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Self-reported sleep in relation to risk of dementia a quarter of a century later at age 90+: *The 90+ Study*

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ABSTRACT

Objective: To examine sex-specific associations of sleep duration and napping self-reported at mean age of 69 years (range: 53–81) with risk of incident dementia 24 years later at age 90 +.

Method: Analytic sample included individuals from a population-based study who reported sleep and napping once in the 1980s and 24 years later (range: 16–38) joined ***The 90+ Study*** and were evaluated in-person. Those without dementia at baseline of ***The 90+ Study*** were prospectively followed. Hazard ratios [HR] and 95% confidence intervals [CI] of dementia risk were estimated by Cox regression.

Results: Of 574 participants 71% were women, mean age at start of dementia follow-up with ***The 90+ Study*** was 93 years (range: 90–102). After 3.3 years (range: 0.4–13.8) of follow-up 47% developed dementia. Higher risk of dementia at age 90+ was seen in women with <6 hours of self-reported sleep per night (adjusted HR = 2.00; 95% CI = 1.15–3.50; p = .01) compared with 8 hours. Lower risk of dementia at 90+ was seen in men with short-to-moderate (<60 minutes) self-reported naps compared with no naps (HR = 0.33; 95% CI = 0.18–0.63; p < .01).

Conclusions: Sleep and nap 24 years earlier are important risk factors for dementia after age 90.

Introduction

Individuals aged 90+ years (oldest-old) are the fastest growing age segment of the population and have highest risk of dementia (Corrada et al., 2010). To reduce dementia burden, it is essential to identify modifiable factors that impact risk of dementia in this age group. Sleep and napping are potential candidates as they are associated with cognition in the younger-old (age 65–89 years). Short (≤5 or ≤6 hours depending on the study) and long (≥8 or ≥9 hours depending on the study) self-reported sleep per night and per 24 hr are associated with increased risk of all-cause cognitive impairment (Chen et al., 2016; Sabia et al., 2021). Short sleep may be associated

with increased pathology accumulation, while long sleep may be a marker, not a cause, of dementia or neurodegeneration (Spira et al., 2013; Westwood et al., 2017). Moderate duration (<60 minutes) self-reported naps are associated with lower risk of cognitive decline (Keage et al., 2012) likely due to their neuroprotective effect (J. Li et al., 2017).

Sleep may be associated with cognition differently in men and women. Sleep deprivation impairs working memory in women but not in men, likely because women require greater neuronal activity and engagement to complete these tests and thus are more vulnerable to sleep loss (Rångtell et al., 2019). Sex-specific risks of incident dementia in relation to sleep are rarely reported, and the results are mixed. One study found that both long and short self-reported sleep are associated with increased 7-year risk of cognitive impairment in women (Chen et al., 2016), while a study of community-dwelling men found no association over 22 years (Luojus et al., 2017). Another study found that self-reported long sleep in women and short sleep in men were associated with increased 1-year risk of dementia (Potvin et al., 2012). Risk of incident dementia in the oldest-old in relation to sleep and napping has not been studied; sex-specific analysis may provide additional insights and allow for tailored interventions in this age group.

We examined whether risk of incident dementia at age 90+ in the men and women of ***The 90+ Study*** is related to sleep duration and napping self-reported on average 24 years prior. We hypothesized that extreme sleep duration is associated with increased risk of dementia, especially in women whose cognition may be affected more by insufficient sleep compared to men, and who report shorter sleep. We further hypothesized that napping is associated with decreased risk of dementia, especially in men who might benefit from naps more than women.

Materials and methods

Participants

We analyzed data from a subset of individuals who participated in both studies described below. Leisure World Cohort Study (LWCS) is a population-based study of residents of a Southern California retirement community, who responded to a one-time postal health and lifestyle survey that was mailed in 1981 to all residents and in 1982, 1983, and 1985 to new residents who later moved into this community (Paganini-Hill et al., 1986). LWCS participants who were alive, aged 90 or older on January 1, 2003, January 1, 2008, or each January 1 thereafter were invited to join ***The 90+ Study***, an ongoing longitudinal study of aging and dementia in people aged 90+ (Kawas, 2008). Analytic sample included 574 individuals who (1) reported sleep duration, napping, and covariates of interest with the LWCS of the 1980s, (2) joined ***The 90+ Study*** in 2003 or later, (3) had an in-person baseline evaluation with ***The 90+ Study*** and were determined to be dementia free at that time, and (4) had at least one follow-up evaluation with ***The 90+ Study***. Of the 13,978 individuals who returned the LWCS survey, 12,826 had complete data on sleep and covariates, of those 10,878 have died and 20 more were alive but younger than 90 years at the time of ***The 90+ Study*** recruitment, leaving 1,928 eligible to join ***The 90 + Study***, of whom 1,560 (81%) did join (Supplementary Figure S1). Of these, 908 had an in-person

evaluation at baseline with ***The 90+ Study***, 624 were free of dementia, and 574 had at least one follow-up (Figure 1).

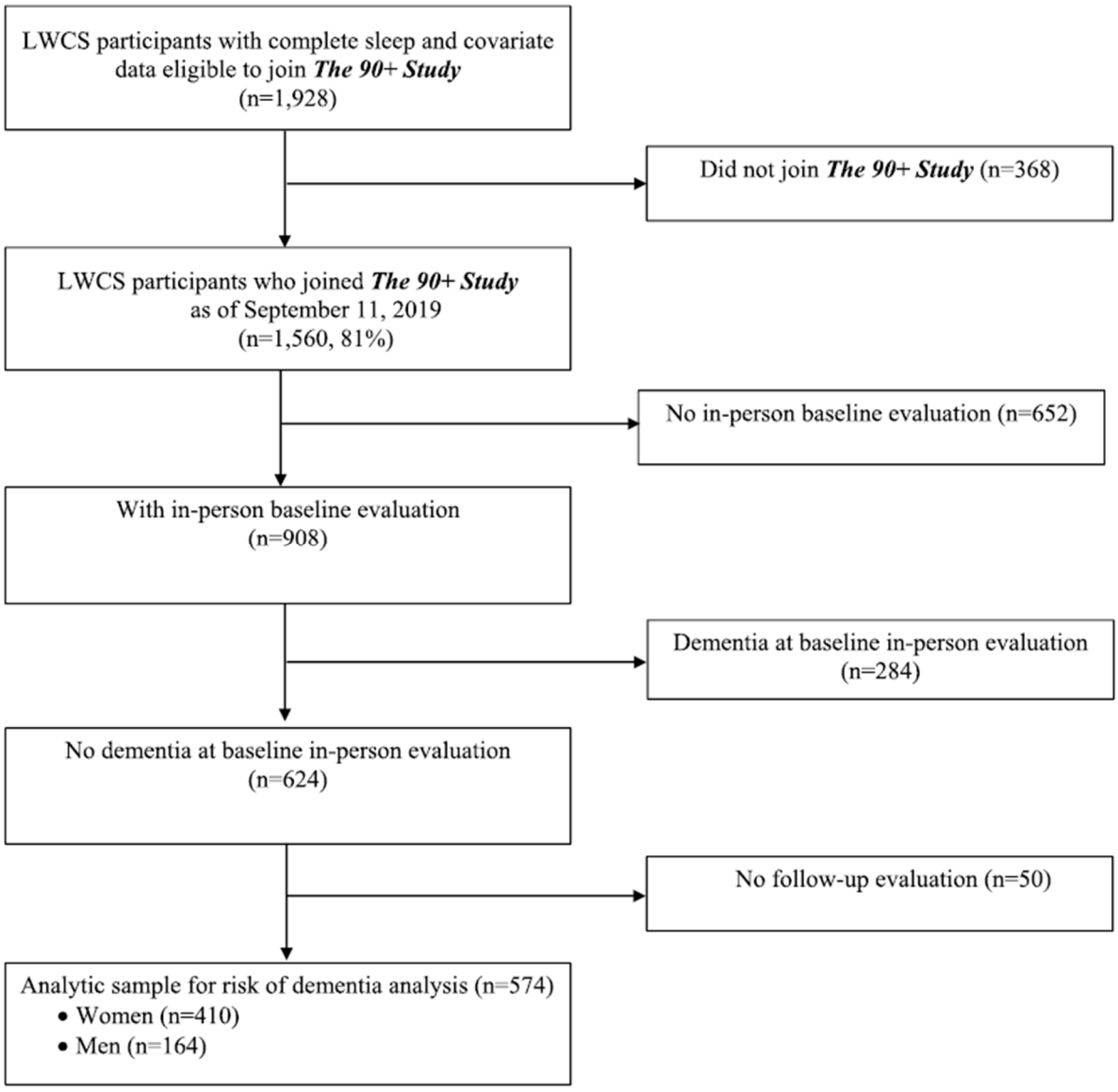

Figure 1. Flowchart of participant inclusion in sleep and risk of dementia analysis. LWCS, Leisure World Cohort Study.

Assessments

Primary independent variables: sleep reported as part of LWCS (1980s)

The one-time LWCS survey from the 1980s included three sleep questions:

(1) “How many hours of sleep do you usually get each night? __hours”,

(2) “Do you usually take a nap during the day? Yes/no”,

(3) “If yes, how long is your usual nap? __ minutes”.

Participants reported sleep and nap durations as integers. Information on sleep quality, sleep disorders, or sleep medications was not collected. We calculated 24-hr sleep duration as night sleep plus nap duration (assuming that naps were daily). Night and 24-hr sleep duration were categorized as: <6 (short), 6, 7, 8 (reference), >8 (long) hours. We chose 8 hours as the reference, because it is the most prevalent category in our group, is consistent with other relevant publications (Chen et al., 2016; Lo et al., 2016), and corresponds to National Sleep Foundation’s sleep duration recommendations for folder adults (Hirshkowitz et al., 2015). Nap duration was categorized as: 0 (no nap, reference), <60 minutes (short-to-moderate), ≥60 minutes (long) in accordance with another relevant study (Keage et al., 2012).

*Primary outcome: Incident dementia determined as part of **The 90+ Study** (2003 or later)*

The 90+ Study assessments occurred every 6 months between January 1, 2003, and September 11, 2019. Baseline and follow-up Diagnostic and Statistical Manual of Mental Disorders-IV dementia status (American Psychiatric Association, 1994) was determined by trained examiners (physicians or nurse practitioners) from their neurological examination, Clinical Dementia Rating scale (Morris, 1993), Mini-Mental State Examination (MMSE; Folstein et al., 1975), and Modified Mini-Mental Examination (3 MS; E. L. Teng & Chui, 1987) scores. No other tests were used for in-person determination of dementia status. For more information see Supplement and a previous paper (Corrada et al., 2010). If in-person follow-up evaluations were not possible, telephone evaluations or informant questionnaires were used for dementia status evaluation.

Covariates: reported as part of LWCS (1980s)

We used the following self-reported variables as covariates: age at LWCS, body mass index ((BMI), ≤24.9 (underweight or normal), >24.9 (overweight or obese) kg/m2; National Heart Lung and Blood Institute, 1998) calculated from self-reported height and weight, exercise (active outdoor and indoor activities, categorized as 0, <1, ≥1 hours/day), alcohol consumption (0, ≤1, >1 drinks/day), caffeine intake (<50, 50–199, ≥200 mg/day), smoking (never vs. ever), hypertension (yes/no; Paganini-Hill et al., 2016) based on their association with sleep and dementia (Benito-León et al., 2009; Paganini-Hill et al., 2011). LWCS participants were asked only the seven items from the Zung depression scale (Zung, 1965) that reflect positive outlook (henceforth “Zung+”). Sum of these items, an indicator opposite to depression, was used as a covariate (Paganini-Hill et al., 2018). Education was collected as part of ***The 90+ Study*** and categorized as high school or less, vocational school or some college, and college graduate or higher (Corrada et al., 2017).

The study was approved by the Institutional Review Boards of the University of California Irvine (HS#2001-2029) and the University of Southern California (HS-815001). All participants provided written informed consent.

Statistical analysis

We examined sex-specific risks of dementia in relation to self-reported sleep duration categories, napping (no/yes) and nap duration categories using Cox regression models with age as the time scale and age at dementia diagnosis (for those who developed dementia) as the primary outcome. Participants were considered at risk for dementia and contributed person-years from the age at the baseline evaluation until either (1) age at the follow-up evaluation when first diagnosed with dementia or (2) if never diagnosed with dementia, age at the last follow-up evaluation when known not to have dementia. Hazard ratios (HRs) for dementia were estimated and adjusted for above covariates. Additionally, night sleep analyses were adjusted for nap duration categories and nap analyses were adjusted for night sleep categories. The proportional hazard assumption for predictors and covariates was verified using the Schoenfeld residuals method, and no major violation was detected. We determined predicted survival curves based on the Cox regression model of the probability of being dementia free, stratified by sex and presented by categories of self-reported sleep duration and napping.

Participant characteristics were summarized as means, standard deviations, and ranges for continuous variables and as frequencies and percentages for categorical variables. Characteristics were compared between the sexes using Kruskal–Wallis test for continuous and chi-square test for categorical variables. Analyses were done using SAS 9.4 (SAS Institute Inc., Cary, NC).

Since we analyzed data only on a subset of the LWCS participants, in supplementary analyses, we explored whether our findings are subject to selection or survival bias. We determined whether the odds of having joined ***The 90+ Study*** vs. not having joined differed in relation to self-reported sleep and napping. We compared those who joined ***The 90+ Study*** (N = 1,560) vs (1) those eligible to join (alive and aged 90+ at the time of recruitment to ***The 90+ Study***), but who did not join (N = 368), (2) those who died before age 90 (N = 7,243), and (3) those who died at age 90+ but before the recruitment to ***The 90+ Study*** started (N = 3,635). The second analysis was done separately for those who died early and late based on median time between LWCS enrollment and death (13 years) to account for potential factors that might have affected sleep at different time points (Supplement).

Results

Characteristics of participants

Of 574 individuals included in the analyses, most were women (71%), had more than a high school education (76%), and White (99%). The LWCS sleep and covariate data were reported at a mean age of 69 years (range: 53–81). The mean age at the entry into ***The 90+ Study*** was 93 years (range: 90–102). The average time interval between reporting sleep and covariate data in the LWCS and the baseline visit with ***The 90+ Study*** was 24 years (range: 16–38). The average follow-up time for dementia after joining ***The 90+ Study*** was 3.3 years (range: 0.4–14). Nearly half (47%, N = 272) developed dementia during follow-up with ***The 90+ Study*** (Table 1, Supplementary Table S1 provides characteristics of those who did and did not develop dementia).

Most participants slept 8 (35%) or 7 (34%) hours per night (range: 4–10). There were no significant sex differences in mean sleep duration per night (7.2 hr, men and women) or per 24 hr (7.3 hours, women; 7.5 hours, men). Thirty percent napped with a mean nap duration of 33 minutes (range: 10– 90). A significantly higher proportion of men (46%) than women (24%) napped (Table 2, Supplementary Table S2 provides sleep characteristics of those who did and did not develop dementia).

Table 1. Characteristics of study participants: data from the Leisure World Cohort Study (1980s) and *The 90+ Study* (2003 or later).

	Entire group (n = 574)	Women(n = 410)	Men(n = 164)	Sex comparisons*p* Value[a]
LWCS (1980s) Self-Reported Characteristics				
Age, y, Mean [Range]	68.6[53–81]	68.5[53–81]	68.8[56–79]	0.49
Body mass index[b], n (%)				
≤24.9 kg/m^2 (underweight or normal)	406(71)	111(68)	295(72)	0.19
>24.9 kg/m^2 (overweight or obese)	168(29)	53(32)	115(28)	
Exercise, n (%)				
0 hours/day	72(12)	54(13)	18(11)	0.59
<1 hours/day	229(40)	163(40)	66(40)	
≥1 hours/day	273(48)	193(47)	80(49)	
Alcohol consumption, n (%)				
0 drinks/ day	109(19)	84(21)	25(15)	<0.01
≤1 drinks/ day	195(34)	157(38)	38(23)	
>1 drinks/ day	270(47)	169(41)	101(62)	
Caffeine consumption, n (%)				
<50 mg/day	141(25)	97(23)	44(27)	0.73
50–199 mg/day	219(38)	158(39)	61(37)	
≥200 mg/day	214(37)	155(38)	59(36)	
Ever smoked, n (%)	305(53)	209(51)	96(59)	0.10
History of hypertension, n (%)	173(30)	131(32)	42(26)	0.13
History of angina, Yes, n (%)	32(6)	20(5)	12(7)	0.25
History of myocardial infarction[c], Yes, n (%)	19(3)	7(2)	12(7)	<0.01
History of stroke, Yes, n (%)	10(2)	6(2)	4(2)	0.42
History of diabetes, Yes, n (%)	14(2)	8(2)	6(4)	0.23
History of cancer, Yes, n (%)	38(7)	31(8)	7(4)	0.15
Zung+, Mean (SD)	25.3(3.1)	25.4(3.0)	24.9(3.2)	0.10
The 90+ Study (2003 or later) – Baseline Visit				
Age, y, Mean [Range]	92.9[90.0–102.5]	92.9[90.0–102.5]	92.8[90.0–100.8]	0.85
Time between sleep and covariate report in the LWCS and entry in*The 90+ Study*,y, Mean [Range]	24.3[16–38]	24.4[17–38]	23.9[16–34]	0.26
MMSE total score, Mean (SD)	26.5(2.6)	26.7(2.6)	26.1(2.6)	<0.01
White, n (%)	567(99)	407(99)	160(97)	0.16
Education, n (%)				
High school or lower	138(24)	102(25)	36(22)	<0.01
Vocational school or some college	197(34)	161(39)	36(22)	
College or higher	239(42)	147(36)	92(56)	
The 90+ Study (2003 or later) – Follow-up				
Follow-up duration, y, Mean [Range]	3.3[0.4–13.8]	3.3[0.4–13.8]	3.1[0.5–11.8]	0.38
Incident dementia, n (%)	272(47)	204(50)	68(41)	0.07

Abbreviations: LWCS = Leisure World Cohort Study; MMSE = Mini-Mental State Examination; Zung+ is sum of 7 items from the Zung depression scale that reflect positive outlook.
[a]*p* Values from chi-square test for categorical and Kruskal–Wallis test for continuous variables.
[b]Body mass index calculated from self-reported height and weight.
[c]History of heart attack or myocardial infarction.

Table 2. Self-reported sleep from the Leisure World Cohort Study (1980s).

	Entire group(n = 574)	Women(n = 410)	Men(n = 164)	*p* Value[a]
Night sleep (hours)				
Mean (SD)[Range]	7.2(1.1)[4.0–10.0]	7.2(1.1)[4.0–10.0]	7.2(1.0)[4.0–9.0]	0.98
Categories, n (%)				
<6	37(6)	29(7)	8(5)	0.37
6	96(17)	71(17)	25(15)	
7	194(34)	132(32)	62(38)	
8	201(35)	141(35)	60(37)	
>8	46(8)	37(9)	9(5)	
24-hour sleep (hours)				
Mean (SD)[Range]	7.4(1.1)[4.0–10.5]	7.3(1.1)[4.0–10.5]	7.5(1.0)[4.0–10.5]	0.10
Categories, n (%)				
<6	35(6)	28(7)	7(4)	0.76
6	93(16)	68(17)	25(15)	
7	189(33)	132(32)	57(35)	
8	201(35)	141(34)	60(37)	
>8	56(10)	41(10)	15(9)	
Nap duration (minutes)				
Mean (SD)[Range]	33.4(17.4)[10.0–90.0]	31.9(17.8)[10.0–90.0]	35.4(16.8)[10.0–90.0]	0.08
Categories				
0	400(70)	312(76)	88(54)	<0.01
<60	143(25)	82(20)	61(37)	
≥60	31(5)	16(4)	15(9)	

[a]*p* Values from chi-square test for categorical and Kruskal–Wallis test for continuous variables.

Risk of incident dementia in relation to sleep duration and napping

Self-reported sleep duration was related to the risk of dementia in women but not in men. Compared with women who slept 8 hours, risk of dementia was approximately doubled in women who slept <6 hours per night (hazard ratio [HR] = 2.00, 95% confidence interval [CI] = 1.15–3.50; p= .01) or per 24-hr period (HR = 1.93, 95% CI = 1.02–3.43; p= .02; Table 3, Figure 2, also illustrated by survival curves on Supplementary Figures S2A, S2B).

Napping was related to the risk of dementia in men but not in women. Compared with men who did not nap, men who napped had a 55% lower risk of dementia (HR = 0.45, 95% CI = 0.26–0.79; p < .001). Men who napped less than 60 minutes, but not those who napped longer, had 67% lower risk of dementia (HR = 0.33, 95% CI = 0.18–0.63; p < .001) than men who did not nap (Table 3, Figure 2, also illustrated by survival curves on Supplementary Figures S2C, S2D).

Table 3. Hazard Ratios (HRs) for incident dementia in the oldest-old by self-reported sleep and nap categories.

	Women			Men		
	HR	95% CI	*p* Value	HR	95% CI	*p* Value
Night sleep (hours)						
<6	2.00	1.15, 3.50	0.01	0.75	0.22, 2.58	0.64
6	1.26	0.82, 1.92	0.29	0.69	0.31, 1.58	0.39
7	1.29	0.91, 1.83	0.16	1.00	0.56, 1.81	0.99
8	1.00	reference	-	1.00	reference	-
>8	1.06	0.61, 1.85	0.84	0.35	0.08, 1.58	0.17
24-hour sleep (hours)						
<6	1.93	1.02, 3.43	0.02	0.91	0.22, 3.75	0.89
6	1.31	0.86, 2.00	0.21	0.67	0.31, 1.45	0.31
7	1.21	0.85, 1.72	0.29	1.01	0.54, 1.89	0.98
8	1.00	reference	-	1.00	-	-
>8	1.11	0.66, 1.87	0.71	1.12	0.39, 3.11	0.84
Nap						
No	1.00	reference	-	1.00	reference	-
Yes	1.21	0.88, 1.66	0.25	0.45	0.26, 0.79	<0.001
Nap duration (minutes)						
0	1.00	reference	-	1.00	reference	-
<60	1.23	0.87, 1.73	0.24	0.33	0.18, 0.63	<0.001
≥60	1.08	0.53, 2.20	0.84	1.76	0.69, 4.44	0.23

Abbreviations: HR, hazard ratio; CI, confidence interval.
*Cox regression models adjusted for education and the Leisure World Cohort Study variables: age at entry, BMI, exercise, alcohol and caffeine intakes, smoking, hypertension, and Zung+ scores. Additionally, night sleep analyses were adjusted for categories of nap duration and nap analyses were adjusted for categories of night sleep.

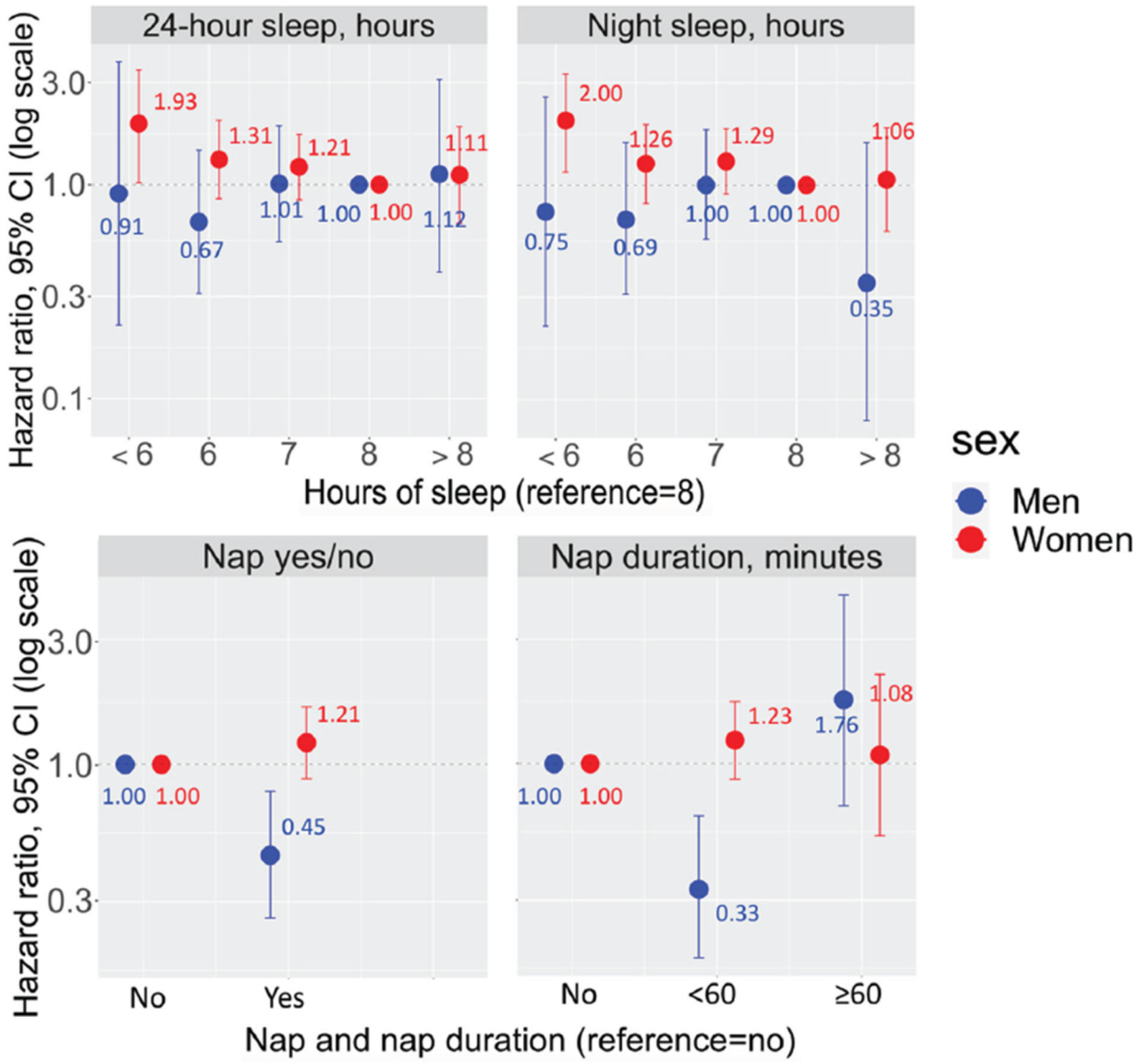

Figure 2. Risk of dementia in relation to self-reported sleep and nap by sex using Cox regression models. Abbreviations: CI, confidence interval. *Cox regression models adjusted for education and the Leisure World Cohort Study variables: age at entry, BMI, exercise, alcohol and caffeine intakes, smoking, hypertension, and Zung+ scores. Additionally, night sleep analyses were adjusted for categories of nap duration and nap analyses were adjusted for categories of night sleep.

Supplementary analyses

(1) The odds of having joined ***The 90+ Study*** vs. being eligible to join (alive and aged 90+ at the time of recruitment to ***The 90+ Study***) but not joining did not differ in self-reported sleep or napping (Supplementary Tables S3, S4). (2) The odds of having joined ***The 90+ Study*** vs. dying before age 90 differed in self-reported sleep and napping only for those who died early (within

13 years of joining LWCS); no difference was observed for those who died late (after 13 years of joining the LWCS). Men with long self-reported sleep (>8 hours), and men and women with long self-reported naps (≥60 minutes) had lower odds of joining ***The 90+ Study***. Those who died early were older and had more comorbidities at LWCS baseline than those who joined ***The 90+ Study*** (Supplementary Tables S5, S6). (3) The odds of having joined ***The 90+ Study*** vs. dying at age 90+ before the recruitment to ***The 90+ Study*** started did not differ in self-reported sleep or napping (Supplementary Tables S7, S8).

Discussion

We found that in oldest-old women risk of incident dementia was approximately doubled if they reported short sleep (<6 hours per night or per 24-hr period) at mean age of 69 years compared with women who reported 8 hours of sleep. We also found that in oldest-old men self-reported napping (at mean age of 69) was associated with 55% lower risk of incident dementia compared with men who reported no napping. While the risk was 67% lower for short-to-moderate self-reported naps (<60 minutes), no association was observed for men reporting long naps (≥60 minutes). In our group 47% of incident dementia rate within 3.3 years (range: 0.4–14) of follow-up is expected given that the risk of dementia doubles every 5 years of age and is the highest in those age 90+ (Corrada et al., 2010; Ganguli et al., 2015; Lobo et al., 2011). The association of short sleep with increased risk of cognitive impairment and of naps with decreased risk has been observed in younger-old (Benito-León et al., 2009; Chen et al., 2016; Keage et al., 2012), and we extend these findings to oldest-old men and women using exceptionally long interval (24 years) between sleep self-report and the beginning of dementia follow-up.

A number of studies with 3 to 25 years of follow-up using self-reported sleep and sleep measured objectively with actigraphy or polysomnography (PSG) found associations between short and long sleep with elevated risk of dementia or cognitive impairment (Benito-León et al., 2009; Chen et al., 2016; Lucey et al., 2021; Lutsey et al., 2018; Sabia et al., 2021). In our study, short self-reported sleep (<6 hours) was associated with higher risk of incident dementia in oldest-old women, but no association of long self-reported sleep (>8 hours) was observed. One explanation could be the decreased representation of participants with long self-reported sleep in our cohort due to the higher odds of them dying before age 90 years (Supplementary Table S6). Purported mechanisms through which short sleep negatively affects cognition include inflammation (Ferrie et al., 2013), increased amyloid and tau accumulation or decreased clearance (López-García et al., 2021; Ooms et al., 2014; Shokri-Kojori et al., 2018; Spira et al., 2013), hippocampal oxidative stress (Silva et al., 2004), inhibited neurogenesis (Mirescu et al., 2006), enhanced apoptosis (Naidoo et al., 2008), and adverse effects on blood pressure and insulin resistance, which might affect brain functioning and ultimately cognition (Buxton et al., 2012). The amyloid-sleep association is thought to be bidirectional in that accumulation of amyloid may lead to circadian disruption and shorter sleep, which in turn may contribute to amyloid accumulation (Musiek et al., 2015). Both sleep and cognition may be affected by a third factor, such as depression or blood pressure variability. Depression may be associated with disrupted and short sleep and increased risk of dementia through vascular damage, hormonal

changes, hippocampal atrophy, inflammation, and deficits in nerve growth factors (Burke et al., 2016; Byers & Yaffe, 2011; Scuteri et al., 2013). Blood pressure variability is linked to shortened REM sleep and dementia through vascular damage, hypoperfusion, hypotension, atherosclerosis, and endothelial dysfunction (X. Liu et al., 2021; Ma et al., 2020; Scuteri et al., 2009). Self-reported sleep duration may reflect qualitative sleep characteristics, such as insomnia (Scarlett et al., 2021); therefore, actigraphically or PSGmeasured sleep may give a better insight into sleep mechanisms associated with cognition at this age. We found the association of short self-reported sleep with increased risk of incident dementia in women but not in men, and studies suggest that for the same cognitive tasks women might need greater neuronal activity and engagement than men, which cannot be attained if sleep is insufficient (Rångtell et al., 2019). Another potential explanation is that women tend to report shorter sleep than men, providing more power to detect the effect (Gildner et al., 2014; Potvin et al., 2012; Van den Berg et al., 2009).

We found that short-to-moderate (<60 minutes) self-reported naps were associated with lower odds of dementia in oldest-old men, long self-repored naps showed no association. This may be because those with long naps had lower odds of survival beyond the first 13 years after joining the LWCS (Supplementary Table S6). Our finding is partially consistent with the only study of self- reported nap duration, where both short-to-moderate and long naps were associated with lower risk of cognitive decline at 2 years of follow-up (Keage et al., 2012). Short-to-moderate naps are known to benefit cognition through facilitation of memory consolidation (McDevitt et al., 2018), restoration of memory encoding capacity (Mander et al., 2011), reduction of oxidative stress (Hill et al., 2018), and lowering vascular demands (Brindle & Conklin, 2012). On the contrary, long naps (≥60 minutes) may disturb nighttime sleep, affect circadian rhythms, or be indicative of health problems (Yamada et al., 2015) which in turn, may negatively affect cognition. Indeed, long actigraphically measured naps have been associated with greater cognitive decline and higher risk of cognitive impairment in community-dwelling individuals (Leng et al., 2019; P. Li et al., 2022). Our finding of lower dementia risk in short-to-moderate naps was only in men, and some studies suggest that naps might have bigger cognitive benefit in men than women, potentially due to higher hippocampal acetylcholine levels in men or because men tend to nap more (Genzel et al., 2012; McDevitt et al., 2014; Nakagawa et al., 2016).

Strengths and limitations

Strengths of this study include high (81%) recruitment rate of LWCS participants into ***The 90+ Study***; short intervals (6 months) between dementia evaluations, use of several sources of information for cognitive diagnosis, and efforts to have complete follow-up data (home visits, telephone, or informant evaluations) to avoid underestimation of dementia incidence rate in this age group with highest dementia risk. Long interval between sleep self-report and start of dementia follow-up (on average 24 years) allows to assume that sleep was reported before or at the very early stages of the accumulation of dementia neuropathology, therefore this study contributes to ongoing efforts to understand whether sleep is a marker of or a factor contributing

to the development of dementia. The results suggest that sleep may be a contributing factor in developing dementia in the oldest-old.

We acknowledge several limitations. We used self-reported and not objectively measured sleep. While subjective and objective sleep measures may not always correspond well, in our study sleep was reported by individuals without dementia who still had good insight into their sleep. We have not collected information on qualitative sleep characteristics and medications. We have collected data on limited number of comorbidities, and their prevalence was low. Out of this limited list, we have adjusted analyses for relevant lifestyle factors and comorbidities. Sleep and covariate data were collected at one time point (rather than repeatedly), so stability of these characteristics is unknown. Generalizability of our results may be limited to primarily White and well-educated individuals.

Since we analyzed data from a subset of the LWCS participants, we conducted sensitivity analyses to explore potential selection and survival biases by examining whether the odds of joining versus not joining ***The 90+ Study*** differed in self-reported sleep and napping. The odds of joining versus not joining did not differ in self-reported sleep or napping in those who lived to age 90 + . The only difference was that more participants who died before age 90 and within the first 13 years of the LWCS reported long sleep (>8 hours, men) and naps (≥60 minutes, men and women) compared with those who joined ***The 90+ Study***. Those individuals were also older and had more comorbidities, so long sleep and naps may be indicative of poor health closer to death. Therefore, it is likely that our findings are relatively robust to the potential selection and survival biases.

Conclusions

Using a long interval between sleep self-report and start of dementia follow-up (average 24 years), we extended sleep-dementia investigations to oldest-old individuals, demonstrating that short self- reported sleep (<6 hours) is associated with increased risk of incident dementia in women and short- to-moderate (<60 minutes) naps are associated with lower risk of dementia in men. We conclude that sleep is an important risk factor for dementia in the oldest-old.

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Disclosure statement

Z.A.M., C.H.K., A.P-H, M.J.P., L.J., M.M.C. have no conflict of interest to declare. B.A.M. has received consulting fees from Eisai.

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Author change form

We have removed Michael J. Phelan, Ph.D., from the authors list because he has retired and asked to remove him from the authors list.

We have added Luohua Jiang, Ph.D., to the authors list because she has contributed significantly to the manuscript revision.

Data availability

The dataset used for the current study is available from the corresponding author on reasonable request.

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