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Sleep disturbances are associated with cognitive impairment in postmenopausal women

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ABSTRACT

To evaluate the association between severe sleep problems and mild cognitive impairment (MCI) in postmenopausal women, we conducted a sub-analysis of a cross-sectional, multinational investigation between January and November 2023 among postmenopausal women younger than 70 years attending gynecological consultations in nine Latin American countries. MCI was assessed using the Montreal Cognitive Assessment (MoCA) tool, and severe sleep problems were evaluated with two validated instruments: the third question of the Menopause Rating Scale (MRS, score ≥3) and the Jenkins Sleep Scale (JSS, total score ≥12). Two adjusted logistic regression models were used to examine the association between the two measures of severe sleep problems and MCI, adjusting for relevant covariates. The analysis included 1,185 postmenopausal women with a mean age of 56.9 years. Severe sleep problems were significantly more frequent among women with MCI compared to those without MCI, whether assessed by the MRS (28.3 percent vs. 16.6 percent) or the JSS (31.6 percent vs. 18.4 percent; both $p < .001$). In adjusted regression models, severe sleep problems remained independently associated with MCI (MRS: aOR = 1.81, 95 percent CI: 1.26–2.60; JSS: aOR = 1.88, 95 percent CI: 1.31–2.69). Additional factors associated with a higher likelihood of MCI included physical inactivity and greater parity, while ever-use of menopausal hormone therapy and higher

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educational attainment were associated with a reduced likelihood of MCI. In this sample of postmenopausal Latin American women, severe sleep problems were associated with a higher likelihood of MCI, and factors such as physical inactivity, educational attainment, parity, and ever use of menopausal hormone therapy were also independently related to this condition.

Introduction

Menopause represents a significant milestone in a woman's life, marked by cessation of ovarian function and a decline in estrogen and progesterone levels. This hormonal reduction can adversely impact both physical and mental health. By 2030, approximately 1.2 billion women worldwide will have reached menopause (Verde et al. 2022; Zhang and Cheng 2024).

Sleep problems are common during the menopausal transition and postmenopause, presenting as frequent nighttime awakenings that affect sleep duration, continuity, satisfaction, and quality (Maki, Panay, and Simon 2024; Proserpio et al. 2020; Zhang and Cheng 2024). The 2005 NIH State-of-the-Science Conference highlighted sleep problems as a major symptom of menopause (NIH 2005).

Multiple biopsychosocial factors contribute to these sleep disturbances during female midlife, including hormonal fluctuations along the hypothalamic-pituitary-gonadal axis, changes in neuronal activity, and alterations in neurotransmitters regulating reproductive and sleep-wake functions (Verde et al. 2022). Hormonal imbalances affect 40–60 percent of postmenopausal women, influencing sleep architecture and reducing REM sleep, total sleep time, and sleep quality (Baker et al. 2018; Hachul et al. 2021; Kang et al. 2022; Liu et al. 2022). Nighttime hot flashes further disrupt sleep, while shorter sleep duration may worsen menopausal symptoms, creating a bidirectional relationship (Y. Li et al. 2021). Additional contributors include mood disturbances, fatigue, social isolation, chronic pain, comorbidities, and life stressors (Hachul et al. 2021; Kang et al. 2022; Liu et al. 2022).

Sleep is essential for restorative physiological processes, including optimal organ function and cellular repair (Baranwal, Yu, and Siegel 2023), and supports memory consolidation and cognitive performance (Brodt et al. 2023). Disrupted sleep is associated with increased risk of cardiovascular, metabolic, mental, and cognitive disorders (Zhang and Cheng 2024). Cognitive impairment has been defined by the WHO (2019) as a condition involving disruptions in brain functions such as memory, attention, and learning, which may be related to normal aging. Mild cognitive impairment (MCI) represents an intermediate stage between normal aging and dementia. Understanding whether sleep problems contribute to MCI in postmenopausal women is critical for early prevention and intervention.

Evidence suggests that sleep problems correlate with poorer cognitive function (Brodt et al. 2023; Kyle et al. 2017; J. Li et al. 2022; Ma et al. 2020), yet data on postmenopausal women remain limited, particularly in diverse populations. Therefore, the objective of this sub-analysis was to investigate the association between severe sleep problems and MCI in postmenopausal women.

Materials and methods

Study design and participants

The present document presents a sub-analysis of a cross-sectional, multinational study (REDLINC XII) conducted between January and November 2023 in general gynecological consultations in nine Latin American countries: Argentina, Bolivia, Brazil, Colombia, Costa Rica, Ecuador, México, Panamá, and Perú. The main objective of the REDLINC XII study was to assess the association of the type of menopause (spontaneous or surgical) and cognitive decline (Espinoza et al. 2024). In this sub-analysis, we explore the association between sleep

problems and MCI. The participants of the REDLINC XII were otherwise postmenopausal women under 70 years of age who attended a routine gynecological checkup (convenience sampling from clinical settings). They were required to be literate in either Spanish or Portuguese (Brazil) language, and most of them had moderate incomes and accessed health-care services from private and state clinical centers (highlighting the clinic-based nature and potential impact on generalizability). We excluded those who declined to participate, as well as women who had undergone chemotherapy or radiotherapy. Additionally, participants who were deaf or blind or had been diagnosed with dementia that impaired their ability to understand the questionnaires were not included in the study.

Studied variables

The following data were collected: age (years), educational attainment (university, yes/no), body mass index (BMI; weight [kg] divided by height squared [m^2]), number of children, current partnership status (yes/no), sexually active (at least one sexual intercourse in the last year, yes/no), smoking status (yes/no), physical inactivity (less than 150 min per week of moderate aerobic activity such as brisk walking, cycling, recreational sports, or dancing recorded as yes/no), postmenopausal stage (defined according to the STRAW +10 criteria as ≥12 months of amenorrhea), type of menopause (surgical, premature, natural), ever use of menopausal hormone therapy (MHT, current or past use), current use of psychotropic medications (including antidepressants, hypnotics, or anxiolytics, recorded as yes or no), and presence of comorbidities (defined as presenting one or more of the following conditions: receiving treatment for dyslipidemia, diabetes mellitus, or hypertension; indicated as yes or no).

Cognitive testing

Cognitive function was evaluated with the Montreal Cognitive Assessment (MoCA) tool. This is a cognitive screening instrument developed in Canada by Nasreddine et al. (2005) to identify individuals who have MCI. MCI is considered a transitional stage between normal aging and dementia, particularly Alzheimer's disease. The prevalence of MCI varies between 3 percent and 42 percent across different studies, depending on the used diagnostic criteria (Ward et al. 2012). Research indicates that approximately every year 10–15 percent of individuals with MCI progress to dementia. Currently, many studies investigate MCI as a preceding stage of dementia (Petersen et al. 2001).

The MoCA assesses six cognitive domains within a 10-min timeframe, including memory, visuospatial ability, executive function, attention, language, and orientation, with a maximum obtainable score of 30 points. In its original version, the cutoff point for MCI was set at 26 points (Panza et al. 2005). An additional point is added if the individual has fewer than 12 years of education. It has been suggested that the MoCA surpasses the Mini-Mental State Examination (MMSE) tool in sensitivity and specificity for the detection of MCI, 90 percent and 87 percent, respectively, for the MoCA, compared to 18 percent and 100 percent, respectively, for the MMSE (Nasreddine et al. 2005).

During the Spanish language validation of the MoCA test, Lozano-Gallego et al. (2009) used a cutoff of 21 points to identify MCI, demonstrating a sensitivity of 71.4 percent and a specificity of 74.5 percent. In Brazil, the Portuguese language version of the MoCA used a cutoff value similar to that of the Spanish language version (that is 20 points or less positive for MCI) (Freitas et al. 2010). In the present sub-analysis, we used a total MoCA score of 20 or less, adjusted for educational level, to define MCI (Freitas et al. 2010; Lozano-Gallego et al. 2009).

In the REDLINC XII study, a physician administered the general questionnaire and the MoCA, and conducted a comprehensive examination of each woman, recording her personal and family medical history. To establish the presence of sleep problems, two tools were used to identify self-perception of

difficulty with sleep: The Jenkins Sleep Scale (JSS) (Jenkins et al. 1988) and the Menopause Rating Scale (MRS) (MRS. ZEG Berlin).

The Jenkins Sleep Scale (JSS)

This is a 4-item instrument that assesses the frequency and intensity of sleep problems over the past 4 weeks: difficulty falling asleep, difficulty staying asleep, waking up several times during the night, feeling tired or worn out after usual sleep (Jenkins et al. 1988). Each item is scored on a Likert scale of six response options: Never (0), 1–3 days (1), 4–7 days (2), 8–14 days (3), 15–21 days (4) and 22–31 days (5). The JSS is a short, easy-to-use instrument with good psychometric properties, where higher scores (per item and total) indicating poorer sleep quality. A total score of ≥12 points is classified as indicative of severe sleep problems (Duruöz et al. 2017). The JSS has been cross-culturally validated in five Spanish-speaking Latin American countries (Palao-Loayza et al. 2024).

The Menopause Rating Scale (MRS)

This scale evaluates 11 menopausal symptoms (11 items), with participants rating each symptom on a 5-point scale from 0 (not present) to 4 (very severe). Item # 3 of the MRS assesses the presence and intensity of sleep problems (difficulty in falling asleep, difficulty in sleeping through the night, waking up early) (Menopause Rating Scale n.d.). For this sub-analysis, severe sleep problems were defined as a score ≥3 on item 3 of the MRS. The MRS been has previously validated in both the Spanish and Portuguese (Brazil) languages, ensuring the reliability and accuracy of the collected data in these linguistic contexts (Menopause Rating Scale, n.d.).

Sample size calculation

Assuming that 20 percent of postmenopausal women experience sleep problems (Arteaga et al. 2025) and aiming to estimate their effect on cognition with an odds ratio of 2 (observed result 1.88), we calculated the required sample size at a 5 percent significance level (two-sided test) and 80 percent power. With a 2:1 ratio of women without severe sleep problems to cases, this resulted in 123 cases with sleep problems and 245 women without severe sleep problems (CDC 2025).

Statistical analysis

Statistical analysis was performed using SPSS software (version 21.0 for Windows; SPSS Inc., Chicago, IL). Data are presented as mean ± standard deviations, percentages (with 95 percent confidence intervals [CI]), odds ratios (OR) and their 95 percent CIs. Levene's test was used to assess the homogeneity of variance, with $p > .05$ indicating homogeneity. The Kolmogorov–Smirnov test was applied to evaluate the normality of the data distribution. Based on these results, differences between numeric variables were analyzed with the Mann-Whitney U test (non-parametric data) or the Student's T test (parametric data). Categorical data were analyzed using the chi-square test. Logistic regression analysis was conducted to assess the association between sleep problems (independent variable) and MCI (dependent outcome), adjusting for relevant covariates. Two models were used: Model 1, incorporating "severe sleep problems" defined by item # 3 of the MRS (score ≥3) and Model 2, incorporating "severe sleep problems" defined by the JSS (total score ≥12). Categorical covariates were included in the models without modification, while continuous variables were dichotomized based on their median values. All relevant sociodemographic and clinical characteristics (Table 1) were initially tested as covariates using a stepwise procedure, with a significance level of 10 percent for entry. Variables not reaching statistical significance ($p > .05$) were not retained in the final models. Variance Inflation Factor (VIF) was used to assess multicollinearity, with VIF < 10 indicating

Table 1. Characteristics of women based on the presence or absence of mild cognitive impairment (MoCA total score 20 or less).

	Mild cognitive impairment		
Characteristics	No (83.5 percent; $n = 989$)	Yes (16.5 percent; $n = 196$;)	p value*
Age (years)	55.4 ± 6.6	55.1 ± 7.9	NS[1]
Body mass index (kg/m^2)	26.3 ± 4.9	27.3 ± 6.4	.049[2]
Number of children	2.2 ± 1.6	3.2 ± 2.4	<.001[2]
Has a partner currently	72.5 (69.7–75.3)	72.5 (66.1–78.8)	NS[3]
Sexually active	68.7 (65.8–71.6)	58.7 (51.7–71.7)	.007[3]
University graduate	47.0 (44.1–50.3)	18.4 (12.9–23.8)	<.001[3]
Surgical menopause	19.8 (17.3–22.3)	25.5 (19.4–31.7)	NS[3]
Premature ovarian insufficiency	23.1 (20.4–25.7)	17.9 (12.5–23.3)	NS[3]
Menopause hormone therapy (ever use)	39.9 (36.9–43.0)	15.5 (10.2–20.4)	<.001[3]
Physical inactivity	48.0 (44.9–51.2)	68.4 (61.8–74.9)	<.001[3]
Smoking status	27.0 (24.2–29.8)	26.5 (20.3–32.8)	NS[3]
Current psychotropic drug use	33.8 (30.8–36.7)	31.1 (24.6–37.7)	NS[3]
Presence of comorbidities	44.1 (41.0–47.2)	49.0 (41.9–56.0)	NS[3]

Data are presented as mean ± standard deviations or percentages (95 percent confidence intervals). *p value as determined with the Student's T test[a], the Mann Whitney U test[b], or the chi-square test[c]. NS, non-significant.

significant multicollinearity. Interactions between variables found to be statistically significant in the bivariate analysis were also considered. For all analyses, a p value <0.05 was considered statistically significant.

Ethical considerations

The REDLINC XII study was approved by the Ethics Committee of the Southern Metropolitan Health Service, Santiago de Chile, Chile (Memorandum 15/2022; June 22, 2022) and conducted in accordance with the Declaration of Helsinki. All participants were informed about the study objectives and the assessment tools used and provided written informed consent prior to participation.

Results

The REDLINC XII study included 1,185 postmenopausal women with varying types of menopause. Among them, 939 experienced spontaneous menopause (263 before and 676 after age 40), while 246 underwent surgical menopause (bilateral oophorectomy: 136 before and 110 after age 40). The participants' mean age was 55.3 years, with an average BMI of 26.4 kg/m^2. On average, women had 2.5 children, 74.2 percent reported having a partner, and 69.2 percent had engaged in sexual activity within the past 12 months. The mean educational attainment was 10.4 years, with 46.0 percent holding a university degree.

Table 1 presents a comparison of characteristics between women with and without MCI. Among the surveyed women, 16.5 percent had MCI. Compared to those without MCI, these women exhibited higher BMI, a greater number of children, and higher levels of physical inactivity. They also reported lower sexual activity, lower educational attainment, and less frequent ever MHT use. No significant differences were observed in age, partner status, age at menopause, smoking habits, current use of psychotropic medications, or comorbidities.

Table 2 presents the assessment of sleep using the MRS and the JSS. Women with MCI showed higher MRS item # 3 mean scores and a greater prevalence of severe sleep problems (MRS item #3 score ≥3). Specifically, 28.3 percent of women with MCI reported severe sleep problems compared to 16.6 percent of women without MCI. Findings from the JSS were consistent, with all four items and the total score indicating poorer sleep quality among women with MCI. According to the JSS, 31.6 percent of women with MCI experienced severe sleep problems, compared with 18.4 percent of women with normal cognition (Figure 1). Rate of severe sleep problems comparing both tools was similar (28.3 percent vs. 31.6 percent).

Table 2. Sleep problem assessment in women with and without mild cognitive impairment.

	Mild cognitive impairment		
Used tools	No (*n*=989)	Yes (*n*=196)	*p* value*
Menopause Rating Scale item #3 (Sleep problems)			
Average obtained score on item #3	1.07 ± 1.27	1.49 ± 1.52	<.001[1]
Severe sleep problem[c]	16.6 (14.3–18.9)	28.3 (19.9–36.8)	<.001[2]
Jenkins Sleep Scale			
Difficulty falling asleep	1.90 ± 1.38	2.23 ± 1.71	.011[1]
Difficulty staying asleep	2.21 ± 1.60	2.64 ± 1.86	.003[1]
Waking up several times during the night	1.85 ± 1.35	2.44 ± 1.79	<.001[1]
Feeling tired or worn out after usual sleep	2.05 ± 1.41	2.48 ± 1.85	.002[1]
Total Jenkins score	8.01 ± 4.69	9.79 ± 6.52	<.001[1]
Severe sleep problem[d]	18.4 (16.0–20.8)	31.6 (25.1–38.2)	<.001[2]

Data are presented as mean ± standard deviations or percentages (95 percent confidence intervals). * *p* value as determined with the Mann Whitney *U* test[a] or the chi-square test[b].
[c]MRS item # 3 score ≥3 points; [d] JSS total score of ≥ 12 points.

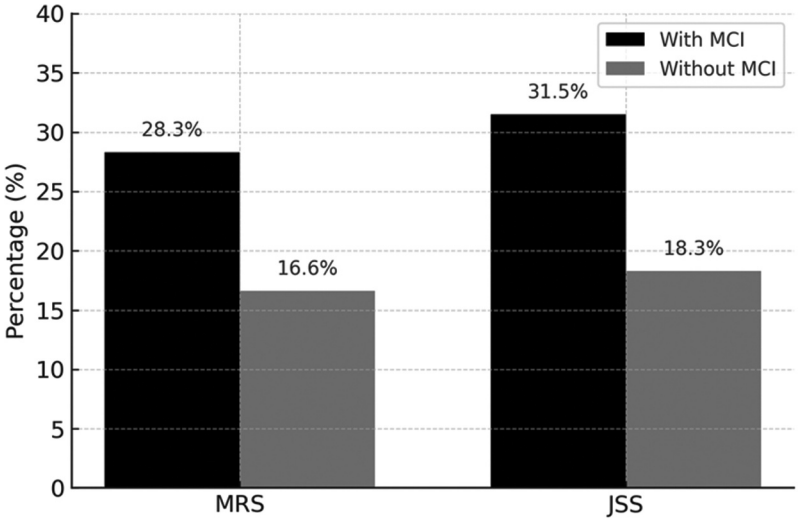

Figure 1. Prevalence of severe sleep problems (MRS and JSS) in women with and without mci, showing higher rates among those with mci.

Table 3 shows two logistic regression models examining the association between severe sleep problems and MCI (dependent variable), adjusting for the relevant covariates listed in Table 1. In Model 1, severe sleep problems, as measured by the MRS, were significantly associated with MCI (OR 1.81; 95 percent CI 1.26–2.60). Other factors positively associated with MCI included physical inactivity (OR 1.61; 95 percent CI 1.14–2.28) and having more than two children (OR 1.50; 95 percent CI 1.07–2.09). Protective factors were ever use of MHT (OR 0.38; 95 percent CI 0.25–0.58) and attainment of a university degree (OR 0.34; 95 percent CI 0.23–0.51). Model 2, using the JSS to define severe sleep problems, showed a similar pattern of associations.

Discussion

The present study found that severe sleep problems, assessed with two validated instruments, were significantly associated with MCI in postmenopausal women across nine Latin American countries. These findings highlight the potential impact of sleep disturbances on cognitive health in this population, even after adjusting for relevant sociodemographic and clinical

Table 3. Adjusted logistic regression analysis of factors associated with mci using two models.

Model 1 Using the MRS	aOR (95 percent CI)	Model 2 Using the JSS	aOR (95 percent CI)
Severe sleep problems[a]	1.81 (1.26–2.60)	Severe sleep problem	1.88 (1.31–2.69)
Physical inactivity	1.61 (1.14–2.28)	Physical inactivity	1.67 (1.18–2.35)
More than two children	1.50 (1.07–2.09)	More than two children	1.53 (1.10–2.14)
Ever use of MHT	0.38 (0.25–0.58)	Ever use of MHT	0.37 (0.24–0.56)
University graduate	0.34 (0.23–0.51)	University graduate	0.34 (0.23–0.51)

[a]MRS item # 3 score ≥ 3 points; [b]JSS total score of ≥ 12 points. aOR, adjusted odds ratio; CI, confidence interval; MRS, Menopause Rating Scale; JSS, Jenkins Sleep; MHT, menopausal hormone therapy.
*In both models, all significant sociodemographic and clinical characteristics shown in Table 1 were included as covariates. Variables that were not significantly associated ($p > .05$) are not presented.

covariates. Our results are consistent with those of Bolge et al. (2010) and Utian (2005), who reported that sleep problems may be associated with cognitive decline and reduced alertness. They are also in line with Weber et al. (2021) and Maki and Jaffe (2022), who emphasized that sleep is a significant predictor of memory impairment and verbal performance in perimenopausal women. Moreover, sleep fragmentation has been linked to cognitive deficits, daytime sleepiness, physical and mental fatigue, anxiety, depression, and memory problems (Yaffe, Falvey, and Hoang 2014). A causal relationship has been suggested between short sleep duration or frequent and prolonged sleep deprivation and adverse health outcomes, including depression, overweight, obesity, diabetes, and cardiovascular disease (J. Li et al. 2022; Zhang and Cheng 2024).

Poor sleep quality, a condition that tends to worsen with age, may lead to neurovascular brain lesions, which can clinically manifest as cognitive impairment (Qi et al. 2023). This concept aligns with the restorative sleep theory, which proposes that a proper circadian cycle allows the body to replenish and repair cellular components depleted during wakefulness (Baranwal, Yu, and Siegel 2023; Zhang and Cheng 2024). Sleep disturbances can negatively affect cognitive function through multiple mechanisms, including the excessive accumulation of β-amyloid – a key factor in the progression of Alzheimer's disease – neuroinflammation, the buildup of free radicals, and ongoing disruptions in the balance of cerebral neurotransmitters (Spira et al. 2013). In women in early postmenopause, sleep problems have been associated with increased white matter hyperintensities in the central nervous system. These hyperintensities suggest small ischemic brain lesions or small vessel disease and are additionally linked to stroke, cognitive decline, dementia, and increased early mortality (Thurston et al. 2020).

Chen et al. (2012) reported that individuals with clinically diagnosed insomnia who use hypnotics long term are twice as likely to develop dementia compared to those without insomnia. This finding aligns with our observations and is further supported by Yaffe, Falvey, and Hoang (2014), who suggested that existing data point to a bidirectional association between sleep problems and cognitive impairment. Although the evidence does not establish a causal link between sleep disturbances and cognitive function, several authors (Kyle et al. 2017) have proposed, based on data from the UK Biobank, that lower cognitive performance does not directly precipitate insomnia symptoms. These findings underscore the complex and potentially bidirectional relationship between sleep quality and cognitive health.

In our study, we also observed that physical inactivity was associated with an increased likelihood of cognitive impairment. More broadly, aerobic physical activity has been shown to enhance cognitive abilities, including memory and executive functions (OR 0.37, 95 percent CI: 0.04–0.69), thereby delaying the neurobiological decline associated with aging (Creasy et al. 2019). Regular aerobic exercise has also been linked to an increase in hippocampal volume, as well as gray and white matter within the temporal and prefrontal cortices, along with elevated levels of brain-derived neurotrophic factor (BDNF), insulin-like growth factor-1 (IGF-1), and cerebral blood volume (Hoffmann, Petrov, and Lee 2021).

In our study, higher parity was also associated with an increased likelihood of MCI. This relationship remains controversial, as longitudinal studies have yet to clarify definitively how parity affects cognitive changes. Zhou et al. (2022) reported that women with a higher number of births, compared to those with no births, experienced slower declines in global cognitive function and, consequently, had a lower risk of developing cognitive impairment or dementia.

Regarding protective factors, we observed that ever MHT use and having a university graduate were associated with a lower likelihood of MCI. These findings are consistent with our previous observations in Latin American women, which indicate that MHT use, having a higher educational attainment and maintaining sexual activity were linked to a reduced likelihood of MCI (Blümel et al. 2022).

Healthcare professionals caring for midlife women should prioritize evaluating sleep complaints. This assessment should include a comprehensive medical history that considers the onset and progression of sleep disturbances, overall health status, psychosocial factors, and living conditions. It is essential to distinguish whether sleep problems are symptoms of menopause or reflect primary sleep/wake cycle disorders, as this differentiation is critical for accurate clinical interpretations and guiding the most appropriate therapeutic interventions.

The *International Classification of Sleep Disorders* of the American Academy of Sleep Medicine (American Academy of Sleep Medicine 2023) and the DSM-5-TR of the American Psychiatric Association (APA 2022) are valuable tools for determining whether sleep disturbances are related to menopause or represent primary sleep disorders. In addition, sleep complaints should be objectively evaluated using methods such as actigraphy or polysomnography, in accordance with established guidelines. It is important to note that self-reported sleep disturbances often appear more severe than those detected by objective measurements (Freedman and Roehrs 2007). A multidisciplinary approach to management and intervention can be beneficial. This may include cognitive behavioral therapy, MHT, prolonged-release melatonin, and respiratory devices, among other options (Maki, Panay, and Simon 2024). Furthermore, education focused on correcting poor sleep habits is essential, as adequate and high-quality sleep is vital for optimal brain health, cognitive function, immune and metabolic health, psychological well-being, and overall quality of life (J. Li et al. 2022; Qi et al. 2023; Xiong et al. 2022; Zhang and Cheng 2024).

This study has several limitations. Firstly, its cross-sectional design precludes causal inference. Second, we did not assess the underlying causes of sleep disturbances or MCI, which may have introduced bias. Third, sleep quality was evaluated solely through subjective measures, and while the frequency of severe sleep problems was recorded, this may not fully reflect the clinical presence of sleep disorders (Scott et al. 2023); future studies incorporating objective measures such as polysomnography are warranted. Fourth, restricting the sample to women in the late postmenopausal stage may have led to inaccuracies in menopausal age and clinical history. Fifth, the overrepresentation of women with menopause before age 40 could be considered a limitation, though it may also be a strength, as this group is more prone to sleep disturbances (Ates et al. 2022). Sixth, the study lacked detailed information regarding the type of used MHT, including the formulation, route of administration, and treatment duration. Seventh, mood disorders (depression and anxiety) may act as potential confounders or mediators; however, psychotropic medication use did not differ by MCI status, which is somewhat reassuring. Eighth, participants were recruited from both public and private healthcare services, which may affect the generalizability of the findings and represents a potential source of selection bias. Ninth, other factors influencing sleep and cognitive function, such as stress and underlying health conditions, were not fully captured and may represent unmeasured confounders. Finally, menopausal symptoms were not included as covariates in the regression models assessing the association with MCI, as the focus of this analysis was on sleep problems; and the relationship between menopausal symptoms and MCI has been evaluated in the same cohort in detail elsewhere (Calle et al. 2024).

Despite the aforementioned limitations, several strengths of the study should be highlighted. Validated and widely recognized tools were used to assess both sleep problems and cognitive function, enhancing the reliability of the findings. The multicenter design minimized the risk of

bias inherent to single-site studies, and the inclusion of participants from both private and public healthcare systems improved the generalizability of the results. Nevertheless, the findings may not fully represent the broader Latin American population, given the region's limited access to preventive health checkups, which introduces potential selection bias. Both validated tools demonstrated comparable effectiveness in identifying women with severe sleep problems and their association with MCI. Notably, we previously evaluated the accuracy of MRS in diagnosing sexual dysfunction among climacteric women (Jara et al. 2009), underscoring the value of validated menopausal instruments that reliably correlate with other health conditions. Finally, all participants were assessed by women's health specialists, and robust statistical methods were employed to control for multiple potential confounders, further strengthening the study's overall rigor.

In conclusion, this multicenter study of postmenopausal Latin American women demonstrates that severe sleep problems are associated with an 80 percent increased likelihood of MCI. In addition, factors such as physical inactivity, lower educational attainment, higher parity, and MHT use were also independently related to MCI risk. These findings highlight the importance of systematically assessing sleep quality and modifiable lifestyle factors in postmenopausal women, as early identification and intervention may play a critical role in reducing the burden of cognitive decline in this population. Clinical practices and intervention strategies promoting healthy sleep habits, along with consideration of MHT, may help protect against MCI. Future longitudinal and interventional studies are needed to determine whether improving sleep in postmenopausal women can mitigate cognitive decline, which would help clarify causality and potential cognitive benefits.

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Authors' contributions

Alvaro Monterrosa-Castro contributed to the conception and design of this sub-analysis, as well as data collection and text revision.

Juan E. Blümel contributed to the conception and design of this sub-analysis, performing statistical analysis, and text preparation and revision.

Peter Chedraui contributed to the conception and design of this sub-analysis, performing statistical analysis, and text preparation and revision.

Alejandra Elizalde contributed to data collection and text revision.

María T. Espinoza contributed to data collection and text revision.

Carlos Escalante contributed to data collection and text revision.

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Mónica Ñañez contributed to data collection and text revision.

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Marcio A. Rodrigues contributed to data collection and text revision.

Carlos Salinas contributed to data collection and text revision.

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María S. Vallejo contributed to data collection and text revision.

Andrés Calle contributed to data collection and text revision.

Maribel Dextre contributed to data collection and text revision.

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Disclaimer

The views expressed in the submitted article are of the authors alone.

Availability of dataset

All required information regarding the REDLINC XII protocol, collected data and the sub-analysis will be made available upon a reasonable request to the corresponding author (Alvaro Monterrosa-Castro).

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