Association of reported sleep disturbances with objectively assessed mild cognitive impairment among adults in the **United States**

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Abstract

Background: Sleep is a multifaceted phenomenon influenced by both duration and quality. Various sleep disturbances have been associated with mild cognitive impairment, but the role of specific disturbances in mild cognitive impairment pathophysiology remains unclear. This study investigated the associations between distinct sleep disturbances and mild cognitive impairment in adults aged 50 and older using nationally representative data.

Methods: Longitudinal data from the Health and Retirement Study were analyzed to explore the association between mild cognitive impairment and three types of sleep disturbances: trouble falling asleep, trouble waking up, and waking up too early. Logistic regression models estimated unadjusted (Model I) and adjusted associations accounting for sex, race/ethnicity, age, social determinants of health (Model 2), general health (Model 3), depression (Model 4), and pain and physical activity (Model 5). **Results:** The study cohort included 8877 participants aged \ge 50 years in 2018 (baseline) who were followed up in 2020. Overall, 15.4% reported trouble falling asleep, 23.2% reported trouble waking up, and 12.8% reported waking up too early and being unable to fall back asleep most of the time. Among older adults, approximately 13.1% reported experiencing mild cognitive impairment; The prevalence of mild cognitive impairment was even higher in those who experienced sleep disturbances. The unadjusted odds ratio (uOR) for experiencing trouble falling asleep most of the time was 1.69 (95% CI: 1.42–2.03), for trouble waking up most of the time was 1.31 (95% CI: 1.10–1.57), and for waking up early most of the time was 1.88 (95% CI: 1.51–2.35). However, these positive associations attenuated depending on the covariate adjustment.

Conclusions: Nearly one in seven adults had mild cognitive impairment. The relationship between sleep disturbances and mild cognitive impairment has been challenging to delineate. Our findings demonstrate a positive association between sleep disturbances and mild cognitive impairment, although these associations were sensitive to covariate adjustments. These findings suggest multifaceted pathways for reducing the risk of mild cognitive impairment.

Keywords

Mild cognitive impairment, depression, sleep disturbances

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Introduction

Mild cognitive impairment (MCI), a symptomatically mild but recognizable change in memory, is a highly prevalent condition with 12%-18% of older adults, aged ≥ 60 years reporting symptoms.^{1,2} The global prevalence of MCI is estimated at 19.7% with 95% confidence intervals (18.3%– 21.1%).³ MCI can lead to negative health consequences including mortality. Compared to those without MCI, individuals with MCI have greater mortality rates.⁴

MCI is often described as an intermediate stage in the trajectory to dementia.⁵ Older adults with MCI have an increased risk of developing dementia including Alzheimer's disease (AD), a public health crisis with devastating humanistic, clinical, and economic burdens.^{6,7} For example, 10%– 15% of individuals with MCI develop AD (Alzheimer's Association, 2022).² An interesting characteristic of MCI is that it is reversible.⁵ The serious sequelae of MCI to dementia as well as the reversibility of MCI have driven significant interest in MCI early identification and its risk factors.

Existing literature suggests that immutable elements such as age and modifiable factors such as cardiovascular risks, depression, anticholinergic burden, smoking, diet, obesity, comorbid conditions, sensory impairments, pain, alcohol consumption, social isolation, and levels of physical and intellectual activity are associated with cognitive decline and MCI.^{8–14} Health conditions such as depression have been shown to have a complex relationship with MCI.¹⁵

While many factors contribute to the development of MCI, emerging literature has begun to focus on sleep disturbances as a potential modifiable pathway to reduce its risk. There is growing evidence suggesting that improving sleep quality may decrease the risk of cognitive decline leading to MCI. For example, using a population-attributable risk calculation, a meta-analysis concluded that 15% of AD could be prevented by treating sleep disorders.¹⁶ As MCI often precedes AD as a transitional cognitive state, these findings suggest that addressing sleep disturbances may also play a crucial role in preventing or delaying the onset of MCI.

Studies have also established a potential link between sleep disturbances and cognitive decline and MCI.^{17–19} Self-reported sleep quality and daytime sleepiness have been associated with cognitive decline over a 3–4-year timeframe, and variations in sleep duration alongside circadian disruptions have been linked to cognitive decline and increased dementia risk.²⁰⁻²² Compared to healthy controls, persons with MCI had greater sleep disturbances (e.g., waking after sleep onset, reduced total sleep time, and longer sleep onset latency) using objective measures.¹⁷ The prevalence of sleep disturbances in individuals with MCI has been studied in both cross-sectional and longitudinal designs.²³ In a systematic review and meta-analysis of the prevalence of sleep disturbances in individuals with MCI, sleep disturbance prevalence was significantly lower in 16 cohort studies compared to the 28 cross-sectional studies.²¹

Although the relationship between sleep and cognition is bidirectional, studies have explored sleep disturbances as a risk factor for MCI. These studies have yielded mixed findings. While sleep disorders such as a history of insomnia or obstructive sleep apnea significantly increased the risk of MCI among older individuals, some measures of sleep disturbances such as wake after sleep onset and total sleep time were not associated with MCI in some sub-populations such as older women.^{24,25} In a cross-sectional comparison of sleep disturbances among those with and without MCI, no significant differences were found in terms of subjective sleep quality, wake-up time, sleep latency, and daytime dysfunction.²⁶ However, in this study, a composite score was significantly higher among those with MCI, suggesting that sleep disturbances may be a risk factor for MCI.²⁶ In healthy adults, a prospective cohort study found that sleep disturbances predicted MCI.27 However, this study relied on a single binary indicator of nighttime behaviors, derived from responses to the question: "Does the patient awaken you during the night, rise too early in the morning, or take excessive naps during the day?" On the other hand, in a longitudinal cohort study, the presence of sleep disturbance symptoms did not affect the rate of decline in measures of global cognition, executive function, or memory performance in cognitively healthy individuals.²⁸ These findings suggest that the relationship of sleep disturbance with MCI may not be consistent.

Furthermore, the variations in measurements of MCI and sleep disturbances may introduce significant limitations in understanding the role of sleep in MCI. For example, there is no single recommended "gold standard" test to measure MCI.²⁹ MCI can be assessed using various methods, including traditional paper-and-pencil neuropsychological tests, neuroimaging techniques (e.g., magnetic resonance imaging [MRI] and positron emission tomography [PET]), and laboratory-based biomarkers (e.g., cerebrospinal fluid measures of A β and genetic markers). A scoping review article identified a total of 52 different cognitive tools.³⁰

Similarly, while in-lab tests of sleep disturbances provide detailed insights, their generalizability may be restricted due to small sample sizes. Conversely, composite sleep disturbance measures may obscure the specific relationship between sleep disturbances and MCI by equally weighing diverse sleep-related issues (e.g., difficulties in sleep initiation vs maintenance). This approach neglects the intricate nature of sleep disturbances and their potential distinct influences on MCI. Furthermore, many studies combine MCI or dementia as the outcome variable.¹⁹ Given that sleep is a complex phenomenon and the varied types of sleep disturbances, it is imperative to understand their individual associations with MCI. Therefore, this study examined individual sleep disturbance variables and their associations with MCI using nationally representative data of adults aged 50 years or older.

Methods

Data source

This retrospective study based on secondary data analysis utilized a cohort design with longitudinal data from the Health and Retirement Study (HRS), a prospective cohort study of adults aged 50 and older. The HRS is sponsored by the National Institute on Aging and conducted by the Institute for Social Research at the University of Michigan. It surveys a nationally representative sample of over 20,000 non-institutionalized Americans aged 50 and above every 2 years. The primary aim of the HRS is to examine the health, economic, and social factors that influence aging and retirement decisions in the United States.³¹ Ethical approval for this study was waived by the Institutional Review Board because the study is based on a public and deidentified data.

Study cohort and study period

The study cohort included 8877 participants aged \geq 50 years in 2018 (baseline period) and followed up in 2020 (followup period). Participants with dementia (based on self-report or objective assessments) at either the baseline or follow-up were excluded, as were those with missing data on key variables including cognition score and sleep disturbances. Our analytic cohort, weighted according to the HRS sampling methodology, represented a population of 54,656,438 individuals aged 50 years or older.

Dependent variable: MCI without dementia (yes/no)

The dependent variable was MCI without dementia. As stated in the introduction, there is no single recommended "gold standard" test to measure MCI.²⁹ Thus, the HRS cognitive provides a simplified assessment of cognitive function and overlaps with parts of both MMSE and MoCA but does not fully replicate either tool's scope. For example, the HRS cognitive measure overlaps significantly with both the MMSE and the MoCA in key cognitive domains such as memory, orientation, attention, and language. However, it lacks the more detailed executive function and visuospatial ability components found in the MoCA and, to a lesser extent, the MMSE.

We identified MCI without dementia in 2020, 2 years after the sleep disturbances were measured. MCI was based on several objective tests. MCI was identified based on a series of tests, including immediate word recall (score range 0-10), delayed word recall (score range 0-10), serial 7s (score range 0-5), and backward count from 20 (0-2) assessed in 2020. Immediate and delayed word recall tests consisted of 10 words read slowly by the interviewer and recalled by the respondent once immediately (within 2 min)

and once at a later point in time. Scoring of word recall is based on the number of words correctly recalled and can range from 0 to 10. In the serial 7s test, the participant subtracted 7 from 100 in the first step and continued subtracting 7 from the previous number in each subsequent step. Scores on each of these tests can range from 0 to 27, with lower scores representing poorer cognitive performance. We used the standard cut points developed by Lang-Weir (12–27 – no cognitive impairment; 7–11 cognitive impairment and no dementia; and 0–6 dementia).³² Thus, a total score between 7 and 11 indicated MCI without dementia.

The threshold cut points used in our study have been validated against the Aging, Demographics, and Memory Study (ADAMS). The ADAMS selected a subset of respondents from the HRS sample to undergo extensive neuropsychiatric assessment as well as detailed medical, functioning, cognitive, and physical exams.³³ ADAMs assign a diagnosis of dementia, cognitive impairment without dementia, and dementia based on objective assessments. Studies have found a strong agreement of "normal" cognition (87.1%) between ADAMS and the HRS. However, concordance between ADAMS and HRS in identifying MCI without dementia is relatively low, limiting its precision in this category.³⁴

Key explanatory variables: Sleep disturbances

Similarly, there are different definitions for sleep disturbances across different studies. For example, sleep disturbance measurements range from clinical evaluations in overnight in-lab assessments to self-reported composite measures like the Pittsburgh Sleep Quality Index,³⁵ the seven-question Insomnia Severity Index,³⁶ and the Jenkins Sleep Scale.³⁷ The Jenkins sleep scale has a high internal consistency (alpha=0.80) and is a practical scale for studying sleep difficulties.³⁷ The HRS provides a 4-question adapted, validated version of the Jenkins Sleep Scale.^{37,38} These questions are routinely and broadly used in evaluating and screening for sleep quality and sleep disturbances in research.

We assessed sleep disturbances at baseline in 2018. These were measured through responses to questions regarding difficulties falling asleep ("How often do you have trouble falling asleep?"), nocturnal awakenings ("How often do you have trouble with waking up during the night?"), and early morning awakenings with the inability to return to sleep ("How often do you have trouble with waking up too early and not being able to fall asleep again?"). After each of the three questions, respondents were prompted with the following: "Would you say most of the time, sometimes, or rarely or never?" These questions are routinely and broadly used in evaluating and screening for sleep quality and sleep disturbances in research.^{38–43}

Other independent variables

We considered biological factors such as sex (male/female), age (50-64, 65-69, 70-74, 75-79, 80, and more years), race and ethnicity (non-Hispanic White (NHW), non-Hispanic Black (NHB), Hispanic, and others), social determinants of health (SDOH) including living alone (yes/no), education (less than high school, high school, some college, college), employment (yes/no), private insurance (yes/no), poverty (poor, low income, middle income, high income), and lifestyle factors including exercise (yes/no), pain severity (no pain, mild, moderate, severe), general health (fair/poor, good, very good/excellent), and depression. Depression was measured using the Short Form Composite International Diagnostic Interview (CIDI-SF).44 This scale uses items such as loss of interest, appetite, trouble falling asleep, trouble concentrating, feeling down, and thoughts of death. We used a threshold of scoring three or more points to define depression as indicated by the instrument's guidelines (yes, no).45 These variables were chosen based on literature and plausible relationship with MCI.⁴⁶ We used general health as a proxy for chronic conditions because of the high predictive ability of chronic conditions with self-perceived general health.⁴⁷

Statistical analysis

The unadjusted associations of sleep disturbances with MCI were examined using Rao–Scott chi-square tests. The adjusted associations for each sleep variable were evaluated using five nested multivariable logistic regression models, each progressively accounting for additional explanatory variables. Model 1 included only sleep disturbance variables without adjustment. Model 2 controlled for sex, age, race/ ethnicity, and SDOH. Model 3 further incorporated perceived general health, while Model 4 accounted for depression. Finally, Model 5 included adjustments for pain and physical activity. All statistical analyses accounted for the complex survey design of the HRS data using SAS 9.4 (SAS Institute Inc., Cary, NC) Survey procedures.⁴⁸

Results

Overall, the study cohort was 54.4% female, 69.6% NHW, 11.8% NHB, and 12.6% Hispanic (not reported in tabular form). A majority of adults (53.5%) were in the age group 50–64 years; 22.5% lived alone. Nearly one-third (30.8%) were college-educated and 46.3% had high income (>400% FPL). About 23.7% of adults perceived their general health as fair or poor. The prevalence of major depression was 18.2%.

Description by sleep disturbances

Among older adults, 15.4% (most of the time) and 33.8% (sometimes) reported trouble falling asleep, 23.2% (most of the time) and 38.9% (sometimes) reported trouble waking up, and 12.8% and 33.3% reported waking up too early and

being unable to fall back asleep most of the time and sometimes, respectively (Table 1).

Table 1 also summarizes group differences in sleep disturbances. Overall, 25.7% of females reported trouble waking up most of the time, compared to 20.3% of males (p < 0.001). Among different age groups, a higher proportion of individuals aged 50–64 reported trouble falling asleep most of the time compared to those aged 80+ (16.6% vs 13.7%, p < 0.001). We also observed that a higher percentage of Hispanic individuals reported waking up early most of the time compared to NHW (18.6% vs 11.0%, p < 0.001).

With regard to SDOH, individuals with less than a high school education had more trouble waking up most of the time than those with a college education or higher (24.4% vs 20.7%, p < 0.001, Table 1). Individuals with lower income and poor poverty status were more likely to experience trouble falling asleep, waking up, and waking up early most of the time compared to those with higher incomes (p < 0.001).

In terms of health variables, adults who reported perceived poor or fair health had higher rates of sleep disturbances most of the time (trouble falling asleep: 27.7% vs 7.3%; nocturnal awakening: 35.6% vs 16.1%; inability to return to sleep: 23.4% vs 8.0%) compared to those with perceived excellent health. Additionally, participants with depression had a significantly higher prevalence of trouble falling asleep most of the time (36.5% vs 10.7%), trouble waking up most of the time (42.8% vs 18.9%), and waking up early most of the time (25.4% vs 10.0%) compared to those without depression (p < 0.001). A higher percentage of adults with severe pain experienced sleep disturbances most of the time compared to those without pain (p < 0.001).

Association of sleep disturbances with MCI

Among older adults without dementia, nearly 1 in 7 (13.1%) had MCI (Table 2). This prevalence was even higher among those who experienced sleep disturbances. Specifically, 18.5% of those who had trouble sleeping most of the time reported MCI, compared to 11.8% of those who never or rarely had trouble sleeping. Similarly, 15.5% of participants with trouble waking up most of the time reported MCI, compared to 12.3% of those who rarely or never had trouble waking up. The prevalence of MCI was 19.0% among those who woke up early and were unable to fall back asleep most of the time, compared to 11.1% among those who rarely or never experienced this issue (Table 2).

Table 3 summarizes the prevalence of MCI by other characteristics of the study cohort. We observed significant differences in MCI status by all characteristics except sex. For example, older adults, NHB, those who live alone, those with less than high school education, low income, fair or poor general health, major depression, severe pain, and less than moderate or vigorous physical activity had a higher prevalence of MCI compared to younger adults, NHW, not living alone, college education, high income, excellent

All	Trouble falling asleep			Trouble waking up			Waking up early												
	Always % 15.4	Some times <u>%</u> 33.8	Rare/never % 50.8	Always % 23.2	Some Times % 38.9	Rare/never % 37.8	Always % 12.8	Some times <u>%</u> 33.3	Rare/never % 53.9										
										Sex									
										Female	18.3	38.0	43.7	25.7	40.0	34.3	13.9	34.4	51.7
Male	11.8	28.9	59.3	20.3	37.7	42.0	11.5	31.9	56.6										
Age in years																			
50–64 years	16.6	32.9	50.5	23.3	37.9	38.8	14.0	31.9	54.1										
65–69 years	14.7	35.1	50.2	21.3	37.1	41.5	12.1	33.0	54.9										
70–79 years	13.5	35.0	51.5	24.0	40.1	35.9	11.8	34.2	54.0										
80+ years	13.7	34.2	52.0	24.4	44.9	30.7	9.5	39.5	51.0										
, Race and ethnicity																			
, NHW	14.7	33.0	52.3	23.9	39.2	36.9	11.0	33.3	55.7										
NHB	18.4	33.5	48.I	21.4	36.0	42.7	15.3	34.7	50.0										
Latino	15.2	38.8	46.0	21.1	40.6	38.3	18.6	33.7	47.7										
Other race	17.4	33.0	49.5	23.8	37.9	38.3	16.5	29.6	53.9										
Living arrangement																			
Alone	19.1	34.0	46.9	26.0	38.8	35.3	14.4	33.9	51.6										
Not alone	14.2	33.7	52.I	22.4	39.0	38.6	12.3	33.1	54.6										
Education																			
Less than high school	19.0	36.3	44.7	24.4	41.6	34.0	18.4	35.4	46.2										
High school	17.2	35.6	47.2	25.I	38.4	36.6	14.8	33.2	51.9										
Some collage	17.3	33.6	49.0	23.7	37.9	38.4	11.9	34.1	54.0										
College	10.4	31.2	58.4	20.7	39.2	40.1	9.4	31.8	58.9										
Employment																			
Employed	11.5	31.8	56.7	20.1	39.4	40.5	11.4	31.6	56.9										
Not employed	18.1	35.3	46.6	25.4	38.8	35.8	13.8	34.6	51.7										
Poverty status																			
Poor	26.6	35.6	37.9	29.9	37.6	32.5	20.8	36.1	43.2										
Low income	21.0	36.9	42.I	27.2	36.8	36.0	16.4	34.3	49.3										
Middle income	15.8	35.1	49.I	21.6	40.6	37.7	11.7	33.9	54.3										
High income	10.7	31.6	57.7	21.2	39.0	39.8	10.4	31.9	57.7										
Private health insurance																			
Yes	11.8	33.5	54.7	21.4	39.4	39.2	11.1	32.5	56.4										
No	20.1	34.0	45.8	25.8	38.3	35.9	15.1	34.3	50.6										
General health																			
Excellent/very good	8.3	30.1	61.6	16.1	39.3	44.6	8.0	29.5	62.4										
Good	15.2	36.5	48.4	23.I	39.3	37.6	11.3	35.1	53.7										
Fair/poor	27.7	36.3	36.0	35.6	37.8	26.6	23.4	37.0	39.6										
Major depression																			
Yes	36.5	38.4	25.I	42.8	36.7	20.5	25.4	38.6	36.0										
No	10.7	32.8	56.5	18.9	39.4	41.7	10.0	32.1	57.9										
Pain																			
None	8.7	31.8	59.5	16.1	39.3	44.6	9.2	30.1	60.7										
Mild	17.5	37.0	45.5	25.9	41.3	32.7	11.8	38.7	49.5										
Moderate	25.4	37.7	36.9	34.8	38.6	26.6	18.0	38.4	43.6										
Severe	38.2	32.9	28.9	43.7	33.6	22.7	29.8	34.8	35.3										
Physical activity																			
Moderate or vigorous activity >1/week	12.4	32.1	55.4	21.3	38.9	39.8	11.8	31.7	56.5										
No	19.6	36.3	44.I	26.1	39.0	35.0	14.3	35.6	50. I										

 Table I. Description of study cohort by sleep disturbance variables older adults aged 50 or older (weighted row percent) health retirement study, 2018–2020.

NHW: non-Hispanic White, NHB: non-Hispanic Black.

Based on 8877 participants, alive as of 2020 and did not have dementia during baseline (2018) and follow-up (2020) periods. Missing data for living arrangement, education, poverty status, employment, and private health insurance are not reported. Rao–Scott chi-squared tests were used to determine significant group differences by sleep disturbance variables. All variables were significantly associated with sleep disturbance except for trouble falling asleep by age (p=0.128) and waking up early by living arrangement (p=0.148).

All	No MCI		MCI	p-Value	
	N	Wt.%	N	Wt.%	
	7336	86.9	1,541	13.1	
Sex				· · · · · · · · · · · · · · · · · · ·	0.507
Women	4.365	87.1	865	12.9	
Men	2.971	86.6	676	13.4	
Age groups	_,				< 0.001
50-64 years	3.791	90.3	631	9.7	
65–69 years	1,165	89.0	195	11.0	
70-74 years	745	86.6	133	13.4	
75–79 years	818	81.9	204	18.1	
$80 \pm \text{vears}$	817	69.3	378	30.7	
Bace/ethnicity	017	07.5	570	50.7	< 0.001
NHW/	4 069	89.8	674	10.2	<0.001
NHB	1,007	76 5	495	23.5	
Hispanic	1,304	70.5	354	20.1	
	1,510	77.7	20	20.1	
	202	00.2	00	11.0	<0.001
		02.1	492	170	<0.001
Alone	1,000	82.1	482	17.9	
Someone Education	5,004	00.3	1,054	11.7	<0.001
	1.0.40	(7.0	F 40	22.2	< 0.001
Less than high school	1,049	67.8	543	32.2	
High school	2,145	83.2	560	16.8	
Some collage	2,045	91.1	276	8.9	
College	2,060	94.6	160	5.4	
Employment					<0.001
Employed	2,925	93.5	319	6.5	
Not employed	4,387	82.1	1,215	17.9	
Poverty status					<0.001
Poor	902	73.8	395	26.2	
Low income	1,247	76.2	425	23.8	
Moderate income	2,173	85.9	444	14.1	
High income	3,000	94.1	268	5.9	
Private health insurance					<0.001
Yes	3,817	92.4	471	7.6	
No	3,466	79.8	1,053	20.2	
General health					<0.001
Excellent/very good	2,798	92.7	348	7.3	
Good	2,702	86.7	532	13.3	
Fair/poor	I,836	77.1	661	22.9	
Major depression					<0.001
Yes	1,352	79.2	456	20.8	
No	5,984	88.6	1,085	11.4	
Pain					<0.001
None	4,366	88.4	828	11.6	
Mild	759	88.6	155	11.4	
Moderate	1,703	85.7	344	14.3	
Severe	485	75.4	205	24.6	
Physical activity					<0.001
Moderate or vigorous activity >1/week	4,221	89.9	685	10.1	
No	3,115	82.4	856	17.6	

Table 2. Description of older adults (age ≥ 50 years) by MCI status (weighted row percent) health and retirement survey 2018 and 2020.

MCI: mild cognitive impairment; NHW: non-Hispanic White; NHB: non-Hispanic Black; Wt: weighted.

Based on 8,877 participants, alive as of 2020 and did not have dementia during baseline (2018) and follow-up (2020) periods. Missing data for living arrangement, education, poverty status, employment, and private health insurance are not reported. Rao–Scott chi-squared tests were used to determine significant group differences by MCI status. **Table 3.** Unadjusted and adjusted odds ratios (aORs) and 95% confidence intervals (CIs) of sleep disturbance variables from logistic regressions on MCI among older adults (age \ge 50 years) health and retirement survey 2018 and 2020.

Model specification	Troubl	Trouble falling asleep		Trouble waking up		Waking up early	
	uOR	95% CI	uOR	95% CI	uOR	95% CI	
Model I unadjusted							
Mostly	1.69	(1.42, 2.03)	1.31	(1.10, 1.57)	1.88	(1.51, 2.35)	
Sometimes	1.09	(0.95, 1.25)	1.03	(0.86, 1.23)	1.30	(1.12, 1.50)	
Rare/never (ref)		· · · ·		· · · · ·		· · ·	
	aOR	95% CI	aOR	95% CI	aOR	95% CI	
Model 2: adjusted for sex, race and ethnicity, ag	e, and SDOH (living	arrangement, edu	ıcation, em	ployment, pover	ty, and pr	ivate health	
insurance)							
Mostly	1.28	(1.05, 1.56)	1.12	(0.92, 1.37)	1.48	(1.14, 1.94)	
Sometimes	0.94	(0.80, 1.09)	0.90	(0.75, 1.08)	1.10	(0.93, 1.30)	
Rare/never (ref)							
Model 3: adjusted for sex, race and ethnicity, age	e, SDOH, and genera	al health					
Mostly	1.14	(0.92, 1.40)	1.00	(0.82, 1.22)	1.33	(1.03, 1.73)	
Sometimes	0.89	(0.76, 1.04)	0.86	(0.71, 1.04)	1.04	(0.88, 1.23)	
Rare/never (ref)							
Model 4: adjusted for sex, race and ethnicity, age	e, SDOH, general he	alth, and depress	ion				
Mostly	1.04	(0.84, 1.30)	0.93	(0.75, 1.15)	1.26	(0.97, 1.64)	
Sometimes	0.86	(0.74, 1.00)	0.84	(0.70, 1.01)	1.02	(0.85, 1.21)	
Rare/never (ref)							
Model 5: adjusted for sex, race and ethnicity, age	e, SDOH, general he	alth, depression,	pain, and p	hysical activity			
Mostly	1.05	(0.83, 1.32)	0.95	(0.76, 1.18)	1.27	(0.96, 1.67)	
Sometimes	0.87	(0.74, 1.01)	0.85	(0.70, 1.02)	1.03	(0.86, 1.22)	
Rare/never (ref)		. ,		. ,		. ,	

MCI: mild cognitive impairment; ref: reference group; uOR: unadjusted odds ratio.

Based on 8877 participants, alive as of 2020 and did not have dementia during baseline (2018) and follow-up (2020) periods.

physical health, no major depression, no pain, and moderate or vigorous physical activity more than once a week.

Figure 1 summarizes the unadjusted and adjusted associations of sleep disturbance variables with MCI. Panel A presents findings related to trouble falling asleep; Panel B represents trouble waking up, and Panel C refers to waking up early and being unable to fall back asleep. In unadjusted (Model 1), those who experienced sleep disturbances most of the time had higher odds of MCI (Figure 1). After adjusting for sex, age, race/ethnicity, and SDOH (Model 2), the positive association of trouble falling asleep (most of the time: adjusted odds ratio (aOR)=1.28, 95% confidence interval (CI): 1.05, 1.56) and waking up early and unable to fall back asleep (most of the time: aOR=1.48, 95% CI: 1.14, 1.94) with MCI remained.

After adjusting for individuals' perceptions of their general health (Model 3), adults who were waking up early and unable to fall back asleep (most of the time) were more likely to have MCI (aOR = 1.33, 95% CI: 1.03, 1.73). Furthermore, after adjusting for depression in Model 4, this positive association disappeared. In the fully adjusted model (Model 5), the associations between all sleep disturbance variables and MCI were statistically insignificant (Figure 1).

Supplemental analyses. We included diabetes, heart disease, COPD, stroke, and hypertension—in the regression models instead of general health status. In these models, the association between sleep disturbances and MCI remained consistent. For example, the aORs (95% CI) were: 1.05 (0.82–1.34) for difficulty falling asleep, 0.97 (0.78–1.21) for nocturnal awakenings, and 1.27 (0.96–1.69) for inability to return to sleep.

To understand the role of sleep disorders on MCI, we included a three-category variable (No sleep disorder, Sleep Apnea, and other sleep disorders) based on the questions: "Have you ever been told by a doctor or other health professional that you have a sleep disorder?" and "What was the sleep disorder?" Controlling for sleep disorders, they did not alter the association between sleep disturbances and MCI. For example, the aORs (95% CIs) were 1.03 (0.81–1.31) for difficulty falling asleep, 0.94 (0.76–1.17) for nocturnal awakenings, and 1.26 (0.96–1.66) for inability to return to sleep.



Figure 1. Illustration of both unadjusted and adjusted associations between various sleep disturbances and MCI. Panel (a) presents the unadjusted (Model I) and adjusted (Models 2–5) odds ratios and their 95% Cls for trouble falling asleep in relation to MCI. Panel (b) displays the unadjusted (Model I) and adjusted (Models 2–5) odds ratios and their 95% Cls for trouble waking up in relation to MCI. Panel (c) shows the unadjusted (Model I) and adjusted (Models 2–5) odds ratios and their 95% Cls for trouble waking up early and difficulty falling back asleep, in relation to MCI. Model I is an unadjusted model. Model 2 is adjusted for sex, race and ethnicity, age, and SDOH, including living arrangement, education, employment, poverty, and private health insurance. Model 3 includes adjustments for sex, race and ethnicity, age, SDOH, and individuals' self-reported general health. Model 4 further adjusts for depression in addition to the variables in Model 3. Model 5 is the final adjusted model, incorporating all variables in Model 4, with the inclusion of pain and physical activity.

MCI: mild cognitive impairment; CI: confidence interval; SDOH: social determinants of health.

Discussion

In this study, we used nationally representative HRS data from 2018 to 2020 to examine the association between sleep disturbances and MCI among U.S. adults aged 50 years and older without dementia. Our study findings suggest that about one in seven (13.1%) older Americans had MCI. However, the prevalence of MCI in this study was somewhat lower than in other studies. In a global systematic review, the prevalence of MCI was 15.56% (95%CI: 13.24%–18.03%).¹¹ For example, a study using the U.S. Census data on individuals aged \geq 51 years reported a prevalence of 22.7% (95% CI: 22.3–23.2).⁴⁹ This variability in prevalence may be due to variations in geographic populations, cultural differences, or methodological differences in MCI measurement across studies.¹

We also found that sleep disturbances are highly prevalent among older adults with 74.6% reporting at least some disturbance across the three measures (data not reported in tabular form). Given the diverse definitions of sleep disturbances across studies, it is difficult to provide meaningful comparisons. However, our findings are in general agreement with a study that reported that the prevalence of sleeping disturbances can reach nearly 70% in the presence of multimorbidity.⁵⁰ In terms of the type of sleep disturbances, 15.4% of participants reported they had trouble sleeping, 23.2% reported trouble waking, and 12.8% reported awakening early and unable to fall asleep again "most of the time." These findings are consistent with findings from the National Health Interview Survey, in which in 2020, 14.5% of adults had trouble falling asleep most days or every day in the past 30 days.⁵¹ Although not specific to trouble falling asleep, among community-dwelling older (65–79 years) persons, 13% reported frequent insomnia.⁵² Using previous 2008 HRS data, another study found that 12.4% of adult participants reported difficulty falling asleep, 25.7% reported waking up during the night, and 12.8% reported waking up too early "most of the time."³⁸

Our findings from bivariate analyses indicated that individuals experiencing sleep disturbances most of the time had a higher prevalence of MCI compared to those who rarely or never experienced sleep disturbances. There may be several pathways from sleep disruption to MCI. One proposed mechanism is that sleep is responsible for decreasing oxidative stress and clearing some of the metabolites that fatigue the brain and disrupt function.⁵³ Another potential mechanism may involve glymphatic clearance. Glymphatic activity is significantly enhanced during deep sleep; therefore, impaired glymphatic function may be associated with reduced sleep quality and subsequent sleep disturbances. Additionally, inefficient glymphatic clearance is linked to the accumulation of metabolic waste, such as beta-amyloid and tau proteins, which may contribute to cognitive decline.54 It is also plausible that sleep disturbances can lead to a higher risk of conditions such as high blood pressure, diabetes, depression, heart disease, and stroke which may in turn lead to cognitive decline and impairment.55,56

A noteworthy finding in our study is that types of sleep disturbances were associated with MCI through distinct and multifaceted pathways. The attenuation of these associations after adjusting for various factors highlights the complexity of the relationships. For example, the disappearance of the relationship between nocturnal awakening (waking up during the night) and MCI after controlling for age, sex, race, ethnicity, and SDOH suggests that these demographic and socioeconomic factors may mediate or confound this association. It is plausible that individuals experiencing nocturnal awakenings most of the time might also be those who are disproportionately affected by adverse social conditions, which in turn could contribute to MCI. Addressing some of these SDOHs can help in reducing the risk of nocturnal awakening and their impact on cognitive health.

The loss of association between trouble falling asleep and MCI upon adjusting for general health indicates that overall health status may play a role. Poor general health may be due to chronic conditions and could lead to difficulties initiating sleep and may independently contribute to cognitive impairment. As shown in Table 2, individuals with poor perception of their general health have a higher prevalence of sleep disturbances across all types. Furthermore, research suggests that individuals with multiple chronic conditions often perceive their overall health as poor, while those with low socioeconomic status or psychiatric disorders may have poor perceptions of their general health.^{47,57–59} Improving general health through lifestyle modifications and management of chronic conditions might alleviate sleep onset problems and reduce the risk of MCI. We cannot rule out the bidirectional relationship between sleep disturbances and general health. In a study that used data from the 2019 National Health Interview Survey, older adults (age \ge 60 years) with sleep problems were more likely to report poor general health.⁶⁰

Without controlling for depression, we observed that adults who reported waking up too early and being unable to fall back asleep most of the time were more likely to have MCI, consistent with a previous study.⁶¹ Researchers using data from the National Social Life, Health and Aging Project 2010–2015 measured cognition in older U.S. adults with a modified Montreal Cognition Assessment along with wrist actigraphy that recorded activity every 15 s for 72 h. Sleep disruption (awakening after onset, fragmented sleep, percent sleep, wakefulness) was assessed. Awakening after sleep onset showed the strongest association with worse cognition performance.⁶¹

The statistically insignificant relationship between waking up too early and MCI after adjusting for depression underscores the complex relationships of sleep disturbances, mood disorders, and cognitive function. Our measure of depression included items assessing trouble falling asleep and difficulty concentrating. These symptoms are also key components of sleep disturbances and cognitive impairment, respectively. Emerging perspectives suggest that cognitive impairment and sleep disturbances are core features of depression, not merely secondary effects.^{62,63} Consequently, when we adjusted for depression in our analysis, we may have inadvertently controlled for variables that are integral parts of both sleep disturbances and MCI. The overlapping symptoms of sleep and cognition in our measure of depression suggest that adjusting for depression may constitute overcontrol, potentially masking significant associations.

Taken together, these findings suggest that the relationship of sleep disturbances with MCI is influenced by a host of demographic, socioeconomic, general health, and psychological factors. There is a need for personalized approaches in both research and clinical practice for prevention and management strategies for MCI related to sleep disturbances. Additionally, interventions for managing MCI may need to adopt a multifactorial approach, considering various contributing factors. Prevention and management strategies may need to be developed within a social-ecological framework. Such a framework will consider both individual-level factors, practices, and behaviors (e.g., physical activity, socioeconomic status, chronic diseases), and social-level factors (e.g., technology).⁶⁴

One key strength of our study is the use of an objective measure for MCI, along with longitudinal data from a robust, nationally representative database. We assessed sleep disturbances during the baseline period (2018) and subsequently recorded the incidence of MCI during the follow-up period (2020). This temporal design helps mitigate the methodological challenge of establishing a sequential relationship inherent in cross-sectional studies that measure both sleep disturbances and MCI within the same time frame⁶⁵ and may be less susceptible to reverse causation. Many cross-sectional and longitudinal studies have been conducted. In a systematic review and meta-analysis of the prevalence of sleep disturbances in individuals with MCI, sleep disturbance prevalence was significantly lower in 16 cohort studies compared to the 28 cross-sectional studies.²³

Furthermore, in a systematic review of cohort and longitudinal studies, most reported associations of sleep disturbances with dementia (61%) or AD (39%).⁶⁶ However, studies on sleep disturbances measures consistent with our study and MCI are sparse. The heterogeneous methodologies for assessing sleep disturbances and cognition⁶⁶ make it difficult to draw conclusive associations between sleep disturbances and MCI. As stated in the introduction, mixed findings have been observed: one prospective cohort study found that sleep disturbances predicted MCI in healthy adults,²⁷ whereas another longitudinal study reported no impact of sleep disturbances on cognitive decline in global cognition, executive function, or memory.²⁸ These discrepancies suggest that the relationship between sleep disturbances and MCI may not be consistent.

Our study also has several limitations. First, the sleep disturbances are self-reported, and research has shown that selfreport measures do not correlate well with objective measures.⁶⁷ Furthermore, there can be considerable variability in sleep disturbances over a period of time due to major life events such as illness or death, and we did not capture this variability.⁶⁷ Additionally, the database lacked certain variables that could have further strengthened our analysis. For instance, sleep duration, an important measure frequently used by researchers to capture the complexities of sleep, was not examined. Although several measures of sleep disturbances were utilized, comparing our findings with other studies remains challenging due to the lack of standardized assessments. Lastly, this is an observational study and no sample size calculation for statistical power was conducted.

Conclusion

Approximately one in seven older Americans without dementia (\geq 50 years old) had MCI. Our findings demonstrated positive associations between sleep disturbances and MCI. However, these associations were sensitive to covariate adjustments and suggested distinct and multifaceted pathways for reducing the risk of MCI.

Author contributions

Chan Shen and Hao Wang: Conception and design, data analysis and interpretation, manuscript writing, and final approval of manuscript. Arthur Nguimatsa Djiotsop, Constance Wiener, Mona Patha, Sophie Mitra, and Patricia A. Findley : Data analysis and interpretation, manuscript writing, final approval of manuscript. Usha Sambamoorthi: Conception and design, data analysis and interpretation, manuscript writing, final approval of manuscript, and supervision of the study.

Declaration of conflicting interests

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Ethical approval

This is a retrospective study based on secondary data analysis. Ethical approval for this study was waived by the Institutional Review Board because the study is based on a public and deidentified data.

Written informed consent statement

This is a retrospective study based on secondary data analysis. The study utilized previously collected survey data, for which written informed consent had been obtained by the survey administrators at the time of data collection.

Trial registration

Not applicable.

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