ASSOCIATIONS BETWEEN SLEEP AND COGNITIVE DECLINE IN OLDER ADULTS

By

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Abstract

Older adults are at an increased risk of sleep disorders as well as cognitive decline in the form of memory problems, dementia, and Alzheimer's Disease. In fact, it is predicted that upwards of 25% of patients with dementia experience disordered sleeping. Due to the observed rate of comorbidities in the older adult population, it has become increasingly important to investigate the relationship between sleep and cognitive decline. The present study of older adults shows an association between sleep characteristics, including difficulty falling asleep and feeling rested, and new onset dementia. A correlation was also found between sleep disorders and new onset dementia. Lastly, the remission, persistence, or development of a sleep disorder over a two-year period was associated with change in memory for better or worse over that same two-year period. Due to the progressive nature of dementia and Alzheimer's Disease, a bidirectional relationship between sleep disturbance and cognitive decline could have important clinical implications pertaining to detection of increased risk for cognitive decline in older adults and potential treatment options. Specifically, sleep interventions could be of use in preventing the onset and progression of cognitive decline.

Introduction

Dementia

Dementia is a general term for cognitive decline that interferes with daily life in consequence to a variety of disease pathologies (Alzheimer's, 2023). Such diseases include dementia with Lewy Bodies, Parkinson's Disease and Vascular Dementia. The leading cause of dementia is Alzheimer's Disease (AD). Alzheimer's is a progressive disease that affects memory

and cognitive function (Alzheimer's, 2023). Presently, there is no cure or treatment for dementia or Alzheimer's that is capable of reversing the damage of the disease. Instead, current efforts are focused on improving the quality of life for those living with dementia. We continue to see increased incidence of dementia as the baby boomer population ages and the average lifespan increases (Alzheimer's, 2016). In 2050, it is expected that 13.8 million people in the United States alone will be living with dementia (Alzheimer's, 2016). Globally, cases of dementia are expected to triple to over 130 million. (Tiwari, Atluri, Kaushik, Yndart, & Nair, 2019). Dementia has a large impact on the health care system and families alike. This impact will only continue to grow as the population continues to age.

Sleep

Sleep is a universal physiological need for all humans. The gravity of the necessity of sleep can be reflected in the push for later grade school start times (Wheaton, Chapman, & Croft, 2016), and the addition of sleep onto the "Life's Essential 8" for the American Heart Association's guideline for cardiovascular health (Sun et al., 2023). Sleep is intimately related to overall brain function and plays a role in regulating the physiological processes of the body. Currently, it is understood that chronic sleep problems increase risk for health issues including obesity, diabetes, hypertension, and cardiovascular disease (Khan & Aouad, 2022). Even with this knowledge, modern pressures and a high prevalence of sleep disorders keep the general population from getting enough, quality sleep on a consistent basis. In fact, the CDC reports that in 1 in every 3 adults in America doesn't get enough sleep, which amounts to around 80 million people.

A typical 8-hour sleep episode is comprised of 4-5 cycles (Patel, Reddy, Shumway, & Araujo, 2022). A sleep cycle includes rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep. NREM sleep is further divided into three stages: N1, N2, and N3. Each stage has keynote characteristics that have notable physiological importance. Sleep is regulated by the homeostatic drive for sleep and the circadian rhythm (Benca & Teodorescu, 2019). The brainstem, hypothalamus, basal forebrain, and thalamus are primary areas of the brain involved in sleep mechanisms (Yaffe, Falvey, & Hoang, 2014). Many of these areas are concurrently involved in memory and cognitive function as well.

As the normal aging process progresses, it is natural for the architecture of sleep to change. Time spent in REM and Slow Wave Sleep (SWS) decreases with age (Benca & Teodorescu, 2019). Arousals during sleep increase, which causes more fragmentated sleep in older adults (Benca & Teodorescu, 2019). Reductions in the fast sleep spindle in the prefrontal cortex can be observed during NREM sleep. (Mander et al., 2014). Decreased sleep duration, efficiency, and difficulty falling asleep are all considered symptoms of an aging brain (Yaffe et al., 2014).

Sleep and Memory

It appears that sleep before and after learning is important for the function of memory mechanisms. This is relevant because one hallmark symptom of cognitive decline is the inability to form new memories (Sperling et al., 2003). This function of the brain takes place during the NREM stage of sleep where the hippocampus reorganizes memories into the neocortex for a longer more stable form of memory storage (Squire, Genzel, Wixted, & Morris, 2015). In a foundational study, fMRI technology showed that compared to healthy older adults, Alzheimer's

patients had less activity in the hippocampus (Sperling et al., 2003) A different study found decreased hippocampal activity during memory encoding after just one night of sleep deprivation (Yoo, Hu, Gujar, Jolesz, & Walker, 2007). Mander et al. (2014) hypothesizes that decreased fast sleep spindles of the prefrontal cortex in the aging brain may explain the decreased activity of these memory mechanisms. In fact, the study found a positive correlation between fast sleep spindles and episodic encoding success in older adults using EEG and fMRI technology (Mander et al., 2014). The combination of fast sleep spindles in the prefrontal cortex and hippocampal functioning appears to determine the ability for the brain to learn the following day (Mander et al., 2014). These findings suggest that decreased activity in the hippocampus, which is a hallmark of both aging and neurocognitive decline, combined with the decrease in fast sleep spindles, may be a crucial part of the explanation for the interconnectedness of sleep and memory impairment.

Sleep Disorders and Cognitive Decline

It is predicted that at least 25% of patients with dementia experience disordered sleeping or sleep disturbances of some kind (Rose & Lorenz, 2010). These sleep disturbances often manifest early in the progression of neurodegenerative diseases and therefore may be useful in the early detection and treatment of dementia in an effort to prolong progression of the disease. Some sleep-wake disturbances seen in dementia patients include circadian rhythm disorders, REM sleep behavior disorder (RBD), excessive daytime sleepiness (EDS), and sleep disordered breathing (SDB) (Rose & Lorenz, 2010). These disorders vary in prevalence based on the type of dementia.

Sleep disordered breathing (SDB) is composed of disorders that contribute to abnormal breathing patterns during sleep including apneas and hypopneas (Yaffe et al., 2014). Ancoli-Israel (2006) predicted an alarming 70-80% of people residing in long term care facilities who are diagnosed with dementia also have obstructive sleep apnea. In a prospective study of women without dementia, the individuals with SDB had a 1.85 adjusted odds ratio of developing mild cognitive impairment (MCI) or dementia (Yaffe et al., 2011). One study investigated the association between Positive Airway Pressure (PAP) treatment for obstructive sleep apnea and Dementia, Alzheimer's, and MCI (Dunietz, Chervin, Burke, Conceicao, & Braley, 2021). Adherence to PAP treatment was associated with lower odds of Alzheimer's and dementia diagnosis as well as MCI. This is just one example of how treatment of sleep disorders may improve cognitive outcomes in older adults.

Circadian rhythm disorders are also relatively common in this patient population. One manifestation of this dysfunction is known as sundowning (Yaffe et al., 2014). Sundowning, which is often seen in the later stages of Alzheimer's, is defined as disruptive behavior caused by confusion in the early evening hours (Gnanasekaran, 2016). This phenomenon is thought to be the result of neurodegeneration, specifically in the suprachiasmatic nucleus (SCN) and cholinergic neurons (Zhong, Naismith, Rogers, & Lewis, 2011). Gehrman et al. (2005) suggested circadian rhythm disturbances were associated with the level of severity of dementia. The severity level of dementia was determined by the Mini Mental State Examination (MMSE) and the severity level of circadian rhythm disturbances was determined by actigraphy. Those with worse dementia had more extreme circadian rhythm abnormalities (Gehrman et al., 2005).

Sindi et al. (2018) reported that both mid-life and late-life insomnia were correlated with increased risk of dementia. The same study also reported that a sleep duration of longer than 9

hours per day increased risk by dementia almost 4-fold. Shi et al. (2018) performed a metanalysis with 246,786 subjects with an average 9.49 year follow up period. According to the study, the presence of insomnia increased risk of AD. Sleep disordered breathing increased risk of AD, dementia, and vascular dementia. Overall sleep disturbance was correlated with a 1.19 times higher risk for dementia. While it is well understood that sleep disorders and dementia are often comorbid, the question persists of whether chronic sleep disturbance plays an active role in the pathogenesis of some dementia causing diseases.

Sleep Duration and Dementia

When discussing sleep and cognitive health, the issue of sleep duration becomes relevant. Chronic sleep duration abnormalities, including both long and short duration have been correlated with cognitive decline and incident dementia (Chen et al., 2016; Sabia et al., 2021). In one prospective study of older women, Chen et al. (2016) found sleep duration of less than 6 hours lead to a 36% increased risk of MCI or dementia and sleep duration of more than 8 hours lead to a 35% increased risk. Similarly, persistent short sleep between ages 50 and 60 was found to increase risk of dementia by 30% (Sabia et al., 2021). Studies with longer follow up periods have become increasingly important to verify the value of this relationship. One study followed participants for 22.5 years on average and found that short and long sleep duration, as well as poor quality sleep produced lower cognitive scores (Virta et al., 2013). The aggregate of these findings suggest a very specific window of sleep duration that decreases risk for cognitive decline: between 7 and 8 hours. It is important to note that conclusions have yet to be drawn as other studies have found a lack of correlation. One self-report study found that frequent sleep disturbance had a 1.58 risk ratio for dementia in men, but no correlation was found for sleep

duration (Luojus et al., 2017). Sleep duration abnormalities, defined by one study as shorter or longer than 7-9 hours, are reportedly seen in around 1/3 of adults (Liu, Wheaton, Chapman, & Croft, 2013). This is an alarming statistic if sleep duration does in fact predict risk of onset dementia and cognitive decline.

Amyloid-β Plaques and Alzheimer's Disease Pathogenesis

Amyloid-β (Aβ) peptides have been examined in an attempt explain the physiological mechanisms linking sleep disturbance and Alzheimer's Disease. The accumulation of Aβ peptides into amyloid plaques is considered a hallmark of the pathogenesis of Alzheimer's (Gouras, Olsson, & Hansson, 2015; Kang et al., 2009; Tiwari et al., 2019). The pathogenic accumulation of Aβ peptides first appears 10-15 years before signs of cognitive decline (Ju, Lucey, & Holtzman, 2014) and develop in the extracellular space of the brain, a process likely dependent on Aβ levels in the interstitial fluid (ISF). Kang et al. (2009) found that Aβ levels in the ISF and cerebrospinal fluid (CSF) were associated with wakefulness in mice and human models. In humans, Aβ levels increased during the day and decreased during the night, suggesting diurnal fluctuation of Aβ independent of light exposure. In sleep deprived mice, Aβ levels in the ISF were significantly higher when compared to periods of light exposure. Furthermore, after sleep recovery, Aβ levels decreased significantly and immediately. Most notably, transgenic mice who were exposed to chronic sleep deprivation showed greater amounts of Aβ plaques characteristic of Alzheimer's Disease. This study suggested the hormone Orexin might play a role. Orexin is part of the mechanism that regulates sleep and wake cycles and has similar diurnal fluctuations seen in Aβ. Mice infused with wakefulness inducing Orexin had significant increased levels of Aβ in the ISF (Kang et al., 2009).

Ju et al. (2014) proposed a bidirectional relationship between Aβ and sleep problems. Amyloid depositions were associated with poor sleep efficiency, even when symptoms of AD were not present (preclinical AD) (Ju et al., 2013). A study performed on mice showed a disruption in the sleep wake cycle after Aβ plaque formation as well as the absence of diurnal fluctuations of ISF Aβ peptides (Roh et al., 2012). This may be explained by the interference of sleep regions of the brain by Aβ plaques.

One longitudinal study showed excessive daytime sleepiness, which is correlated with sleep disturbance, was associated with 2.5 times the risk of developing β-amyloid deposition in the brain 15 years later (Spira et al., 2018). Irwin and Vitiello (2019), suggested a possible biological link between sleep and Aβ deposition in the brain: inflammation. Sleep disturbance has been shown to increase systemic inflammation in the body (Irwin, Olmstead, & Carroll, 2016). Partial sleep deprivation led to expression of proinflammatory cytokines, and the CNS inflammatory response activated by inflammatory signaling pathways (Irwin et al., 2016).

Methods

The present study is correlational study that investigates the association between sleep problems and disorders, and cognitive decline in the form of dementia, Alzheimer's, and change in memory. Data was assessed from 17,146 older adults from the 2018 Health and Retirement Survey. Data from the 2016 Health and Retirement Survey was used as comparative reference.

New onset dementia and Alzheimer's was determined by filtering data to specify for participants that marked "no" on survey questions pertaining to the presence of dementia or Alzheimer's as diagnosed by a doctor or health professional in the previous wave (2016) survey and "yes" in the new wave (2018) survey. Therefore, participants included in new onset

dementia or Alzheimer's groups indicated a new diagnosis of dementia or Alzheimer's sometime between the previous wave (2016) and the new wave (2018).

Sleep characteristics were assessed from survey data by asking participants if they had difficulties initiating or maintaining sleep as well as if they experienced early morning awakenings and if they felt rested upon awakening. All 4 of these symptoms were coded as "never", "sometimes," or "most of the time." Data indicating sleep characteristics as "sometimes" or "most of the time" were included in the analysis. Data involving the presence or absence of a sleep disorder did not specify the type or cause of sleep disorder and instead was characterized by any sleep disorder as diagnosed by a doctor or medical professional. The presence or absence of a sleep disorder was asked in both 2016 and 2018. Data was then coded by "no sleep disorder", "remit sleep disorder", "new sleep disorder" or "sustained sleep disorder."

Memory change was assessed using a survey item on the 2018 survey asking if the respondent's memory was "worse", "better", or "the same" as compared to two years prior in 2016.

Statistical analysis was performed using the R statistical software package studio version 1.4.1103. Poisson regressions were performed to assess the relationships between sleep disorders and dementia or Alzheimer's, and sleep characteristics and dementia or Alzheimer's. For the sleep disorder analyses, sleep disorder was the predictor, and the outcome was dementia or Alzheimer's. For the sleep characteristics analyses, the characteristics were the predictors, and dementia or Alzheimer's was the outcome. Multinomial logistic regression was used to assess the correlation between memory change and sleep disorders. Covariates include sex, age, race,

ethnicity, and depression. Basic descriptive statistics was used to describe characteristics of the sample.

Results

The average age of participants in 2016 was 65.2 years old and the average age of participants in 2018 was 67 years old, making the average birth year 1951. Around 59% of the sample was female and 41% was male. 2% of the sample reported dementia in the previous wave (2016) and 2.7% of the sample reported dementia in the current wave (2018). 1% of the sample reported Alzheimer's Disease in the previous wave (2016) and 1.5% of the sample reported Alzheimer's Disease in the current wave (2018).

Difficulty maintaining sleep "sometimes" was associated with a 0.995 incident risk ratio in patients with new onset of Alzheimer's Disease (IRR = 0.995, 95% [CI]: 0.993 to 0.998, p = 0.004) when adjusted for age, race, ethnicity, sex, and depression. Early morning awakenings "sometimes" had a similar result when adjusted, showing a 0.995 incident risk ratio in patients with new onset Alzheimer's Disease (IRR = 0.995, 95% [CI]: 0.993 to 0.998, p < 0.001). Feeling rested and difficulty initiating sleep showed no association with new onset AD.

Results adjusted for age, race, ethnicity, sex and depression showed that difficulty initiating sleep "most of the time" had a 0.06% increased risk for new onset dementia (IRR = 1.006, 95% [CI]: 1.001 to 1.011, p = 0.019) For those who reported feeling rested "most of the time", there was an adjusted 0.08% decreased risk for new onset dementia (IRR = 0.992, 95% [CI]: 0.987 to 0.997, p = 0.004).

Table 4 evaluates the association between both dementia and Alzheimer's and any sleep disorder as diagnosed by a health professional. Having a sleep disorder was associated with a

0.06% increased risk for new onset dementia (IRR = 1.006, 95% [CI]: 1.001 to 1.012, p = 0.013) when adjusted for age, race, ethnicity, sex, and depression. No statistically significant association was seen between Alzheimer's Disease and sleep disorders.

Table 5 reports associations between sleep disorders and change in memory over a two-year period. The remission of a sleep disorder between 2016 and 2018 was associated with a 2.24 odds ratio for change in memory for the better during a two-year period when adjusted for age, race, ethnicity, sex, and depression (OR = 2.21, 95% [CI]: 1.49 to 3.27, p < 0.001). Contradictory data showed an adjusted odds ratio of 1.39 between those with a remit sleep disorder and a change in memory for the worse during a two-year period (OR = 1.43, 95% [CI]: 1.13 to 1.80, p = 0.006). A newly developed sleep disorder in 2018 was associated with twice the odds of a change in memory for the worse in a two-year period (OR = 2.03, 95% [CI]: 1.65 to 2.50, p < 0.001). A sustained sleep disorder between 2016 and 2018 had an increased odds ratio of 1.58 for worse memory two years later (OR = 1.58, 95% [CI]: 1.40 to 1.77, p < 0.001)

Discussion

Presence of sleep characteristics that might indicate the status of overall sleep health were associated with dementia. Results suggest that difficulty initiating sleep represents an increased risk for onset of dementia by 0.06%. The characteristic of having a difficult time falling asleep is a commonly seen symptom of insomnia. The associated sleep characteristics used in the present study might indicate the presence of underlying sleep disorders which were also correlated to an increased risk of dementia by 0.06%. Although the data was not specific to different types of sleep disorders, this may explain the similarity in the correlation. This data shows consistency with existing literature that suggest sleep disorders and sleep disturbances increase risk for

dementia (Shi et al., 2018; Sindi et al., 2018). Feeling rested is another sleep characteristic that was associated with dementia, but this time showed a decreased risk of onset of dementia by 0.08%. The sleep characteristic of feeling rested may indicate quality sleep health and the absence of sleep problems that would lead to daytime sleepiness or the lack of feeling rested.

The other notable finding of the present study involves change in memory and status of sleep disorders. A change in memory for the better was correlated with twice the odds of the remission of a sleep disorder. The development of new sleep disorders and sustained sleep disorders were associated with worsening memory over the two-year period. These findings suggest that treating sleep disorders may be useful in addressing cognitive deficits in older adults. This data is supported by relevant literature in the field that highlights the importance of sleep in the proper functioning of memory mechanisms (Mander et al., 2014; Sperling et al., 2003). Surprisingly, the remission of a sleep disorder was also correlated to higher odds of worsening memory over a two-year period. Although, this association was smaller.

One limitation of the study that should be mentioned was the use of self-report data. Self-report data may not yield accurate results in some cases. For example, inquiring about sleep characteristics using qualitative measures such as “sometimes” and “most of the time” may have slightly different meaning to different participants. More objective questioning or actigraphy data should be used in future studies to determine characteristics of sleep. More objective data should also be used in measures of memory. Self-report data about change in memory over a two-year period may not be accurate. Instead, fMRI data looking at activity of structures in the brain involved in memory mechanisms, such as the hippocampus, in combination with self-report questionnaires would be more insightful.

Future studies should specify types of sleep disorders and sources of dementia more specifically. Different sleep disorders have different underlying causes, treatments, and diagnosis criteria. Similarly, different causes of dementia have very different pathologies. In order to gain insight into why there is so much overlap in the older population, specific sources of dementia, cognitive deficits, and sleep disturbances should be used.

While the associations found in this study might appear fairly small, it is worth noting with the sheer number of dementia patients amplifies the significance of these associations. Finding ways to decrease risk for dementia, such as prioritizing proper sleep and treatment of sleep disorders, might save the health care system a significant amount of time, money, and resources. For example, based on projected rates of dementia, if only 0.01% of dementias could be prevented by addressing sleep disorders, then that would result in a cost savings of about 1 billion dollars per year for the United States alone.

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Table 1. Characteristics of the Sample

Characteristic	Subtype	2016 Interview	2018 Interview (N=17,146)*
Age	-	65.2 (11.31)	67.0 (11.40)
Sex	Male	-	7,033 (41.0%)
	Female	-	10,113 (59%)
Race	White	-	11,249 (66.2%)
	Black	-	3,769 (22.2%)
	Other	-	1,977 (11.6%)
Ethnicity	Non-Hispanic		14,208 (83.4%)
	Hispanic		2,823 (16.6%)
Depression	-	-	1,021 (6.0%)
Dementia	-	342 (2.0%)	448 (2.7%)
Alzheimer's Disease	-	165 (1.0%)	251 (1.5%)
Sleep Disorder	-	2,530 (15.7%)	2,722 (15.9%)
Early Morning Awakening (EMA)	Rarely or never	-	8,770 (51.3%)
	Sometimes	-	5,968 (34.9%)
	Most of the time	-	2,360 (13.8%)
Difficulty Initiating Sleep (DIS)	Rarely or never	-	8,367 (49.0%)
	Sometimes	-	6,050 (35.4%)
	Most of the time	-	2,670 (15.6%)
Difficulty Maintaining Sleep (DMS)	Rarely or never	-	6,458 (37.8%)
	Sometimes	-	6,768 (39.7%)
	Most of the time	-	3,843 (22.5%)
Feeling Rested	Rarely or never	-	2,840 (16.6%)
	Sometimes	-	5,766 (33.7%)
	Most of the time	-	8,483 (49.6%)

Table 2. Relationship Between Alzheimer's Disease and Sleep Characteristics as Reported in 2018

		Unadjusted			Adjusted**			Adjusted (with depression)		
Characteristic	**Subtype**	**IRR*** **	**95% CI[1]**	**p value**	**IRR*** **	**95% CI[1]**	**p value**	**IRR*** **	**95% CI[1]**	**p value**
Difficulty Initiating Sleep	Sometimes	0.998	(0.996, 1.006)	0.147	0.998	(0.996, 1.001)	0.152	0.998	(0.996, 1.001)	0.145
	Most of the time	1.001	(0.997, 1.004)	0.759	1.002	(0.998, 1.005)	0.399	1.001	(0.998, 1.006)	0.422
Difficulty Maintaining Sleep	**Sometimes**	**0.996**	**(0.993, 0.999)**	**0.004***	**0.995**	**(0.993, 0.998)**	**<0.001***	**0.995**	**(0.993, 0.998)**	**<0.001***
	Most of the time	1.000	(0.996, 1.003)	0.814	0.999	(0.996, 1.003)	0.715	0.999	(0.996, 1.003)	0.707
Early Morning Awakening	**Sometimes**	**0.996**	**(0.994, 0.998)**	**0.001***	**0.995**	**(0.993, 0.998)**	**<0.001***	**0.995**	**(0.993, 0.998)**	**<0.001***
	Most of the time	1.000	(0.996, 1.003)	0.841	1.000	(0.996, 1.004)	0.957	1.000	(0.996, 1.004)	0.953
Feeling Rested	Sometimes	0.998	(0.994, 1.002)	0.293	0.997	(0.993, 1.001)	0.107	0.997	(0.993, 1.001)	0.121
	Most of the time	1.000	(0.996, 1.003)	0.821	0.997	(0.993, 1.001)	0.102	0.997	(0.993, 1.001)	0.118

**Adjusted for Age, Race, Ethnicity, Sex
***IRR=Incidence Risk Ratio
****$p<0.05$ significance
[1] CI=Confidence Interval

Table 3. Relationship Between Dementia and Sleep Characteristics as Reported in 2018

		Unadjusted			Adjusted**			Adjusted (with Depression)		
Characteristic	**Subtype**	**IRR*** **	**95% CI[1]**	**p value**	**IRR*** **	**95% CI[1]**	**p value**	**IRR*** **	**95% CI[1]**	**p value**
Difficulty Initiating Sleep	Sometimes	1.002	(0.998, 1.005)	0.277	1.002	(0.999, 1.006)	0.224	1.002	(0.999, 1.006)	0.206
	Most of the time	1.005	(0.997, 1.004)	0.559	**1.006**	**(1.001, 1.001)**	**0.012***	**1.006**	**(1.001, 1.011)**	**0.019***
Difficulty Maintaining Sleep	Sometimes	0.999	(0.996, 1.003)	0.741	0.998	(0.994, 1.002)	0.274	0.998	(0.994, 1.001)	0.228
	Most of the time	1.002	(0.997, 1.006)	0.604	1.000	(0.996, 1.005)	0.847	0.999	(0.994, 1.003)	0.667
Early Morning Awakening	Sometimes	1.001	(0.998, 1.005)	0.385	1.001	(0.997, 1.004)	0.641	1.001	(0.997, 1.004)	0.703
	Most of the time	1.003	(0.998, 1.008)	0.272	1.004	(0.998, 1.009)	0.124	1.003	(0.995, 1.001)	0.303
Feeling Rested	Sometimes	0.996	(0.991, 1.002)	0.174	0.995	(0.990, 1.001)	0.083	0.995	(0.990, 1.001)	0.072
	Most of the time	0.996	(0.991, 1.000)	0.755	**0.992**	**(0.987, 0.997)**	**0.002***	**0.992**	**(0.987, 0.997)**	**0.004***

**Adjusted for Age, Race, Ethnicity, Sex
***IRR=Incidence Risk Ratio
****$p<0.05$ significance
[1] CI=Confidence Interval

Table 4. Relationship between Dementia, Alzheimer's Disease (AD), and Diagnosed Sleep Disorder in 2018

	Unadjusted			Adjusted**			Adjusted with Depression		
	IRR* **	**95%CI[1]**	**p value**	**IRR*** **	**95%CI[1]**	**p value**	**IRR*** **	**95%CI[1]**	**p value**
Dementia + Sleep Disorder	**1.006**	**(1.001, 1.011)**	**0.026***	**1.007**	**(1.002, 1.012)**	**0.008***	**1.006**	**(1.001, 1.012)**	**0.013***
AD + Sleep Disorder	1.001	(0.998, 1.005)	0.395	1.003	(0.999, 1.006)	0.099	1.003	(0.999, 1.007)	0.090

**Adjusted for Age, Race, Ethnicity, Sex
***IRR=Incidence Risk Ratio
****$p<0.05$ significance
[1] CI=Confidence Interval

Table 5. Change in Sleep Disorder Categorized by Change in Memory Across 2 Years

		Unadjusted			Adjusted*			Adjusted+Depression		
		OR* **	**95%CI[1]**	**p-value**	**OR*** **	**95%CI[1]**	**p-value**	**OR*** **	**95%CI[1]**	**p-value**
Better Memory	No Sleep Disorder	—	—	-----	---	---	---	---	---	---
	New Sleep Disorder	1.22	0.74, 2.01	0.4	1.13	0.69, 1.87	0.6	1.02	0.61, 1.71	>0.9
	Remit Sleep Disorder	**2.31**	**1.58, 3.39**	**<0.001***	**2.21**	**1.49, 3.27**	**<0.001***	**2.24**	**1.51, 3.31**	**<0.001***
	Sustained Sleep Disorder	1.16	0.89, 1.51	0.3	1.16	0.89, 1.52	0.3	1.03	0.78, 1.37	0.8
Worse Memory	No Sleep Disorder	—	—	---	---	---	---	---	---	---
	New Sleep Disorder	**1.89**	**1.55, 2.30**	**<0.001***	**2.15**	**1.75, 2.63**	**<0.001***	**2.03**	**1.65, 2.50**	**<0.001***
	Remit Sleep Disorder	**1.34**	**1.06, 1.68**	**0.013***	**1.43**	**1.13, 1.80**	**0.003***	**1.39**	**1.10, 1.77**	**0.006***
	Sustained Sleep Disorder	**1.57**	**1.40, 1.75**	**<0.001***	**1.75**	**1.56, 1.96**	**<0.001***	**1.58**	**1.40, 1.77**	**<0.001***

**Adjusted for Age, Sex, Race, Ethnicity
***OR = Odds Ratio
****p<0.05 significance
[1] CI=Confidence Interval