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Association between sleep duration from midlife and the risk of physical frailty in late life

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Abstract (200 words)

Sleep duration has been contemporaneously associated with physical frailty, but their prospective association remains unclear. In this study, we used data from 10,792 participants in the Singapore Chinese Health Study who were followed up over 20 years. Sleep durations were recorded at baseline (mean age: 52y), second follow-up (mean age: 64y) and third follow-up (mean age: 72y). Physical frailty was assessed using a modified frailty phenotype at the third follow-up. Compared to 7h/day, short sleep durations of ≤5h/day at baseline and second follow-up were associated with increased likelihood of physical frailty [ORs (95% CIs): 1.43 (1.14-1.79) and 1.29 (1.04-1.60)]. Long sleep durations of ≥9h/day at baseline and second follow-up were also associated with increased likelihood of physical frailty [ORs (95% CIs): 1.62 (1.26-2.08) and 1.27 (1.06-1.53)]. Compared to those who maintained 6-8h/day of sleep at both time-points, baseline short sleepers who prolonged their sleep by ≥2h at second follow-up, as well as baseline long sleepers who shortened their sleep by ≥2h at second follow-up, still had increased likelihood of physical frailty at third follow-up. In this cohort, both short and long sleep durations at midlife, irrespective of changes thereafter, were associated with increased likelihood of physical frailty in late life.

Keywords: sleep duration, sleep length, frail, longitudinal, cohort, Asian

Introduction

Physical frailty is a geriatric syndrome marked by diminished strength, endurance, and physiological function that is associated with a higher risk of adverse outcomes, such as loss of independence and mortality [1]. Physical frailty was first described by Fried et al. [2] in the Cardiovascular Health Study (CHS) cohort, and it was defined as a specific physical phenotype that could be objectively identified based on the presence of 5 possible components: weight loss, exhaustion, low activity, slowness, and weakness [2]. As the global population ages [3], the health burdens associated with physical frailty will inevitably place increasing strain on healthcare systems [4]. Therefore, it is imperative to identify modifiable risk factors of physical frailty, and to develop early interventions to potentially prevent or delay its progression within aging populations [5].

Aspects of sleep have emerged as significant factors associated with physical frailty [6-8]. Sleep disorders, such as daytime drowsiness, sleep disordered breathing, prolonged sleep latency, and poor sleep quality, have all been found to be associated with increased risks of physical frailty [6-8]. Notably, a recent meta-analysis showed that both short (<6 hours) and long (>8 hours) sleep durations were associated with increased odds of physical frailty [6]. However, the majority of evidence linking sleep duration with physical frailty thus far has come from cross-sectional studies [6], and prospective studies that have examined the longitudinal associations have yielded conflicting results [9-11]. Furthermore, to our best knowledge, only 1 other study had investigated how changes in sleep duration affected this relationship [12].

As such, our study aimed to fill the gap in the literature by using data from a population-based cohort of Chinese adults living in Singapore who had reported their sleep durations at 3 time-points over a period of 20 years from midlife, and then underwent an assessment for physical frailty at late life. The goal of our study was to elucidate the temporal relationship between sleep duration at midlife, as well as any subsequent changes to it, with the risk of physical frailty at late life.

Methods

Study Population

This study was nested within the Singapore Chinese Health Study (SCHS), a prospective, population-based cohort of Chinese adults living in Singapore [13]. In brief, a total of 63,257 participants, aged between 45 to 74 years old, were recruited into this cohort between 1993 and 1998. Participants belonged to 1 of the 2 major dialect groups of Chinese in Singapore: the Hokkien and the Cantonese, who originated from the adjacent provinces of Fujian and Guangdong in southern China, respectively. All participants were either Singapore citizens or permanent residents, and they lived in government-built housing flats, where 86% of all Singapore residents lived during the recruitment period. This study was approved by the Institutional Review Board of the National University of Singapore, and written informed consent was obtained from all participants. All research was performed in accordance with the principles as described in the Declaration of Helsinki.

After the baseline interviews, participants were re-contacted for interviews every 5 to 6 years (Figure 1). The first follow-up interviews were conducted between 1999 and 2004, and the second follow-up interviews took place between 2006 and 2010. These interviews were conducted either in-person or over the phone to update selected lifestyle factors and medical histories. The third follow-up interviews were conducted via home visits between 2014 and 2017 and included assessment of aging-related outcomes.

Assessment of Sleep Duration

Participants self-reported their sleep duration at the baseline interviews, the second follow-up interviews (average of 12.3 years after the baseline), and the third follow-up interviews (average of 19.6 years after the baseline) (Figure 1). At each of these interviews, they were asked the question: "On the average, during the last year, how many hours in a day did you sleep (including naps)?" Participants responded by choosing from 1 the following options: ≤5 h/day, 6 h/day, 7 h/day, 8 h/day, 9 h/day, or ≥10 h/day.

Assessment of Covariates

During the baseline interviews, a structured, interviewer-administered questionnaire was used to collect information on participants' demographics (age, gender, dialect group, and educational level), self-reported height and weight, history of physician-diagnosed medical conditions (hypertension, diabetes, and cardiovascular diseases), smoking status, engagement in physical activities, and alcohol consumption. Body mass index (BMI) was calculated by dividing weight by the square of height (kg/m^2), and physical activity was assessed by the hours that participants spent weekly on moderate activities, strenuous sports, and vigorous work. Information on physical activity and alcohol consumption were updated in the second follow-up interviews, while self-reported height and weight, smoking status, and medical conditions were updated in both the second and third follow-up interviews.

Assessment of Physical Frailty

Physical frailty was assessed during the third follow-up interviews using a modified version of the Cardiovascular Health Study (CHS) frailty phenotype [2,14], which has been used in various studies, and has been reported to be a robust frailty assessment tool for clinicians and researchers [15]. Our frailty assessment encompassed the components of slowness, weakness, weight loss, and exhaustion, The criterion of low activity in the original CHS phenotype was not included in our analysis as we did not collect the relevant data for this measure at the third follow-up interviews [16]. The criterion of slowness was assessed with the timed up-and-go (TUG) test. During this test, participants were asked to stand up from a chair of approximately 46cm in height, walk at their usual speed for 3 meters, turn around at the marked area, return to the chair, and sit back on the chair. The time taken for participants upon completion was recorded and rounded to the nearest second [17]. The slowness criterion was met if participants' measured TUG time fell within the slowest gender-specific quintile [18,19]. The criterion of weakness was determined using handgrip strength. This was measured using a digital grip strength dynamometer (Model T.K.K.5401 GRIP D; Takei Scientific Instruments Co., Ltd., Tokyo, Japan), that participants were asked to grasp with their arms let down naturally while standing upright. Participants were asked to grip the dynamometer with maximum force and measurements were recoded to the nearest 0.1 kg [17]. The weakness criterion was met if participants' measured handgrip strength was in the weakest gender-specific quintile [18]. The weight loss criterion was met if participants had lost 10% or more of their self-reported body weight since the second follow-up interviews [16], which occurred a mean duration of 7.3 years (SD = 1.0 years) before the third follow-up interviews. The exhaustion criterion was met if participants responded "No" to the question, "Do you feel full of energy?" [18]. Participants who met 2 or more of the 4 criteria were classified as being physically frail [16,18].

Statistical Analyses

In this study, we only included participants who had complete information on sleep duration at all 3 time-points, and had completed all physical frailty assessments at the third follow-up interviews. In addition, since our aim was to study sleep starting at midlife, we limited our participants to those below 65 years of age at the baseline. A total of 17,048 individuals completed the third follow-up interviews. After excluding those with incomplete information on physical frailty (N = 4,465) and sleep duration (N = 1,447), as well as individuals who were aged 65 and above (N = 344) at the baseline, a total of 10,792 participants were included in our analysis (Figure 1).

We compared the means and standard deviations of continuous variables using Student's *t*-test or one-way analysis of variance (ANOVA), and we compared the proportions of categorical variables using Pearson's χ^2 test. Multivariable logistic regression models were used to compute odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between sleep duration at different time-points and the likelihood of physical frailty at late life, as well as for the associations between changes in sleep duration and physical frailty.

When the associations between sleep duration and physical frailty (or its individual components) were modelled, participants who reported sleep durations of 7 h/day were used as the reference group. We included age at measurement of sleep duration (years), follow-up time from measurement of sleep duration to assessment of physical frailty (years), gender, dialect group (Hokkien, Cantonese), and level of education (no formal education, primary, secondary and above) as covariates in Model 1. In Model 2, we added BMI (<18.5, 18.5-22.9, 23.0-27.4, >27.5 kg/m^2), smoking status (never smoker, former smoker, current smoker), alcohol consumption (never, monthly, weekly or daily), and participation in physical activities [time spent on strenuous sports or vigorous work (<0.5, 0.5-4, ≥4 h/week), time spent on moderate activities (<0.5, 0.5-4, ≥4 h/week)], using data collected either at the same time-point as the sleep duration being analyzed, or at earlier time-points if such data was not available. In Model 3, we further added history of physician-diagnosed chronic diseases (hypertension, cardiovascular diseases, diabetes) at each respective time-point.

In further, separate analyses, we examined the associations between changes in sleep duration and physical frailty. In these analyses, participants were first categorised into 3 groups based on their sleep duration at the baseline interviews—short (≤5 h), recommended (6-8 h) and long (≥9 h)—and participants in the recommended (6-8 h) group were used as the reference group. Changes in sleep duration were then defined as a difference of 2 or more hours from the baseline to the second follow-up interviews, as individuals may have rounded up or down when reporting their sleep duration. Using this definition, participants were ultimately categorized into 7 mutually exclusive groups based on changes in sleep duration.

To test the robustness of our analyses, we conducted a sensitivity analysis that excluded 661 participants who had a history of cardiovascular diseases or diabetes at the baseline interviews, as such participants were more likely to have already been physically frail at the time of recruitment. All statistical analyses were conducted using STATA/SE 18.0 software (StataCorp LLC, College Station, TX, USA). All *p*-values presented were 2-sided, and *p*-values <0.05 were considered statistically significant.

Results

At baseline interviews (1993-1998), the participants were aged 45 to 64 years, with a mean age of 52 (SD = 5.08) years. At the second follow-up interviews (2006-2010), they were aged 53 to 80 years, with a mean age of 64 (SD = 5.35) years. At the third follow-up interviews (2014-2017), they were aged 61 to 87 years, with a mean age of 72 (SD = 5.30) years. At all 3 time-points, among the 5 categories of sleep duration (≤5 h/day, 6 h/day, 7 h/day, 8 h/day and ≥9 h/day), the largest proportion of participants reported a sleep duration of 7 h/day (baseline: 35.69%; second follow-up: 27.68%; third follow-up: 25.82%). Compared to those who reported 7 h/day of sleep, both short and long sleepers were more likely to be female, older, and have a history of cardiovascular diseases and diabetes at the baseline interviews (Table 1). The proportion of short sleepers (≤5 h/day) increased from 7.41% at baseline to 10.91% at the second follow-up interviews, while the proportion of long sleepers (≥9 h/day) increased from 5.24% at baseline to 16.03% at the second follow-up interviews. In contrast, 30.65% of participants reported the same sleep duration at baseline and the second follow-up interviews. At the third follow-up, 12.04% of participants were classified as physically frail. Compared to non-frail individuals, physically frail participants were more likely to be older, smoking, and less physically active, as well as have higher BMIs, and a history of cardiovascular diseases, hypertension, and diabetes at the baseline interviews (Supplementary Table S1).

We first used data from the baseline and second follow-up interviews, which were conducted an average of 19.6 and 7.3 years prior to the third follow-up, to evaluate the longitudinal associations between sleep duration and physical frailty (Table 2 and Figure 2). In our fully adjusted models (Model 3), both short and long sleep durations at the baseline and second follow-up interviews were found to be prospectively associated with physical frailty at the third follow-up. At the baseline interviews, compared to those who slept 7 h/day, the OR (95% CI) for physical frailty was 1.43 (1.14-1.79) among participants who slept ≤ 5h/day, and was 1.62 (1.26-2.08) among those who slept ≥9 h/day. At the second follow-up interviews, compared to those who slept 7 h/day, the OR (95% CI) was 1.29 (1.04-1.60) among participants who slept ≤5 h/day, and was 1.27 (1.06-1.53) among those who slept ≥9 h/day. When the individual components of the physical frailty phenotype were analyzed (Table 3), both short and long sleep durations at baseline were most strongly and significantly associated with weak handgrip strength at the third follow-up. At the second follow-up, short sleep duration was most strongly and significantly associated with exhaustion, while long sleep duration was significantly associated with all components of the frailty phenotype except for slowness.

We then analyzed the contemporaneous associations, and found that both short and long sleep durations at the third follow-up interviews were associated with physical frailty (Table 2 and Figure 2). Compared to participants who were sleeping 7 h/day, the OR (95% CI) for physical frailty was 1.67 (1.39-2.02) among those who were sleeping ≤5 h/day, and was 1.94 (1.56-2.41) among those who were sleeping ≥9 h/day. When individual components of the physical frailty phenotype were analyzed (Table 3), both short and long sleep durations were strongly and significantly associated with all the components in the phenotype. Moreover, in sensitivity analyses which excluded participants who had cardiovascular diseases or diabetes at the baseline interviews, these associations with physical frailty, both longitudinal and contemporaneous, remained substantially unchanged (Supplementary Table S2).

Finally, we evaluated whether changes in sleep duration from the baseline to the second follow-up interviews affected the risk of physical frailty at the third follow-up (Table 4). In these analyses, participants who maintained the recommended sleep duration (6-8 h/day) at both the baseline and second follow-up interviews were used as the reference group. As expected, participants who maintained short and long sleep durations at both time-points had increased odds of physical frailty. Among participants who had reported changes in their sleep duration, those who had the recommended sleep duration at baseline but shortened it by ≥2 h/day at the second follow-up had increased odds of physical frailty [OR (95% CI): 1.30 (1.04-1.63)]. Importantly, however, we found that short sleepers at baseline who lengthened their sleep at the second follow-up continued to have increased odds of physical frailty [OR (95% CI): 1.51 (1.13-2.01)]. In a similar manner, long sleepers at baseline who shortened their sleep at the second follow-up also continued to have increased odds of physical frailty [OR (95% CI): 1.57 (1.08-2.28)].

Discussion

In this prospective, population-based study, both short and long sleep durations at midlife were longitudinally associated with an increased risk of physical frailty at late life. Notably, in our study population, adjustments in sleep duration by lengthening short sleep or shortening long sleep did not significantly mitigate this association.

To our best knowledge, only 4 prospective studies in the current literature have examined the longitudinal associations between sleep duration and physical frailty, and these studies have yielded conflicting results. Our findings concurred with those from 2 studies conducted in the Mexican population. The first study followed 309 older adults aged 70 and above for an average of 4.4 years, and showed that compared to those who reported 7-8 hours of sleep per day, participants who reported a baseline sleep duration of ≤5 hours or ≥9 hours had higher risks of physical frailty at the follow-up [11]. The second study used data from 2,722 participants aged 50 and above, and found that after a follow-up of 9 years, short sleepers who further shortened their sleep from a baseline average of 5.7 hours, as well as long sleepers who further lengthened their sleep from a baseline average of 9.3 hours, had higher likelihoods of physical frailty compared to those who had maintained an optimal sleep duration (average of 7.6 hours) since the baseline [12]. Notably, however, the study did not investigate the risk for short sleepers who prolonged their sleep, or the risk for long sleepers who shortened their sleep over the period of follow-up. Our study extended their findings to show that short sleepers who prolonged their sleep after midlife, as well as long sleepers who shortened their sleep after midlife, did not significantly mitigate their increased risk of physical frailty in late life.

On the contrary, 2 other prospective studies reported conflicting findings with ours. The first study, conducted across 23 provinces in China, followed 7,623 older adults aged 65 and above for a median of 4.4 years, and found that only long sleep duration (≥10 hours) was associated with a higher risk of physical frailty when compared to those who reported >6 to <10 hours of sleep per day [10]. The second study, conducted in 6 regions of the United States, followed 2,505 men aged 67 and above for an average of 3.4 years, and did not find a significant association between a short sleep duration (≤5 hours) and physical frailty when compared with participants who had >5 hours of sleep per day [9]. The discrepancies between our findings and those from these studies were likely due to the differences in the range of sleep duration used for the referent group. In our study, we used participants with 7 hours of sleep duration as the referent group; in contrast, by using participants with a wider range of sleep duration as the reference (>6 to <10 hours in the China study, and >5 hours in the US study), these 2 studies could have inadvertently included those with increased risks for physical frailty in their referent groups, and thus underestimated the associations.

We found that short sleep duration at midlife was associated with weak handgrip strength in late life, thus suggesting that inadequate sleep might have an adverse effect on muscle strength. This is supported by findings from randomized controlled studies of acute sleep deprivation in healthy young adults over periods of 1 to 5 nights [20,21]. These studies reported that acute sleep deprivation could reduce muscle protein synthesis, decrease plasma testosterone, and increase plasma cortisol, and suggested that even a single night of total sleep deprivation was sufficient to induce anabolic resistance and a procatabolic environment [20,21].

Similarly, we also found that long sleep duration at midlife was associated with weak handgrip strength in late life. This concurred with findings from a 4-year prospective study of older community-dwelling individuals in Japan, which showed that those who slept ≥9 h/day had significantly lower handgrip strength compared to those who slept for 6.1 to 8.9 h/day [22]. Research suggests that long sleep duration is associated with greater declines in physical performance, potentially due to factors such as sleep fragmentation, fatigue, and underlying health conditions [23,24], which may contribute to muscle loss by disrupting the underlying physiology of muscle function [25]. Moreover, an observational study of adults without diabetes found that long sleep duration (≥9 h/day) was associated with higher insulin resistance and insulin secretion [26], factors which could also decrease skeletal muscle protein synthesis [27].

The strengths of our study included its large sample size, long follow-up period, repeated assessments of sleep duration, and comprehensive collection of potential covariates at various time-points. However, several limitations must be acknowledged. First, in our study, physical frailty was only assessed at the third follow-up interviews. Unfortunately, during the baseline interviews, we did not collect any of the data required to assess participants for physical frailty, and thus could not identify participants who might have already been physically frail at the time of recruitment. To address this limitation, we conducted sensitivity analyses in which we removed participants who had a history of cardiovascular disease or diabetes at the baseline interviews. We believed that such participants were more likely to already have been physically frail at the time, as the presence of such chronic diseases are strong risk factors for the onset and progression of physical frailty [5,28-33]. In these sensitivity analyses that excluded 661 participants, we noted that our findings remained unchanged (Supplementary Table S2). Second, we used a modified version of the CHS physical frailty phenotype that categorized participants who met 2 out of 4 criteria as frail; in doing so, we might have included those who would otherwise have been considered as pre-frail in the original frailty phenotype (2 out of 5 criteria), and thus potentially overestimated the prevalence of frailty in our cohort, thereby underestimating the true association between sleep duration and physical frailty. Third, we used self-reports of sleep duration, which could have led to non-differential misclassifications and an underestimation of the risk estimates in this prospective study design. Nonetheless, previous research has indicated minimal disparity between self-reported average time in bed and actigraphy-based sleep duration, with self-reporting being more accessible and cost-effective [10]. In addition, previous studies in this cohort have reported associations between sleep duration and other health outcomes, such as mortality, cognitive impairment, and risk of end-stage kidney disease [34-36], further supporting the validity of the self-reported sleep duration.

Fourth, our study only included 10,792 of the 63,257 participants originally recruited in the SCHS cohort (Figure 1). Thus, there was the potential for selection bias. When these 10,792 participants were compared against the 52,465 who were not included in the present study, the included participants were more likely to have reported a sleep duration of 7 h/day, and were less likely to have been short (≤5 h/day) or long (≥9 h/day) sleepers at the baseline interviews (Supplementary Table S3). In addition, at the baseline interviews, the included participants were more likely to have been younger, have higher levels of education, and have participated in vigorous work or strenuous sports; furthermore, they were also less likely to have had a history of smoking or other physician-diagnosed comorbidities. Thus, as the participants included in our study were less likely to have had exposure to the risk factors (short or long sleep), and were also less likely to have developed the outcome (physical frailty), it is possible for us to have underestimated the true association between sleep duration and physical frailty. Fifth, our study did not measure other parameters beyond sleep duration, and hence we could not investigate the associations between sleep quality or other sleep disorders with physical frailty. Sixth, it should be noted that short sleepers at baseline who lengthened their sleep at the second follow-up (N=358; 3.31%) and long sleepers at baseline who shortened their sleep at the second follow-up (N=246; 2.28%) made up relatively small groups of the study population. As such, there was greater uncertainty in the risk estimates for physical frailty in these groups, as evidenced by the wider 95% CIs in Table 4. Finally, it remains possible that certain characteristics of the participants that were not captured could have led to residual confounding, which, in turn, could have biased the observed associations between sleep duration and physical frailty. Therefore, further studies in different populations are still needed to confirm both the validity and generalizability of our findings.

Conclusion

In conclusion, we found that both short and long sleep durations at midlife were longitudinally associated with an increased risk of physical frailty at late life. Notably, in our study population, adjustments in sleep duration by lengthening short sleep or shortening long sleep did not significantly mitigate this association. Thus, although further studies are still required, these results suggest that the maintenance of an optimal sleep duration from midlife onwards could be important in reducing the risk of physical frailty in older age.

Data availability

The datasets generated and/or analysed during the current study are not publicly available due to data privacy laws, but they are available from the corresponding author on reasonable request.

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Additional information

Competing interests

The authors declare no competing interests.

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List of Figures / Figure Legends

Figure 1.

Title: Flowchart of participants included in the present study.

Figure 2.

Title: Associations between sleep duration at different time-points and risk of physical frailty in late life [OR (95% CI)].

Legend: Adjusted for age at sleep duration measurement, years of follow-up time (sleep duration measurement to frailty assessment), gender, dialect group, educational level, body mass index (BMI), smoking status, alcohol consumption, participation in physical activities at each respective time-point, as well as presence of hypertension, cardiovascular diseases, and diabetes at each respective time-point.

Table 1. Baseline characteristics of participants by categories of sleep duration.

	Sleep Duration at Baseline					*p*-value [a]
	≤ 5 h/day	**6 h/day**	**7 h/day**	**8 h/day**	**≥ 9 h/day**	
N (percent in study population)	800 (7.41)	2,568 (23.80)	3,852 (35.69)	3,006 (27.85)	566 (5.24)	
Mean age at baseline ± SD, y	53.28 ± 5.01	52.25 ± 5.04	51.98 ± 5.06	51.38 ± 5.05	52.32 ± 5.31	<0.001
Mean age at second follow-up ± SD, y	65.31 ± 5.35	64.48 ± 5.32	64.39 ± 5.35	63.81 ± 5.34	64.68 ± 5.37	<0.001
Mean age at third follow-up ± SD, y	73.77 ± 5.30	72.97 ± 5.28	72.87 ± 5.31	72.26 ± 5.31	73.12 ± 5.39	<0.001
Sleep duration at second follow-up (%)						<0.001
≤ 5 h/day	258 (32.25)	440 (17.13)	299 (7.76)	157 (5.22)	23 (4.06)	
6 h/day	184 (23.00)	709 (27.61)	765 (19.86)	432 (14.37)	61 (10.78)	
7 h/day	182 (22.75)	710 (27.65)	1,209 (31.39)	781 (25.98)	105 (18.55)	
8 h/day	100 (12.50)	481 (18.73)	1,025 (26.61)	948 (31.54)	193 (34.10)	
≥ 9h/day	76 (9.50)	228 (8.88)	554 (14.38)	688 (22.89)	184 (32.51)	
Gender (%)						<0.001
Men	256 (32.00)	1,095 (42.64)	1,643 (42.65)	1,332 (44.31)	198 (34.98)	
Women	544 (68.00)	1,473 (57.36)	2,209 (57.35)	1,674 (55.69)	368 (65.02)	
Dialect group (%)						0.037
Hokkien	370 (46.25)	1,299 (50.58)	1,916 (49.74)	1,554 (51.70)	302 (53.36)	
Cantonese	430 (53.75)	1,269 (49.42)	1,936 (50.26)	1,452 (48.30)	264 (46.64)	
Level of education (%)						<0.001
No formal education	173 (21.63)	372 (14.49)	548 (14.23)	409 (13.61)	94 (16.61)	
Primary school	372 (46.50)	1,130 (44.00)	1,676 (43.51)	1,315 (43.75)	286 (50.53)	
Secondary school and above	255 (31.87)	1,066 (41.51)	1,628 (42.26)	1,282 (42.65)	186 (32.86)	
Hypertension (%)	163 (20.38)	462 (17.99)	667 (17.32)	536 (17.83)	102 (18.02)	0.37
Cardiovascular diseases (%)	23 (2.88)	46 (1.79)	79 (2.05)	52 (1.73)	25 (4.42)	<0.001
Diabetes (%)	47 (5.88)	100 (3.89)	155 (4.02)	131 (4.36)	33 (5.83)	0.045
Smoking status (%)						0.16
Never smoker	663 (82.88)	2,029 (79.01)	3,073 (79.78)	2,340 (77.84)	452 (79.86)	
Former smoker	56 (7.00)	221 (8.61)	320 (8.31)	264 (8.78)	42 (7.42)	
Current smoker	81 (10.13)	318 (12.38)	459 (11.92)	402 (13.37)	72 (12.72)	
Frequency of alcohol consumption (%)						0.15
Never	652 (81.50)	2,023 (78.78)	3,056 (79.34)	2,362 (78.58)	470 (83.04)	
Monthly	60 (7.50)	252 (9.81)	350 (9.09)	275 (9.15)	36 (6.36)	
Weekly or daily	88 (11.00)	293 (11.41)	446 (11.58)	369 (12.28)	60 (10.60)	

Body mass index (BMI) ± SD, kg/m^2	23.27 ± 3.15	23.21 ± 3.26	23.05 ± 3.14	23.06 ± 3.28	22.91 ± 3.24	0.06
Physical activity [b] (%)						0.14
< 0.5 h/week	521 (65.13)	1,584 (61.68)	2,343 (60.83)	1,825 (60.71)	373 (65.90)	
0.5-4 h/week	175 (21.88)	639 (24.88)	968 (25.13)	742 (24.68)	128 (22.61)	
≥ 4 h/week	104 (13.00)	345 (13.43)	541 (14.04)	439 (14.60)	65 (11.48)	

[a]: *p*-value by analysis of variance test for continuous variables and chi-square test for categorical variables.

[b]: Hours per week spent on moderate activities, strenuous sports, and vigorous work.

Table 2. Associations between sleep duration at different time-points and risk of physical frailty in late life.

	Sleep Duration				
	≤ 5 h/day OR (95% CI)	**6 h/day OR (95% CI)**	**7 h/day OR (95% CI)**	**8 h/day OR (95% CI)**	**≥ 9 h/day OR (95% CI)**
Baseline					
Cases/N	133/800	290/2,568	424/3,852	353/3,006	99/566
Model 1	1.47 (1.18-1.83)	1.02 (0.87-1.21)	Ref	1.16 (1.00-1.36)	1.70 (1.32-2.18)
Model 2	1.45 (1.17-1.81)	1.01 (0.86-1.19)	Ref	1.17 (1.00-1.36)	1.67 (1.30-2.15)
Model 3	1.43 (1.14-1.79)	1.02 (0.87-1.20)	Ref	1.16 (0.99-1.36)	1.62 (1.26-2.08)
Second Follow-up					
Cases/N	159/1,177	223/2,151	302/2,987	328/2,747	287/1,730
Model 1	1.31 (1.06-1.62)	1.11 (0.92-1.34)	Ref	1.16 (0.97-1.37)	1.39 (1.16-1.66)
Model 2	1.31 (1.06-1.63)	1.10 (0.91-1.33)	Ref	1.15 (0.97-1.36)	1.32 (1.10-1.59)
Model 3	1.29 (1.04-1.60)	1.09 (0.90-1.32)	Ref	1.14 (0.96-1.36)	1.27 (1.06-1.53)
Third Follow-up					
Cases/N	330/2,094	306/2,862	243/2,786	225/2,090	195/960
Model 1	1.72 (1.44-2.07)	1.23 (1.02-1.47)	Ref	1.21 (0.99-1.47)	2.15 (1.74-2.66)
Model 2 [a]	1.70 (1.41-2.04)	1.23 (1.02-1.47)	Ref	1.20 (0.98-1.46)	2.08 (1.68-2.58)
Model 3 [a]	1.67 (1.39-2.02)	1.23 (1.02-1.48)	Ref	1.19 (0.97-1.45)	1.94 (1.56-2.41)

[a]: Data on alcohol consumption and physical activity collected in second follow-up were used as the relevant data were not collected at third follow-up interviews.

Model 1: adjusted for age at sleep duration measurement, years of follow-up time (sleep duration measurement to frailty assessment), gender, dialect group, and educational level.

Model 2: adjusted for Model 1 and body mass index (BMI), smoking status, alcohol consumption, and participation in physical activities at each respective time-point.

Model 3: adjusted for Model 2 and presence of hypertension, cardiovascular diseases, and diabetes at each respective time-point.

Table 3. Associations between sleep duration at different time-points and the individual physical frailty criteria in late life.

	Sleep Duration				
	≤ 5 h/day	**6 h/day**	**7 h/day**	**8 h/day**	**≥ 9 h/day**
Baseline					
Frailty criteria					
Weakness (handgrip strength in the weakest sex-specific quintile)					
Cases/N	162/800	381/2,568	578/3,852	502/3,006	112/566
OR (95% CI) [a]	1.30 (1.06-1.59)	0.98 (0.85-1.13)	Ref	1.22 (1.07-1.40)	1.35 (1.07-1.71)
Slowness [timed up-and-go (TUG) test time in the slowest sex-specific quintile]					
Cases/N	132/800	299/2,568	467/3,852	353/3,006	86/566
OR (95% CI) [a]	1.24 (0.99-1.56)	0.92 (0.78-1.09)	Ref	1.04 (0.88-1.21)	1.18 (0.90-1.56)
Weight loss (lost ≥10% of self-reported body weight since the previous follow-up interview)					
Cases/N	84/800	266/2,568	396/3,852	292/3,006	68/566
OR (95% CI) [a]	0.96 (0.74-1.23)	1.00 (0.85-1.18)	Ref	0.97 (0.83-1.14)	1.15 (0.87-1.51)
Exhaustion (answered “no” to the question, “Do you feel full of energy?”)					
Cases/N	154/800	452/2,568	628/3,852	513/3,006	118/566
OR (95% CI) [a]	1.18 (0.97-1.44)	1.10 (0.96-1.25)	Ref	1.07 (0.94-1.21)	1.28 (1.03-1.60)
Second Follow-up					
Frailty criteria					
Weakness (handgrip strength in the weakest sex-specific quintile)					
Cases/N	203/1,177	293/2,151	444/2,987	436/2,747	359/1,730
OR (95% CI) [a]	1.13 (0.93-1.36)	0.96 (0.82-1.13)	Ref	1.04 (0.90-1.21)	1.21 (1.03-1.42)
Slowness [timed up-and-go (TUG) test time in the slowest sex-specific quintile]					
Cases/N	150/1,177	204/2,151	335/2,987	348/2,747	300/1,730
OR (95% CI) [a]	1.05 (0.84-1.31)	0.86 (0.71-1.05)	Ref	1.07 (0.90-1.27)	1.10 (0.91-1.32)
Weight loss (lost ≥10% of self-reported body weight since the previous follow-up interview)					
Cases/N	121/1,177	216/2,151	272/2,987	277/2,747	220/1,730
OR (95% CI) [a]	1.10 (0.87-1.38)	1.12 (0.92-1.35)	Ref	1.08 (0.91-1.30)	1.27 (1.04-1.54)
Exhaustion (answered “no” to the question, “Do you feel full of energy?”)					
Cases/N	224/1,177	370/2,151	467/2,987	469/2,747	335/1,730
OR (95% CI) [a]	1.21 (1.02-1.45)	1.13 (0.97-1.31)	Ref	1.09 (0.94-1.25)	1.20 (1.02-1.40)
Third Follow-up					
Frailty criteria					
Weakness (handgrip strength in the weakest sex-specific quintile)					

Cases/N	390/2,094	420/2,862	367/2,786	335/2,090	223/960
OR (95% CI) [a, b]	1.37 (1.16-1.61)	1.11 (0.95-1.30)	Ref	1.22 (1.03-1.44)	1.61 (1.32-1.95)
Slowness [timed up-and-go (TUG) test time in the slowest sex-specific quintile]					
Cases/N	294/2,094	321/2,862	266/2,786	244/2,090	212/960
OR (95% CI) [a, b]	1.26 (1.04-1.53)	1.17 (0.97-1.40)	Ref	1.15 (0.95-1.40)	1.81 (1.45-2.25)
Weight loss (lost ≥10% of self-reported body weight since the previous follow-up interview)					
Cases/N	238/2,094	277/2,862	233/2,786	225/2,090	133/960
OR (95% CI) [a, b]	1.23 (1.01-1.51)	1.15 (0.95-1.39)	Ref	1.32 (1.08-1.61)	1.51 (1.19-1.92)
Exhaustion (answered "no" to the question, "Do you feel full of energy?")					
Cases/N	496/2,094	496/2,862	384/2,786	306/2,090	183/960
OR (95% CI) [a, b]	1.84 (1.58-2.14)	1.31 (1.13-1.52)	Ref	1.07 (0.90-1.26)	1.38 (1.13-1.68)

[a]: Adjusted for age at sleep duration measurement, years of follow-up time (sleep duration measurement to frailty assessment), gender, dialect group, and educational level, plus lifestyle factors [body mass index (BMI), smoking status, alcohol consumption, participation in physical activities] and presence of chronic diseases (hypertension, cardiovascular diseases, and diabetes) at each respective time-point.

[b] Data on alcohol consumption and physical activity collected at the second follow-up were used as the relevant data were not collected at the third follow-up interviews.

Table 4. Associations between change in sleep duration from baseline to second follow-up, and risk of physical frailty at the third follow-up interviews.

Change in sleep duration [a]		Cases/N	Sleep duration, mean (SD), h		OR (95% CI) [c]
Baseline	**Second Follow-up**		**Baseline**	**Second Follow-up**	
Recommend (6-8 h)	Maintained [b]	730/7,062	7.05 (0.76)	7.08 (1.00)	Ref
	Decreased by ≥ 2h	112/888	7.66 (0.47)	5.49 (0.50)	1.30 (1.04-1.63)
	Increased by ≥ 2h	225/1,476	6.66 (0.72)	8.96 (0.78)	1.16 (0.98-1.37)
Short (≤ 5 h)	Maintained [b]	65/442	5.00 (0.00)	5.42 (0.49)	1.37 (1.03-1.83)
	Increased by ≥ 2h	68/358	5.00 (0.00)	7.77 (0.94)	1.51 (1.13-2.01)
Long (≥ 9 h)	Maintained [b]	62/320	9.20 (0.40)	8.82 (0.80)	1.66 (1.22-2.26)
	Decreased by ≥ 2h	37/246	9.45 (0.50)	6.80 (0.90)	1.57 (1.08-2.28)

[a]: Change in sleep duration over an average of 12.3 years of follow-up, calculated a mean of 7.3 years before the third follow-up interviews.

[b]: Change in duration < 2h.

[c]: Adjusted for age at baseline interview, years of follow-up time (baseline to second follow-up), years of follow-up time (second follow-up to frailty assessment), gender, dialect group, educational level, body mass index (BMI), smoking status, alcohol consumption, and participation in physical activities, hypertension, cardiovascular diseases, and diabetes at baseline.