

1 Title: Daily sleep duration and the risk of incident disability among younger-elderly Japanese  
2 in the New Integrated Suburban Seniority Investigation (NISSIN) Project: a prospective  
3 study using competing event analysis

4

5 Short running title: Sleep duration and incident disability

6

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#### 6 Author contributions

7 LZ contributed to the conception, analysis and interpretation of data, and preparation of  
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10 feedback. MA, KW, and TK contributed to the design, acquisition of data, critical review and  
11 feedback. AT contributed to the design, acquisition of data, interpretation of data, critical  
12 review and feedback.

13

1 Abstract

2

3 Aim: This study aimed to investigate the association between daily sleep duration and  
4 incident disability among younger-elderly individuals in Japan.

5 Methods: We conducted a prospective cohort study, the New Integrated Suburban Seniority  
6 Investigation Project, including 1,895 (962 men and 933 women) Japanese physically and  
7 socially independent individuals aged  $\geq 65$  years. Information on daily sleep duration,  
8 demographic, lifestyle characteristics, and medical status were collected by questionnaire  
9 and health check-up in every year from 1996 through 2005. Dates of incident disability were  
10 confirmed using the certification for the Long-term care insurance in Japan. We treated  
11 censored cases due to death as competing events. Competing risk model was used to  
12 calculate the hazard ratio (HR) and 95% confidence interval (CI) for incident disability.

13 Results: During a median of 12.7 years of follow-up, 256 participants (114 men and 142  
14 women) incident disability. Compared with a sleep duration of 7-7.9 hours/day, sleeping <  
15 6hours/day was increased risk of incident disability (HR 1.64; 95%CI, 1.13-2.38 for total; HR  
16 1.90; 95%CI, 1.19-3.03 for women).

17 Conclusions: The present findings suggest that shorter sleep duration was associated with a  
18 higher risk of incident disability among Japanese elderly people.

19

20 Key Words: Disability, Prospective cohort study, Sleep duration.

21

1 Introduction

2 Sleep is considered to be a fundamental lifestyle along with dietary habit and physical activity

3 <sup>1</sup>. Previously, several observational studies for elderly population revealed that short or long  
4 sleep duration is associated with the incident stroke <sup>2</sup>, ischemic heart disease<sup>3</sup>, as well as  
5 all-cause mortality<sup>4</sup>.

6 With the population aging, the number of elderly individuals disability is increasing  
7 worldwide<sup>5</sup>. Especially, the number of people with disability aged 65 or older is constantly  
8 increasing in Japan where facing the super-aging society and reached around 0.63 million  
9 people (18.1% of elderly people)<sup>6</sup>, and costed approximately 184.1 thousand yen (100 yen =  
10 0.88 dollars) per person on long-term care in 2016<sup>7</sup>. Although, there is one prospective cohort  
11 study included 4,756 elderly Japanese participants suggested that long sleep duration was  
12 associated with higher rate of incident disability<sup>8</sup>, the association between sleep duration and  
13 incident disability has not yet been fully elucidated. Thus, additional prospective evidence  
14 regarding the association between daily sleep duration and subsequent incident disability is  
15 needed.

16 Because risks of incident disability coincide with a decline in functional status and  
17 cognitive decline, risks of incident disability are also linked to mortality risk in the older adult  
18 population, and evidences suggest that predictors of incident disability are often those that  
19 also predict mortality<sup>2</sup>, but the previous study does not recognize death as a censored event  
20 related to loss of information<sup>8</sup>. Therefore, the present study aimed to investigate the  
21 association between daily sleep duration and incident disability with treating all-cause

1 mortality as a competing event among physically and socially independent elderly people  
2 based on a Japanese age-specific cohort.

3

#### 4 Methods

##### 5 Study population

6 The New Integrated Suburban Seniority Investigation (NISSIN) Project is an age-specific  
7 prospective cohort study and has been reported in detail elsewhere<sup>9</sup>. Briefly, 3,073  
8 community-dwelling elderly individuals who were aged 64/65 years and lived in the city of  
9 central Japan were enrolled in this study. They completed baseline comprehensive medical  
10 examination and asked to complete a self-reported questionnaire every June between 1996  
11 and 2005. We excluded individuals who registered before 2000 (n=1,107) because the  
12 Long-term Care Insurance in Japan has started in 2000, those with lower level physical and  
13 social functioning (n=39) and missing information on physical and social functioning (n=32).  
14 Accordingly, 1,895 (962 men and 933 women) individuals were analyzed in the present study.  
15 The physical and social functioning was assessed by using the Tokyo Metropolitan Institute  
16 of Gerontology index of competence which measures the functional capacity and has been  
17 adapted for and validated in the senior Japanese population<sup>10</sup>. A higher score indicated higher  
18 independence of elderly individuals, so a score of 10 or higher was treated as an independent  
19 in this paper<sup>10</sup>. This study was approved by the Ethics Committees of Nagoya University  
20 Graduate School of Medicine, the National Center for Geriatrics and Gerontology of Japan,  
21 Aichi Medical University School of Medicine, and Hokkaido University Graduate School of

1 Medicine.

2

3 Assessment of Sleep Duration

4 Information on sleep duration was assessed by asking the following question: “How many  
5 hours a day do you sleep over the last year?” The answer was categorized into the following  
6 five groups: <6, 6-6.9, 7-7.9, 8-8.9,  $\geq 9$  hours/day<sup>11</sup>.

7

8 Follow-up

9 Dates of incident disability were confirmed using the certification for the Long-term  
10 care insurance (LTCI) by the local government of Nisshin city, which launched in April 2000  
11 in Japan<sup>12</sup>. Dates of death were confirmed using death certificates. We treated relocation out  
12 of the city as a censored case. All participants were followed until December 31, 2015,  
13 whichever came first.

14 The LTCI is one of the mandatory national insurance plans for elderly people in Japan,  
15 and it was instituted to support the independence of elderly people, rather than simply  
16 providing personal care<sup>12</sup>. The certification for LTCI has been reported in detail elsewhere<sup>13</sup>.  
17 Briefly, all individuals aged 65 years or older, or those aged 40–64 years who suffer from  
18 age-related diseases are eligible for LTCI benefits in Japan. When a person applies to their  
19 municipality for LTCI benefits, an authorized care manager examines their physical and  
20 mental status using a standardized questionnaire. Then the certification board, which includes  
21 medical doctors and nurses, determines the level of long-term care needed based on the

1 estimated time required for care, as well as on comments from the applicant's family  
2 physician. The LTCI certifications consist of the following eight levels: independent, support  
3 levels 1–2 and care levels 1–5. We defined a person who certified LTCI in the support level 1,  
4 described as a person is independent in basic activities of daily living but requires some  
5 assistance in instrumental activities of daily living, or higher as a disability.

6

## 7 Statistical Analysis

8 Baseline characteristics of the participants were expressed as numbers (percentages). The  
9  $\chi^2$ -test was used to compare categorical variables. Sex-specific multivariable hazard ratios  
10 (HRs) and confidence intervals (CIs) for an incident disability were calculated by Cox  
11 proportional model. And then, we conducted further analysis using competing risk model<sup>14</sup>.  
12 We treated all-cause mortality as a competing event according to previous study<sup>11</sup>. Potential  
13 confounders such as year of participation (continuous variable), body mass index (BMI,  
14 <18.5, 18.5-24.9,  $\geq 25$  Kg/m<sup>2</sup>), Educational attainment (lower junior high school, upper high  
15 school), working status (employed, unemployed), marital status (married, other), smoking  
16 status (never, past, current smokers), drinking status (never, current drinkers), daily walking  
17 time (<1,  $\geq 1$  hour/day), depressive tendency (presence, absence), physical and social  
18 functioning (independent, dependent), a history of cardiovascular disease (yes, no/missing),  
19 cancer (yes, no/missing), diabetes mellitus (yes, no/missing), hypertension (yes, no/missing),  
20 hyperlipidemia (yes, no/missing) were introduced in the model. BMI was calculated as  
21 weight in kilograms divided by height in meter squared. The depressive tendency was

1 assessed by the short-form Geriatric Depression Scale which is a self-rated  
2 depression-screening tool for elderly people<sup>15</sup>. The presence of depressive tendency was  
3 defined a total score of 6 or higher<sup>16</sup>. Hypertension was defined as individuals with systolic  
4 blood pressure  $\geq 140$ mmHg, or diastolic blood pressure  $\geq 90$ mmHg, or use of antihypertensive  
5 medication. Hyperlipidemia was defined as individuals with self-reported hyperlipidemia, or  
6 a total cholesterol level of  $\geq 220$  mg/dl or the self-reported use of medications for  
7 hyperlipidemia. Hyperglycemia was defined as a fasting plasma glucose  $\geq 126$  mg/dl,  
8 hemoglobin A1c (HbA1c)  $\geq 6.5\%$ , or the self-reported use of medications for hyperglycemia.  
9 The HbA1c levels were converted from the format of the Japan Diabetes Society (JDS) to the  
10 National Glycohemoglobin Standardization Program [NGSP: NGSP (%) =  $1.02 \times$  JDS (%) +  
11 0.25 (%)]. We decided to treat sleep duration of 7-7.9 hours as the reference category because  
12 the mortality risk was considered to be the lowest in people who sleep 7-7.9 hours per night  
13 in the previous studies<sup>16,17</sup>. An alpha level of 0.05 was considered statistically significant. All  
14 statistical analyses were executed using SAS Version 9.4 (SAS Inc, Cary, NC, USA).

15

## 16 Results

17 During a median of 12.7 years of follow-up, 256 participants (114 men and 142 women)  
18 were certain of incident disability, and 133 (95 men and 38 women) died.

19 Baseline characteristics of the participants according to sleep duration are presented in  
20 Table 1. Overall, the most frequent sleep duration was 7-7.9 hour, 38.7% of the participants  
21 reported sleep 7-7.9 hours, 10.7% of participants reported sleeping less than 6 hours, 29.0%



1 reported 6-6.9 hours, 18.7% reported 8-8.9 hours, and 2.9% reported more than 9 hours.  
2 Compared with participants who sleep in 7-7.9 hours/day among women, shorter sleepers  
3 were associated with a significantly less likely to have a history of diabetes mellitus or  
4 hyperlipidemia. Whereas, no significant associations were found among men.

5 The association of average daily of sleep duration with an incident disability was shown  
6 in Table2. After adjusting for potential confounders, daily sleeping < 6hours/day was  
7 increased risk of incident disability (HR 1.64; 95%CI, 1.13-2.38; for total, HR 1.46; 95%CI,  
8 0.71-3.00 for men; HR 1.90; 95%CI, 1.19-3.03 for women).

9

## 10 Discussion

11 This age-specific prospective cohort study revealed that shorter sleep duration (<6  
12 hours/day) was increased risk of incident disability, compared with a sleep duration of 7-7.9  
13 hours/day. To our knowledge, this is the first study reported the association between short  
14 sleep duration and an incident disability defined a person who certified support level 1 or  
15 higher. According to the National Nutrition Survey, the major causes for needing long-term  
16 care among Japanese elderly people were stroke (17.2%), dementia (16.4%), bone fracture or  
17 falls (12.2%), arthropathy (11%), and cardiovascular diseases (4.7%) in 2013<sup>2</sup>.

18 The mechanisms that the association between shorter sleep duration and incident  
19 disability is not fully understood. However, several previous studies showed the association  
20 between shorter sleep duration and an increased risk of poor physical function<sup>3</sup>, falls<sup>18</sup>, low  
21 cognitive function such as executive function<sup>19</sup>, and incident diseases such as stroke<sup>20</sup>,

1 ischemic heart disease<sup>21</sup>, osteoporosis<sup>22</sup>, and sarcopenia<sup>23</sup> through adverse endocrinologic or  
2 metabolic effects such as decreases of testosterone<sup>24</sup> and melatonin secretion<sup>25</sup>, through the  
3 induction of chronic, low-grade inflammation such as elevated C-reactive protein<sup>26</sup>, through  
4 increases vascular damage such as coronary artery calcification, or through increases in  
5 cortisol secretion<sup>27</sup> or altered growth hormone metabolism<sup>28</sup>. They support our results.

6 The strength of this study is the design of age-specific cohort. All the participants were  
7 enrolled at the age of 64/65 years, and therefore we can get rid of the influence of age on the  
8 association between sleep duration and incident disability. Additionally, several  
9 meta-analyses reported that shorter sleep duration is a risk factor for all-cause mortality<sup>4</sup>. It  
10 could lead to an underestimation of the incident disability because all-cause mortality might  
11 be a competing event. Although we found no significant association between sleep duration  
12 and all-cause mortality in this study (data not shown), to reduce this bias, we conducted a  
13 competing risk analysis.

14 The limitations of the study also need to be addressed. First, we obtained information on  
15 the sleep duration based on self-reported and therefore our results could include some  
16 misclassification. Particularly, self-reported long sleepers are more likely to over reported  
17 their total sleep time, and their sleep time is almost their time in bed<sup>29</sup>. If we assess objective  
18 sleep characteristics using actigraphy<sup>30</sup>, our results would be more reliable. Second, although  
19 we adjusted potential confounders as far as possible in the statistical model, some residual  
20 confounders which could be associated with sleep duration could not be eliminated. For  
21 example, this study did not include information on sleep complaint, sleep disorders such as

1 insomnia, sleep apnea, and napping, or history of shift works which may be influenced by  
2 normal sleep duration. Third, we only assessed daily sleep duration at baseline. Sleep  
3 duration might be changed due to subsequent their health condition. Forth, our results might  
4 be included detection bias because not all candidates applied for LTCI certification. Fifth,  
5 because we did not consider causes of incident disability, the mechanisms association  
6 between sleep duration and incident disability remained unidentified. Sixth, although the  
7 results in the subgroup analysis of each confounder may provide them some hints of the  
8 biological mechanism underlying the findings observed in this study, we could not obtain  
9 sufficient calculations due to a small number of incident disability in each sub-group.

10 In conclusion, shorter sleep duration was associated with a higher risk of incident  
11 disability among Japanese elderly individuals.

12

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### 20 Disclosure statement

21 The authors declare no conflict of interest.

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**Table1. Baseline characteristics according to sleep duration(n=1,895)**

Variables	Average daily sleep duration (h/day)					p-value	Women (n=933)					p-value
	Men (n=962)						<6 (n=133)	6-6.9 (n=295)	7-7.9 (n=353)	8-8.9 (n=139)	≥9 (n=13)	
<b>BMI (Kg/m<sup>2</sup>)</b>												
<18.5	3 (4.3)	7(2.8)	14 (3.7)	10 (4.7)	3 (7.0)	0.68	5 (3.8)	18 (6.1)	15 (4.2)	8 (5.8)	1 (7.7)	0.96
18.5-24.9	43 (62.3)	185 (72.8)	264 (69.3)	145 (67.4)	31 (72.1)		103 (77.4)	217 (73.6)	268 (75.9)	101 (72.7)	9 (69.2)	
≥25	23 (33.3)	62 (24.4)	103 (27.0)	60 (27.9)	9 (20.9)		25 (18.8)	60 (20.3)	70 (19.8)	30 (21.6)	3 (23.1)	
<b>Educational attainment</b>												
Lower junior school	21 (30.4)	49 (19.3)	102 (26.8)	53 (24.7)	15 (34.9)	0.08	45 (33.8)	86 (29.2)	122 (34.6)	54 (38.8)	4 (30.8)	0.34
Upper high school	48 (69.6)	205 (80.7)	279 (73.2)	162 (75.3)	28 (65.1)		88 (66.2)	209 (70.8)	231 (65.4)	85 (61.2)	9 (69.2)	
<b>Working status</b>												
Employed	29 (42.0)	108 (42.5)	164 (43.0)	106 (49.3)	20 (46.5)	0.66	93 (69.9)	215 (72.9)	250 (70.8)	111 (79.9)	10 (76.9)	0.41
Unemployed	38 (55.1)	142 (55.9)	214 (56.2)	107 (49.8)	22 (52.1)		40 (30.1)	76 (25.8)	100 (28.3)	28(20.1)	3 (23.1)	
<b>Marital status</b>												
Married	65 (94.2)	243 (95.7)	365 (95.8)	207 (96.3)	42 (97.7)	0.92	99 (74.4)	255 (86.4)	306 (86.7)	116 (83.5)	10 (76.9)	0.07
Other	4 (5.8)	11 (4.3)	16 (4.2)	8 (3.7)	1 (2.3)		33 (24.8)	40(13.6)	46 (13.0)	22 (15.8)	3 (23.1)	
<b>Smoking status</b>												
Never	14 (20.3)	56 (22.0)	73 (19.2)	35 (16.3)	5 (11.6)	0.21	120 (90.2)	267 (90.5)	325 (92.1)	124 (89.2)	13 (100)	0.72
Past	31 (44.9)	138 (54.3)	201 (52.8)	110 (51.2)	18 (41.9)		7 (5.3)	18 (6.1)	14 (4.0)	11 (7.9)	0.0	
Current	24 (34.8)	60(23.6)	106 (27.8)	70(32.6)	20 (46.5)		6 (4.5)	10 (3.4)	14 (4.0)	4 (2.9)	0.0	
<b>Drinking status</b>												
Never/past	20 (29.0)	89 (35.0)	122 (32.0)	61 (28.4)	11 (25.6)	0.61	106 (79.7)	223 (75.6)	289 (81.9)	111 (79.9)	12 (92.3)	0.26
Current	49 (71.0)	164 (64.6)	259 (68.0)	154 (71.6)	32 (74.4)		27 (20.3)	72(24.4)	64 (18.1)	28(20.1)	1 (7.7)	
<b>Walking status (h/day)</b>												
<1	37 (53.6)	143 (56.3)	186 (48.8)	99 (46.0)	27 (62.8)	0.07	52 (39.1)	98 (34.4)	103 (29.2)	43 (30.9)	7 (53.8)	0.31
≥1	31 (44.9)	111 (43.7)	194 (50.9)	116 (54.0)	16 (37.2)		81 (60.9)	185 (64.9)	247 (70.0)	96 (69.1)	6 (46.2)	
<b>Depressive tendency</b>												
Absence	50 (72.5)	193 (76.0)	306 (80.3)	175 (81.4)	32 (74.4)	0.37	90 (67.7)	216 (73.2)	267 (75.6)	99 (71.2)	11 (84.6)	0.11
Presence	17 (24.6)	53(20.9)	60(15.7)	36 (16.7)	8 (18.6)		41 (30.8)	66 (22.4)	69 (19.5)	30 (21.6)	1 (7.7)	
<b>History of disease</b>												
Cardiovascular disease	2 (2.9)	18 (7.1)	29 (7.6)	19 (8.8)	5 (11.6)	0.44	8 (6.0)	16 (5.4)	15 (4.2)	6 (4.3)	1 (7.7)	0.88
Cancer	1 (1.4)	7 (2.8)	9 (2.4)	11 (5.1)	1 (2.3)	0.34	8 (3.0)	16 (5.4)	18 (5.1)	6 (4.3)	1 (7.7)	0.96
Diabetes mellitus	5 (7.2)	29 (11.4)	55 (14.4)	34 (15.8)	5 (11.6)	0.32	5 (3.8)	18 (6.1)	22 (6.2)	19 (13.7)	2 (15.4)	0.01
Hypertension	33 (47.8)	127 (50.0)	169 (44.4)	123 (57.2)	21 (48.8)	0.06	48 (36.1)	105 (35.6)	146 (41.4)	61 (43.9)	6 (46.2)	0.36
Hyperlipidemia	35 (50.7)	136 (53.5)	205 (53.8)	113 (52.6)	24 (55.8)	0.98	82 (61.7)	186 (63.1)	245 (69.4)	108 (77.7)	8 (61.5)	0.02

All values shown are as n (%). The proportion of each variable does not always add up to 100% owing to missing data.

p-values were calculated by  $\chi^2$ -test.

**Table2. Association of average daily sleep duration with incident disability**

	Average daily sleep duration (h/day)				
	<6	6-6.9	7-7.9	8-8.9	≥9
<b>Total</b>					
Person-years	2,418	6,556	9042	4,312	685
No. of case	36	70	95	54	10
No. of death	8	32	56	31	6
Sex adjusted HR (95% CI) <sup>a</sup>	1.63 (1.11-2.39)	1.11 (0.81-1.52)	1.00	1.19 (0.85-1.67)	1.30 (0.68-2.51)
Adjusted HR (95% CI) <sup>a</sup>	1.61 (1.09-2.40)	1.09 (0.79-1.50)	1.00	1.14 (0.81-1.61)	1.31 (0.68-2.54)
Adjusted HR (95% CI) <sup>b</sup>	1.64 (1.13-2.38)	1.09 (0.80-1.48)	1.00	1.16 (0.82-1.62)	1.27 (0.66-2.42)
<b>Men</b>					
Person-years	800	2,973	4,655	2,612	513
No. of case	9	29	48	28	9
No. of death	4	20	41	24	6
Clude HR (95% CI) <sup>a</sup>	1.27 (0.62-2.59)	1.06 (0.67-1.69)	1.00	1.01 (0.63-1.61)	1.82 (0.89-3.74)
Adjusted HR (95% CI) <sup>a</sup>	1.42 (0.68-3.00)	1.15 (0.70-1.87)	1.00	1.01 (0.63-1.65)	1.74 (0.83-3.62)
Adjusted HR (95% CI) <sup>b</sup>	1.46 (0.71-3.00)	1.14 (0.70-1.85)	1.00	1.01 (0.63-1.62)	1.66 (0.82-3.37)
<b>Women</b>					
Person-years	1,618	3,583	4,387	1,700	172
No. of case	27	41	47	26	1
No. of death	4	12	15	7	0
Clude HR (95% CI) <sup>a</sup>	1.86 (1.15-3.00)	1.17 (0.77-1.80)	1.00	1.49 (0.92-2.42)	0.38 (0.05-2.73)
Adjusted HR (95% CI) <sup>a</sup>	1.91 (1.16-3.15)	1.17 (0.76-1.81)	1.00	1.39 (0.84-2.29)	0.42 (0.06-3.07)
Adjusted HR (95% CI) <sup>b</sup>	1.90 (1.19-3.03)	1.16 (0.77-1.75)	1.00	1.36 (0.84-2.22)	0.43 (0.06-3.11)

HR, Hazard Ratio; CI, Confidence Interval.

<sup>a</sup>Cox proportional model, <sup>b</sup>competing risk model

Adjusted for year of participation, body mass index, education, working status, marital status, smoking, drinking, daily walking, depressive tendency, and history of cardio vascular disease, cancer, hypertension, hyperlipidemia, and diabetes mellitus.