)	6.69 ± 1.2	6.80 ± 1.1	<b>-0.11 [-0.18 to -0.05]<sup>b</sup></b>	<b>-0.12 [-0.21 to -0.02]<sup>b</sup></b>
Insomnia (onset)	Requiring more than 30 min to fall asleep for at least 3/wk, % (n)	20.6 (575)	15.0 (336)	<b>1.47 [1.27 to 1.70]</b>	<b>1.31 [1.03 to 1.65]</b>
	Possible sleep-onset insomnia disorder, % (n)	10.5 (212)	7.0 (124)	<b>1.56 [1.24 to 1.96]</b>	<b>1.49 [1.01 to 2.18]</b>
Insomnia (maintenance)	Waking up and having difficulty falling asleep again for at least 3/wk, % (n)	27.9 (779)	26.2 (588)	1.09 [0.96 to 1.23]	1.02 [0.84 to 1.24]
	Possible sleep-maintenance insomnia disorder, % (n)	15.6 (288)	13.8 (201)	1.16 [0.95 to 1.40]	0.96 [0.70 to 1.32]
Daytime somnia	Finding difficulty to stay awake during normal hours for at least 3/wk, % (n)	7.1 (197)	6.6 (147)	1.08 [0.86 to 1.35]	1.25 [0.88 to 1.78]
	Possible daytime somnolence disorder, % (n)	1.3 (31)	1.3 (24)	1.04 [0.61 to 1.77]	1.10 [0.45 to 2.66]
OSA	Snoring loudly, % (n)	23.4 (575)	18.7 (379)	<b>1.33 [1.15 to 1.54]</b>	1.02 [0.81 to 1.28]
	Stopped breathing in sleep, % (n)	9.5 (250)	7.4 (157)	<b>1.30 [1.06 to 1.60]</b>	1.12 [0.80 to 1.56]
	Possible obstructive sleep apnea, % (n)	14.5 (378)	10.1 (212)	<b>1.52 [1.27 to 1.81]</b>	<b>1.39 [1.04 to 1.87]</b>
RBD	Acting out on dreams while asleep, % (n)	9.9 (274)	11.2 (251)	0.87 [0.72 to 1.04]	1.07 [0.81 to 1.41]
	Possible RBD (excluding confounds), % (n)	3.7 (72)	4.3 (72)	0.84 [0.60 to 1.17]	0.90 [0.54 to 1.50]
RLS	Experiencing uncomfortable feeling in legs while sitting or lying down, % (n)	35.1 (978)	30.9 (693)	<b>1.20 [1.07 to 1.36]</b>	1.19 [0.99 to 1.44]
	Experiencing urge to move legs while sitting or lying down, % (n)	36.4 (1013)	32.3 (723)	<b>1.20 [1.07 to 1.35]</b>	1.16 [0.97 to 1.39]
	Possible restless leg syndrome, % (n)	24.9 (531)	21.3 (379)	<b>1.22 [1.05 to 1.42]</b>	1.08 [0.85 to 1.36]

The above table compares distribution of each sleep condition in postmenopausal and pre/perimenopausal women, excluding hormone therapy (HT) users. OSA, obstructive sleep apnea; PTSD, post-traumatic stress disorder; RBD, rapid eye movement sleep behavior disorder; RLS, restless leg syndrome. <sup>a</sup>Odds ratio adjusted for age, marital status, child numbers, education, income, satisfaction with income, BMI, physical activity, smoke, alcohol, diet, anxiety, depression, PTSD, psychological distress, physician-diagnosed thyroid dysfunction, cancer and hypertension. (Please note that HT use is not included in the adjustment model.)

<sup>b</sup>For this cell, mean difference (B-coefficient and 95% CI) is presented, instead of odds ratio, because “sleep hours” is a continuous variable.

studies did not find higher sleep disorders in postmenopausal women compared with premenopausal women.<sup>27-30</sup> Moreover, there has been no consensus on which specific sleep disorders are associated with menopausal status. Our study, which included a very large sample, the assessment of numerous sleep disorders, and the ability to adjust for key confounds, was able to address this important area.

### Menopausal status and insomnia

Our primary finding was an increase in sleep-onset insomnia in the postmenopausal state. Some previous large cohorts have examined the interaction between menopause and insomnia, with conflicting results. A subcohort of the Study of Women’s Health Across the Nation (SWAN) study of 3,045 women compared insomnia in different stages of the menopause cycle prospectively over 7 years’ follow-up. Similar to our results, they showed increased difficulty falling asleep with menopause. However, contrary to our study, postmenopausal and late perimenopausal women also had a higher rate of multiple awakenings during night and early morning awakening compared with premenopausal and early perimenopausal.<sup>6</sup> In a multinational study across 6,079 women aged 40 to 59 years in 11 Latin American countries, there was progressively poorer scores on the Pittsburgh Sleep Inventory and Athens Insomnia scale from the premenopausal to the late postmenopausal period.<sup>50</sup> Because age and other factors were not adjusted for, the effects of age could not be disentangled from menopause itself. The British

Birth Cohort study evaluated trouble sleeping over the prior 2 weeks in a sample of 1,498 women all aged 47 years; they found a 3.4-fold higher prevalence of trouble sleeping in the postmenopausal state, and 1.5-fold increase in the perimenopausal state, compared with premenopausal women. Hot flashes, and psychological and somatic symptoms were described as possible etiologies for this difference.<sup>51</sup> By only including 47-year-old women, age effects were controlled; however, only 76 women (5.1%) were postmenopausal at the time of study. Moreover, the study included only one question regarding ‘trouble sleeping,’ so discrete sleep disorders could not be measured. Finally, a cohort study of 2,400 Korean women found a higher frequency of onset of insomnia, maintenance insomnia, and daytime somnolence in perimenopausal versus premenopausal women. However, no differences were seen comparing postmenopausal with premenopausal women.<sup>27</sup> The different findings can be explained by a higher age difference between post and premenopausal women (12 years) in their study. Because we restricted the age group, our study had less age difference between post and pre/perimenopausal groups (ie, 6 years), and postmenopausal women had a more recent transition to menopause. If sleep complications secondary to menopause peak around menopause transition period, but then resolve, they would no longer be present if women were interviewed too late after the menopause transition. Future studies examining prospective changes in sleep in our cohort will be able to address this possibility.

### Menopausal status and sleep apnea symptoms

We also found a link between menopause and possible OSA diagnosis (although there were no significant differences in individual subcriteria for apnea screening).

Mirer et al, in the Sleep in Midlife Women Study, assessed OSA in 219 women with different menopausal states, by measuring apnea-hypopnea index (AHI), using in-home polysomnography. After adjustment for age, BMI, and waist and neck circumferences, they found increasing trend of higher AHI from premenopausal, to perimenopausal, and postmenopausal stages.<sup>52</sup> Results of 50,473 Nurses' Health Study (NHS) and 53,827 Nurses' Health Study II (NHSII) participants showed an association between OSA symptoms and earlier menopause age.<sup>53</sup> In a study on 1,691 women aged 40 to 65 years, possible OSA was more common in postmenopausal compared with pre and perimenopausal women, after adjusting for age, smoking, and BMI.<sup>54</sup> It is unclear why menopause and OSA would be linked. Reproductive hormones are suggested as protective factors for OSA; for example, progesterone has a stimulatory effect on ventilation drive and also on expanding the upper airway tract.<sup>55</sup> Therefore, its reduction in menopause may increase apnea risk. Furthermore, alterations in sex hormones can change the distribution of fat after menopause, increasing fat mass in trunk and abdomen, increasing neck circumference, and thereby increasing risk of apnea.<sup>56,57</sup>

### Menopausal status, sleep satisfaction, RLS, and RBD

We did not find significant differences in sleep satisfaction between postmenopausal and pre/perimenopausal women. This is similar to the results of the study by Tao et al<sup>28</sup> and Freeman et al.<sup>29</sup> However, other studies have reported increased prevalence of overall sleep dissatisfaction after menopause.<sup>22,58,59</sup> In a study by Young et al,<sup>30</sup> postmenopausal participants had higher self-reported sleep dissatisfaction, but showed longer and deeper sleep on objective polysomnography measures. Of note, sleep satisfaction is a construct that is dependent on mental status and psychological distress (eg, for the same amount of objective sleep disturbance, those experiencing anxiety or depression may report different subjective satisfaction). Because of the comprehensive nature of our cohort, we were able to adjust for psychological disorders.

Similarly, we found no significant decrease in self-reported sleep hours after menopause (ie, only a 4-minute differences between groups), consistent with polysomnographic studies of Xu et al<sup>60</sup> and Freedman and Roehrs,<sup>61</sup> which showed no difference in total sleep time before and after menopause.

Until now, there has been little known about the association between menopause and possible RBD. In sleep clinics, approximately 80% of RBD patients comprised of men,<sup>62</sup> suggesting a role of sex in RBD. However, controlled epidemiologic studies often find no true sex difference,<sup>63</sup> which may suggest the possibility of sex-specific selection/presentation bias. Here we found no significant difference between

postmenopausal and pre/perimenopausal groups, suggesting that hormonal changes may not be directly responsible for any sex differences in RBD.

The prevalence of RLS in our study was similar between women before and after menopause. This is consistent with findings by a 5000-participant Swedish study, and a 334-participant Italian study.<sup>64,65</sup> As iron deficiency has an important role in the pathophysiology of RLS,<sup>66,67</sup> one might have expected a higher prevalence of RLS in premenopausal women (because of iron deficiency due to menstruation). It is possible that differences in iron level may be counterbalanced by increased recognition of RLS symptoms simply due to sleep-onset insomnia (ie, one has to be awake to experience RLS, so those with subclinical RLS may be unaware of their symptoms if they fall asleep before they can be experienced). It should be noted that there was no clinician interview to rule out possible RLS confounds. Absence of clinician interview reduces specificity; one study found a reduction of specificity from 94% to 45%, translating to a positive predictive value of 55% for a positive RLS screen in the general population.<sup>68-70</sup> Any nonspecificity could reduce power to see true differences.

Some limitations of our study should be noted. First, in the CLSA, vasomotor symptoms of menopause were not evaluated, and so could not be directly assessed for their role in determining sleep disorders. Our study did not also distinguish premenopausal from perimenopausal states (the perimenopausal state can be difficult to reliably identify cross-sectionally, so the item queried whether periods had stopped for 1 year). Therefore, those sleep disorders that are associated with the immediate perimenopausal period would be added into the premenopause group, tending to wash out differences between groups. Further questions related to menopausal symptoms (hot flashes, changes in menstrual frequency, irregular rhythm, etc) would have been useful to assess this state. Fortunately, because the CLSA has a prospective follow-up in which menopausal state will be reassessed, we will be able to directly measure the effect of the perimenopausal transition in future studies. This will also allow us to assess the stability and evolution of sleep changes over time in these women. Second, with regards to OSA, there was no direct measurement of neck circumference, preventing full evaluation of the Snoring, Tiredness, Observed apnea, blood Pressure, Body Mass Index, Age, Neck Circumference and Gender (STOP-BANG) questionnaire. Moreover, the data were self-reported. We also did not have input from bed partners or caregivers, symptoms of RBD or daytime somnolence, in particular, may be under-reported, as participants themselves may not be aware of symptoms. Finally, although we could assess some medications which were self-reported for specific symptoms (eg, anxiety/depression), the full CLSA medication module was not yet available, and therefore we could not fully adjust for all medication use.

On the contrary, our study has notable strengths. Based on our knowledge to date, this is among the largest population-based studies to systematically assess sleep disorders.

Moreover, rather than restricting to overall sleep satisfaction or single sleep disorders, we were able to simultaneously assess a more comprehensive list of sleep symptoms and disorders. Finally, because of the comprehensive nature of the CLSA, we had the ability to adjust for many possible confounding variables.

### CONCLUSIONS

In conclusion, we observed a specific effect of menopause on sleep-onset insomnia and OSA, which persists after adjusting for age and numerous covariates. Further research is warranted to explore the mechanisms of this effect and the potential for specific treatments.

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