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博　士　論　文

Sleep duration and excessive daytime sleepiness are associated with incidence of disability in community-dwelling older adults.

（地域在住高齢者において、

睡眠時間と過度の日中の眠気は障害発生に関連する）

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神戸大学大学院保健学研究科保健学専攻

中窪　翔

INTRODUCTION

Disability in older adults, which is a growing public health concern, is associated with poorer physical and mental health, greater use of medical care, and a higher rate of institutionalization [1, 2]. Identifying risk factors for incident disability is therefore important for the development of preventive strategies.

Sleep disturbances are common among older adults, with over half of community-dwelling older adults reporting chronic sleep complaints [3]. Sleep complaints have been associated with various adverse health outcomes, including disability in older adults [4]. Previous studies have identified insulin resistance [5], autonomic nervous system dysregulation [5, 6], metabolic derangement [7], and inflammation [8] as potential mediators between sleep disturbances and incident disability. Only one longitudinal study has examined the association between sleep complaints and incident disability among older adults.[4] Change in sleep duration with aging is common, and a longitudinal study has revealed that long sleepers tend to have relatively poorer sleep quality.[9] However, the association between sleep duration and incident disability has not yet been fully elucidated.

In contrast, many studies have investigated excessive daytime sleepiness (EDS) in older adults. EDS is one of the most common sleep disturbances, and presents in 15% to 30% of community-dwelling older adults [10-12]. EDS is associated with several adverse health outcomes, including psychiatric disorders [13], falls [14], and cognitive deficits [15, 16]. Although a few cross-sectional studies have shown an association between disability and sleep complaints, such as difficulty falling asleep or awakening during the night or early morning [4, 17], the impact of EDS on the risk of disability is not well understood. Thus, additional evidence is needed to reveal these associations.

No longitudinal study has examined the impact of both sleep quality and quantity on incident disability. In the current study, we examined whether EDS, sleep duration, and their combination affect subsequent incident disability in community-dwelling older adults. We hypothesized that those who have both long sleep durations and EDS would reflect the worsened sleep conditions and show more risk of disability than those with either EDS or long sleep durations only.

MATERIALS AND METHODS

Setting and participants

The Obu Study of Health Promotion for the Elderly (OSHPE) is an observational study designed to investigate physical and cognitive function among the elderly population. The study enrolled 5,104 community-dwelling older adults. Participants were recruited from Obu, Japan, which is a residential suburb of Nagoya. Inclusion criteria required that participants were aged 65 years or older at examination in 2011 or 2012, lived in Obu, and had not participated in another study in the past. After the baseline assessment, monthly information on participants' health status, including incident disability as assessed by the Japanese public long-term care insurance (LTCI) system, death, or relocation from Obu was obtained from the Obu city office. Three hundred and forty-eight participants were excluded based on the following criteria: 1) missing values at baseline assessment; 2) a history of Parkinson's disease, Alzheimer's disease, or depression; 3) severe cognitive impairment as indicated by Mini Mental State Examination (MMSE) scores < 18 [18]; and 4) already certified by LTCI at any level during the baseline assessment. The final analysis sample consisted of 4,755 participants. Informed consent was obtained from all participants before their inclusion in the study, and the Ethics Committee of the National Center for Gerontology and Geriatrics approved the study protocol.

Measures

Certification of need for care in the LTCI system

The nationally uniform criteria for long-term care need certification was objectively established by the Japanese government, and certification of need with respect to levels of care for older adults is determined based on evaluation results by the Certification Committee for Long-Term Care Need in municipalities in accordance with these basic guidelines. The process of eligibility for certification of need for care in the LTCI system is as follows: (1) an elderly person or caregiver contacts the municipal government to request official certification of the care needs of the applicant; (2) a trained local government official then visits the home to evaluate nursing care needs based on current physical and mental status; (3) after completion of the assessment, the results are entered into a computer to calculate the standardized scores on physical and mental status, estimate the time required for the care of the individual (grooming, bathing, eating, toileting, transferring, assistance with instrumental activities of daily living (IADL), behavioral problems, and rehabilitation and medical services), and assign a care-need level based on the total estimated care time; (4) the care needs certification board reviews the data, which include a report from the primary physician of the applicant; and (5) finally, the applicant is assigned to the level of care required (certified support-level ranging from 1–2 or care-level ranging from 1–5). Every 6 months, the eligibility of the individual receiving care via the LTCI system is re-evaluated. In the present study, incident disability was defined as the onset of certification at support-level 1–2 or care-level 1–5.

Assessment of sleep habits

At baseline assessment, participants were asked about usual sleep and wake times, and the answers were used to calculate sleep durations. EDS was assessed using the question “How often do you have daytime sleepiness requiring a nap?” with the following options: “almost always,” “sometimes,” and “rarely or never.” EDS was deemed to be present when it was reported to occur “almost always.”

Other measurements

Sociodemographic variables including sex, age, and education level (years) were collected along with medical history, weight (kg), and height (m). Body mass index (BMI) was derived as weight in kilograms divided by the square of height in meters. Participants were asked about medical diagnoses and medications via face-to-face interviews. Depressive symptoms were measured with the Geriatric Depression Scale [19] (range 0–15), with higher scores indicating more depressive symptoms. The Geriatric Depression Scale includes 15 items, and participants whose total score was ≥6 were defined as having depressive symptoms. Global cognitive function was measured using the

MMSE. Physical activity was assessed by the total amount of time spent walking on an average day. For smoking and alcohol drinking status, participants were categorized as current, past, or never smokers or alcohol drinkers, respectively.

Statistical Analysis

All analyses were performed using SPSS 21.0 J for Windows (SPSS Japan Inc., Tokyo, Japan). Participants were divided into three groups according to sleep duration (short: ≤6.0 h, mid: 6.1 to 8.9 h, long: ≥9.0 h)[20-22] and categorized with respect to presence or absence of EDS. Furthermore, we also divided participants according to the combination of sleep duration and EDS as follows: 1) short sleep duration and absence of EDS (short & no EDS); 2) short sleep duration and presence of EDS (short & EDS); 3) mid sleep duration and absence of EDS (mid & no EDS, control); 4) mid sleep duration and presence of EDS (mid & EDS); 5) long sleep duration and absence of EDS (long & no EDS); and 6) long sleep duration and presence of EDS (long & EDS). Continuous data are presented as means ± standard deviations (SDs). Characteristics were summarized as means ± SDs for continuous variables and as counts and percentages for categorical variables. Comparisons were performed using analysis of variance and Pearson's chi-square test for categorical data. Kaplan-Meier survival analysis for the incidence of disability was performed to compare sleep duration or presence of EDS. Furthermore, univariate and multivariate Cox's proportional hazard regression models were conducted to assess hazard ratios (HR) with 95% confidence intervals (CI) for the risk of incident disability. In multivariate analysis, potential confounders included age, sex, BMI, education level, number of medications, MMSE score, chronic disease, depressive symptoms, smoking habits, alcohol consumption, and physical activity. The significance level was set at $p < 0.05$ for all tests.

RESULTS

The number (%) of participants in each age range exhibiting short sleep duration was as follows: 65-69 years: 232 (12.1%), 70-74 years: 156 (10.5%), 75-79 years: 79 (5.1%), 80-84 years: 19 (5.1%), 85 years ≤: 4 (3.0%), total: 490 (10.3%). The number (%) of participants in each age range exhibiting long sleep duration was as follows: 65-69 years: 212 (11.1%), 70-74 years: 252 (17.0%), 75-79 years: 206 (24.1%), 80-84 years: 128 (34.0%), 85 years ≤: 55 (41.7%), total: 853 (17.9%). Further, the prevalence of EDS tended to increase with participant age: 65-69 years: 218 (11.4%), 70-74 years: 205 (13.9%), 75-79 years: 167 (19.6%), 80-84 years: 66 (17.6%), 85 years ≤: 33 (25.0%), total: 689 (14.5%) (p for trend < 0.01). Descriptions of the baseline characteristics of these 6 groups are presented in Table 1; all variables except history of respiratory illness were significantly different among groups. Of the 4,755 participants initially included, 198 participants (5.4%) developed a disability during the 24-month follow-up period. Incident disability rates in each group were as follows: 1) short & no EDS, n = 10 (2.6%); 2) short & EDS, n = 5 (4.8%); 3) mid & no EDS (control), n = 95 (3.2%); 4) mid & EDS, n = 20 (4.4%); 5) long & no EDS, n = 47 (6.5%); and 6) long & EDS, n = 21 (16.2%).

Kaplan-Meier survival curves showed the highest rate of incident disability in the long sleep duration group and in the presence of EDS (Fig. 1 and 2, $p < 0.01$ for both). In this analysis, the mean time period for new incident disability was 23.2 months in the presence of EDS and 23.6

Table 1
Baseline Characteristics of 6 Groups

	Total, n = 4756	Short and No EDS, n = 386	Short and EDS, n = 104	Mid and No EDS, n = 2957	Mid and EDS, n = 455	Long and No EDS, n = 723	Long and EDS, n = 130	P^*
Age, y, mean ± SD	71.94 ± 5.46	70.66 ± 4.72	71.02 ± 4.44	71.32 ± 5.14	72.82 ± 5.62	73.95 ± 6.02	76.27 ± 6.27	<.001
Women, n (%)	2380 (50.1)	226 (58.5)	57 (54.8)	1575 (53.3)	220 (48.4)	253 (35.0)	49 (37.7)	<.001
BMI, kg/m^2, mean ± SD	23.44 ± 3.13	23.83 ± 3.36	24.44 ± 3.15	23.34 ± 3.07	23.75 ± 3.22	23.27 ± 3.18	23.58 ± 3.01	<.001
Education, y, mean ± SD	11.37 ± 2.54	11.79 ± 2.56	11.33 ± 2.50	11.46 ± 2.49	11.26 ± 2.65	11.00 ± 2.58	10.43 ± 2.58	<.001
Medications, n, mean ± SD	2.01 ± 2.07	1.88 ± 1.99	2.34 ± 2.60	1.87 ± 1.97	2.31 ± 2.21	2.27 ± 2.17	2.82 ± 2.57	<.001
MMSE, mean ± SD	26.28 ± 2.59	26.41 ± 2.53	26.64 ± 2.49	26.49 ± 2.49	26.29 ± 2.46	25.55 ± 2.85	24.88 ± 2.90	<.001
Physical activity, min/d, mean ± SD	279.53 ± 159.50	298.56 ± 173.09	264.81 ± 161.32	288.27 ± 160.38	264.79 ± 160.26	253.68 ± 145.41	231.50 ± 139.27	<.001
Depressive symptoms (GDS ≥ 6), n (%)	669 (14.1)	54 (14.1)	25 (24.0)	344 (11.7)	79 (17.5)	133 (18.4)	34 (26.2)	<.001
Sleep duration, h, mean ± SD	7.74 ± 1.26	5.64 ± 0.62	5.52 ± 0.72	7.59 ± 0.64	7.60 ± 0.64	9.58 ± 0.95	9.67 ± 0.89	<.001
Smoking, n (%)								<.001
Never	2807 (59.0)	247 (64.0)	55 (52.9)	1828 (61.8)	267 (58.8)	344 (47.6)	66 (50.8)	
Past	1472 (31.0)	95 (24.6)	32 (30.8)	859 (29.0)	135 (29.7)	302 (41.8)	49 (37.7)	
Current	475 (10.0)	44 (11.4)	17 (16.3)	270 (9.1)	52 (11.5)	77 (10.7)	15 (11.5)	
Alcohol consumption, n (%)								.011
Never	2197 (46.2)	189 (49.0)	48 (46.2)	1402 (47.4)	216 (47.6)	287 (39.7)	55 (42.3)	
Past	356 (7.5)	31 (8.0)	9 (8.7)	197 (6.7)	37 (8.1)	67 (9.3)	15 (11.5)	
Current	2201 (46.3)	166 (43.0)	47 (45.2)	1358 (45.9)	201 (44.3)	369 (51.0)	60 (46.2)	
Chronic disease, n (%)								
Hypertension	2220 (46.7)	169 (43.8)	58 (55.8)	1330 (45.0)	228 (50.1)	361 (49.9)	74 (56.9)	.002
Stroke	241 (5.1)	18 (4.7)	10 (9.6)	113 (3.8)	23 (5.1)	61 (8.4)	16 (12.3)	.001
Heart disease	786 (16.5)	75 (19.4)	18 (17.3)	451 (15.3)	82 (18.0)	123 (17.0)	37 (28.7)	.001
Diabetes	643 (13.5)	52 (13.5)	23 (22.1)	362 (12.2)	65 (14.3)	111 (15.4)	30 (23.1)	.001
Respiratory illness	530 (11.1)	44 (11.4)	15 (14.4)	302 (10.2)	59 (13.0)	95 (13.1)	15 (11.5)	.146

GDS, 15-item Geriatric Depression Scale.
*Continuous variables were analyzed by analysis of variance, and categorical variables were analyzed by χ^2 test.

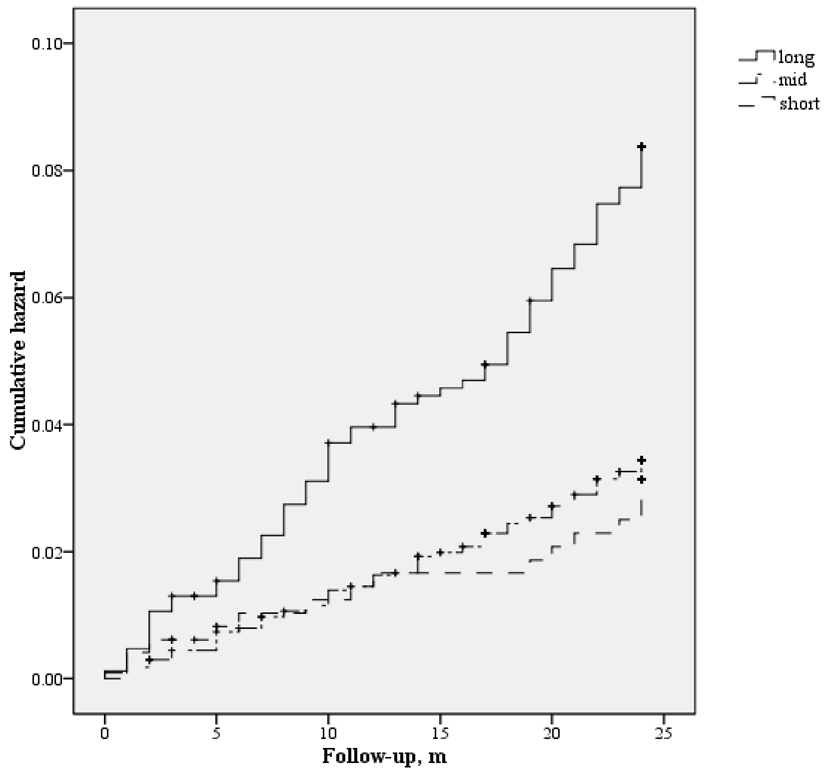

Fig.1 Kaplan-Meyer survival curves of older adults showing the relationship between incident disability and sleep duration

months in the absence of EDS. Regarding sleep duration, the mean time period for new incident disability was 23.1 months for long sleep duration and 23.6 and 23.7 months for mid and short sleep durations, respectively.

Moreover, in the crude model, Cox's proportional hazard regression showed that the long sleep duration group had a higher rate of incident disability compared with the mid sleep duration group (HR: 2.43, CI 95%: 1.80-3.28), whereas the short sleep duration group did not differ from the mid sleep duration group (HR: 0.91, CI 95%: 0.53-1.56). These results were also sustained in adjusted models for age, sex, BMI, and education level (HR: 1.55, CI 95%: 1.13–1.23) and fully

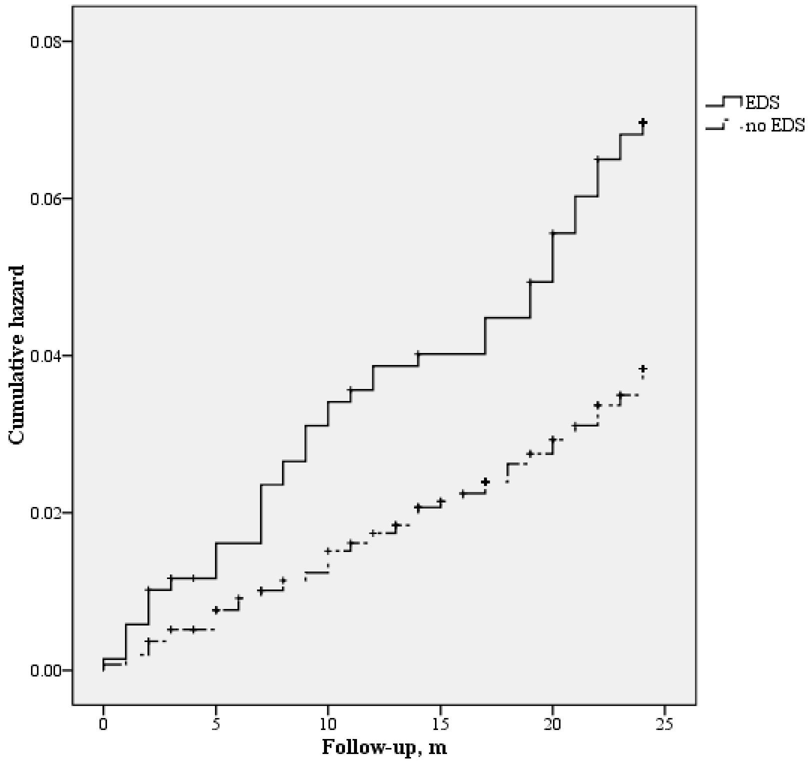

Fig.2 Kaplan-Meyer survival curves of older adults showing the relationship between incident disability and excessive daytime sleepiness (EDS)

adjusted models (HR 1.43, CI 95% 1.04–1.97). However, the presence of EDS group also had a higher rate of incident disability than the no EDS group (HR: 1.82, CI 95%: 1.31–2.53). These results were also sustained in adjusted models for age, sex, BMI, and education level (HR: 1.51, CI 95% 1.08–2.11) and fully adjusted models (HR 1.41, CI 95% 1.01–1.98). Furthermore, the long & no EDS group and the long & EDS group showed significantly higher hazard rates of incident disability compared with that in the control group in adjusted model 1. In adjusted model 2, however, only the long & EDS group showed a higher rate of incident disability (Table 2, Fig. 3).

Table 2
Crude and Multivariate Cox Proportional Hazard Regression Models

	Hazard Ratio (95% Confidence Interval)		
	Crude Model	Adjusted Model 1	Adjusted Model 2
Short and no EDS	0.81 (0.42–1.55)	0.95 (0.50–1.84)	0.94 (0.49–1.82)
Short and EDS	1.52 (0.62–3.74)	1.83 (0.74–4.51)	1.84 (0.74–4.56)
Mid and no EDS	ref.	ref.	ref.
Mid and EDS	1.38 (0.85–2.24)	1.14 (0.70–1.85)	1.11 (0.68–1.80)
Long and no EDS	2.06 (1.45–2.92)	1.34 (0.92–1.93)	1.27 (0.88–1.83)
Long and EDS	5.45 (3.40- 8.74)	2.74 (1.68–4.47)	2.25 (1.36–3.70)

Significance set at $P < .05$.
Adjusted model 1: adjusted for age, sex, BMI, and education level.
Adjusted model 2: adjusted for model 1 covariates, number of medications, MMSE score, chronic disease, depressive symptoms, smoking habit, alcohol consumption, physical activity.

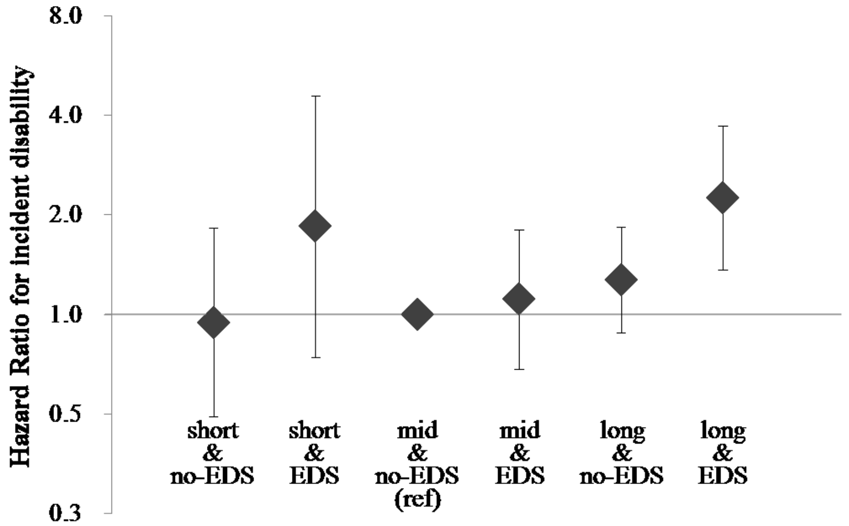

Fig. 3 Multivariate Cox's proportional hazard regression models adjusted for age, sex, BMI, education level, number of medication, MMSE score, chronic disease, depressive symptoms, smoking habit, alcohol consumption, and physical activity.

DISCUSSION

Our study revealed that both long sleep duration and EDS were risk factors associated with incident disability among older adults. Furthermore, the combination of longer sleep duration and EDS was associated with a higher risk of disability. These results were sustained in multivariate analyses adjusted for age, sex, education level, BMI, number of medications, MMSE score, chronic disease, depressive symptoms, smoking habits, alcohol consumption, and physical activity.

Emerging evidence indicates that sleep complaints are associated with a wide variety of adverse health consequences, including cognitive decline [15, 16, 23, 24], decrease of physical function [20], and mortality [25]. One cross-sectional study indicated that complaints of frequent awakenings or daytime sleepiness were independently associated with self-reported IADL impairment in older women [13]. Furthermore, another cross-sectional study of more than 9,000 older adults found that high scores on a self-reported measure of poor sleep quality and related daytime complaints were associated with self-reported impairment in ADL and related tasks [26]. A longitudinal study revealed that reports of trouble falling asleep were a risk factor for IADL impairment, and reports of waking up at night and not feeling rested in the morning were associated with incident ADL disability [4]. Moreover, daytime sleepiness, taking naps, or not feeling rested in the morning increased the risk of developing mobility disability [4]. Together these studies reveal that sleep complaints indicate a risk of disability, although the outcomes of sleep complaints varied among studies. EDS is one of the most important complaints, and therefore, our evidence of the relationship between EDS and disability further extended this relationship.

Long sleep duration also was related to incident disability in our study. The ability to initiate and maintain sleep declines with aging and causes a progressive decrease in sleep quality. In fact, the prevalence of sleep disorders is elevated in older adults; despite spending more time in bed, older adults report more complaints about sleep [27]. Long sleepers also were found to have a greater wake after sleep onset (WASO) frequency and lower sleep efficiency [27], and both are associated with decline of physical function [28] and cognitive function [29]. The long sleep duration group in our study may have had poor sleep characteristics in common with those studies. In a study using objective sleep assessment, incident IADL impairment was associated with greater WASO in unadjusted models and lower sleep efficiency in adjusted models [30]. Thus, our findings are consistent with the results of other studies.

This study adds to the available evidence that co-existence of EDS and long sleep duration has a negative impact on incident disability. Excessive sleepiness, as defined by Ohayon, consists of excessive sleep quantity and excessive somnolence at inappropriate times [31]. In other cases, the deteriorated quality of wakefulness during daytime is part of the impairment/consequences associated with the sleep disorder (e.g., insomnia, restless legs syndrome). In fact, our study showed that the proportion of EDS considerably increased among older adults with long sleep duration (more than 9 hours of sleep) compared with the mid sleep duration group (between 7 and 9 hours). Thus, those who slept for long durations and experienced EDS may require greater amounts of sleep, reflecting worse sleep conditions, and have a greater risk of incident disability.

The mechanisms underlying the association between long sleep duration/EDS and higher incidence of disability remain unknown. Several studies have observed that long sleep duration is associated with a sedentary lifestyle and low levels of daytime physical activity[32-34], suggesting that sedentary lifestyle may account for part of the increased risk for decline in physical function observed in this group. Other studies have suggested that sleep duration is related to muscle mass and muscular performance independent of testosterone levels.[35] Furthermore, Lee *et al.* revealed that long sleep duration was associated with 5-year mortality in older adults, while insomnia and daily napping were specifically associated with 5-year mortality in older men.[36] Several researchers have hypothesized that long sleep duration may reflect an increased need for sleep, which has in turn been associated with decreased physical strength, poor health status, and comorbidity.[37-39] Although analysis in the present study also adjusted for specific confounding factors including disease history, other factors such as neuroendocrine dysfunction or subclinical inflammation may be involved. Further research is required to elucidate these mechanisms.

This study had several limitations. First, self-reported measures of sleep duration and EDS were utilized, rendering the study incapable of performing a truly objective assessment of sleep characteristics, such as an assessment performed using actigraphy. Previous research has suggested that self-reported long sleepers [40] as well as average sleepers [41] tend to overestimate their total sleep time, and that their self-reported sleep time largely corresponds to time in bed. Mortality risks associated with self-reported long sleep might be partly attributable to long time in bed. However, given the high correlation of time in bed with total sleep time, reported long sleep is likely to be indicative of long physiologic sleep, as confirmed recently [9]. Thus, it is necessary to verify whether individuals among those in the long sleep duration group required longer sleep due to non-restorative sleep caused by underlying conditions or simply naturally required more sleep. Future studies must also verify the association of sleep duration/EDS with incident disability using objective methods of assessment, such as wrist actigraphy. Second, "long sleep duration" was defined in the present study as sleep duration of nine hours or longer. However, some studies have used a cut-off point of 10 hours rather than 9. Such differences in cut-off value may affect the results of the studies and their comparison. Thirdly, we did not determine whether participants had other sleep disorders, such as obstructive sleep apnea (OSA) or restless legs syndrome. This is particularly important to address in future studies because OSA is one significant cause of EDS, and may be associated with functional decline. Finally, we did not assess any underlying physiological changes (e.g. melatonin, growth hormone secretion) that may have been associated with increases or decreases in sleep duration.

CONCLUSION

Long sleep duration and EDS were associated with a higher risk of incident disability among community-dwelling older adults after adjusting for possible confounders. These findings suggest that excessive quantities of sleep increase the risk of developing negative conditions in older adults. Further studies using objective assessments of sleep are needed to reveal the impact of inappropriate sleep on incident disability.

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