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Sleep Disturbances and Frailty Status in Older Community-Dwelling Men

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Abstract

Objectives—Test the hypothesis that sleep disturbances are independently associated with greater evidence of frailty in older men.

Design—Cross-sectional analysis of prospective cohort study

Setting—Six U.S. centers

Participants—3133 men ≥ 67 years

Measurements—Self reported sleep parameters (questionnaire); objective parameters of sleep wake patterns (actigraphy data collected for an average of 5.2 nights); and objective parameters of sleep disordered breathing, nocturnal hypoxemia, and periodic leg movements with arousals (PLMA) (in-home overnight polysomnography). Frailty status classified as robust, intermediate stage or frail using criteria similar to those used in the Cardiovascular Health Study frailty index.

Results—The prevalence of sleep disturbances including poor sleep quality, excessive daytime sleepiness, short sleep duration, reduced sleep efficiency, prolonged sleep latency, sleep fragmentation (greater nighttime wakefulness and frequent long wake episodes), sleep disordered breathing, nocturnal hypoxemia and frequent PLMA was lowest among robust men, intermediate among men in the intermediate stage group, and highest among frail men (p-for-trend ≤ 0.002 for all sleep parameters). After adjusting for multiple potential confounders, self-reported poor sleep quality (Pittsburgh Sleep Quality Index < 5 , multivariable odds ratio (MOR) 1.28, 95% CI 1.09–1.50), sleep efficiency $< 70\%$ (MOR 1.37, 95% CI 1.12–1.67), sleep latency ≥ 60 minutes (MOR 1.42, 95% CI 1.10–1.82), and sleep disordered breathing (respiratory disturbance index ≥ 15 , MOR 1.38, 95% CI 1.15–1.65) were each independently associated with an increased odds of greater frailty status.

Conclusion—Sleep disturbances including poor self-reported sleep quality, reduced sleep efficiency, prolonged sleep latency and sleep disordered breathing are independently associated with greater evidence of frailty.

Keywords

sleep disturbances; frailty; aging

INTRODUCTION

Self-reported sleep disturbances including chronic insomnia are increasingly common with advancing age.^{1–4} In addition, age-related changes in sleep/wake patterns as ascertained by actigraphy including lower sleep efficiency, longer sleep latency, greater nighttime wakefulness, and higher number of long wake episodes have been reported in population-based cohorts of older men and women.^{5,6} Prior population-based studies in older people using polysomnography have also reported a high prevalence of sleep disordered breathing^{7–10} and periodic leg movements in sleep, including movements causing arousals.^{11–13}

Frailty, a term typically used in clinical geriatric medicine to describe the presence of multisystem impairment and expanding vulnerability, is also highly prevalent with increasing age.^{14–18} Although many factors are thought to characterize frailty in older

adults¹⁹, Fried and colleagues¹⁶ have proposed a standard definition of frailty in which three or more of the following criteria are present: unintentional weight loss, poor endurance or energy, weakness, slow walking speed and low physical activity. In their analysis of data collected in the Cardiovascular Health Study (CHS), frailty as defined by this index (CHS index) was predictive of falling, hospitalization, disability, and mortality. While a number of instruments have been developed to operationalize the construct of frailty, the CHS index has been most extensively studied and the predictive validity of the CHS index has been confirmed in several cohorts of older people.^{14,15,18,20,21}

Although frailty definitions including the CHS index usually incorporate a component of poor energy (feeling of fatigue or exhaustion) and self-reported poor sleep and sleep disordered breathing have been associated with fatigue^{22–24}, the associations between sleep disturbances and frailty status in older people are uncertain. We tested the hypothesis that poorer sleep as defined by subjective and objective sleep parameters is independently associated with greater evidence of frailty as defined by the CHS phenotype in a cohort of 3133 older community-dwelling men enrolled in the Outcomes of Sleep Disorders in Older Men (MrOS Sleep) study.

METHODS

Participants

From March 2000 through April 2002, 5995 men who were at least 65 years of age were recruited for participation in the baseline examination of the prospective Osteoporotic Fractures in Men (MrOS) study.²⁵ Men were recruited from population based listings in six regions of the United States.²⁶ Men with a history of bilateral hip replacement and men who were unable to walk without the assistance of another person were excluded.

From December 2003 through March 2005, MrOS participants were invited to participate in an ancillary study to identify outcomes of sleep disorders in older men (MrOS Sleep study). A total of 381 participants from the overall cohort died or terminated study participation prior to the sleep exam leaving 5614 men available for recruitment into the sleep substudy. Of these, 3133 (56%, >100% of recruitment goal) men completed the MrOS Sleep examination and provided data for frailty components in the CHS index. All 3133 men provided data on self reported sleep parameters, 3054 underwent objective actigraphic recordings to determine sleep wake patterns, and 2909 had overnight polysomnographic recordings to determine the presence of sleep disordered breathing, nocturnal hypoxemia, and periodic leg movements of sleep. The Institutional Review Board (IRB) at each center approved the study protocol and written informed consent was obtained from all subjects.

Sleep Parameters

Self-Reported Sleep Parameters—At the sleep examination, participants completed the Pittsburgh Sleep Quality Index (PSQI), a validated measure of subjective sleep quality and sleep disturbances over a one-month time period. The questionnaire is divided into sections that assess subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of sleeping medication and daytime dysfunction. Global PSQI scores range from 0–21. A score >5 is indicative of poor sleep quality and has a sensitivity of 89.6% and specificity of 86.5% in distinguishing good vs. poor sleepers.²⁷

Participants also completed the Epworth Sleepiness Scale (ESS), a self-administered questionnaire which classifies subjective daytime sleepiness among people with sleeping disorders. Participants were asked to rate how likely (from 1–3, with 1 being unlikely and 3

being highly likely) they were to doze off in eight typical daily situations. Scores on the ESS range from 0–24, with a score >10 indicating excessive daytime sleepiness.^{28,29}

Objective Actigraphic Parameters of Sleep-Wake Patterns—As a part of the sleep examination, parameters of sleep-wake patterns were measured using an actigraph (Ambulatory Monitoring, Inc., Ardsley, NY), a small device used to detect movement that is similar in appearance to a wristwatch. An accelerometer within the actigraph measured movement several times per second and digitally stored the information every minute. Actigraphy has been shown to provide an objective and reliable estimate of sleep/wake patterns.³⁰ Actigraphy data collected in the digital integration mode were analyzed with ActionW- 2 software (Ambulatory Monitoring, Inc., Ardsley, NY). Details of the actigraphy scoring algorithms used in this study have been published elsewhere.³¹

Participants were instructed to wear the actigraph continuously for 5 nights/6 days, removing it only for bathing, or situations in which it might get submerged in water. They were also asked to keep a sleep log in which they recorded whether the actigraph recording represented their normal sleep/wake patterns as well as their time to bed, time of final arising, and any times the actigraphy was removed. Sleep logs were used to aid in editing the actigraph data. Actigraphy data was collected for an average of 5.2 ± 0.9 24-hour periods.

Sleep-wake parameters examined in this analysis were actigraphy-based estimates of total sleep time (total hours slept while in bed), sleep efficiency (percentage of time participant was sleeping while in bed), sleep latency (amount of time until onset of sleep, defined as when participant achieved sleep for 20 continuous minutes after getting into bed), time awake after sleep onset (defined as total minutes of time scored as awake from the onset of sleep until the end of the last sleep episode while in bed), and number of long wake episodes (number of awakenings 5 minutes or more in duration while in bed). For all analyses, the average of a given parameter over all nights was used to minimize night-to-night variability.

Objective Polysomnographic Parameters of Sleep Disordered Breathing, Nocturnal Hypoxemia, and Periodic Leg Movements with Arousals: As a part of the sleep examination, in-home sleep studies were completed using unattended, portable polysomnography (Safiro, Compumedics, Inc.®, Abottsfield, AU). The recording montage was as follows: C₃/A₂ and C₄/A₁ electroencephalograms (EEG), bilateral electrooculograms and a bipolar submental electromyogram to determine sleep status; thoracic and abdominal respiratory inductance plethysmography to determine respiratory effort; airflow (by nasal-oral thermocouple and nasal pressure cannula); finger pulse oximetry; lead I EKG; body position (mercury switch sensor); and bilateral tibialis leg movements (piezoelectric sensors). Centrally-trained and certified staff performed home visits to set up the unit, verify the values of the impedances for each channel, confirm calibration of position sensors and note any problems encountered during set-up, similar to the protocol used in the Sleep Heart Health Study.³² Staff returned the next morning to collect the equipment and download the data to the Case Western Reserve Sleep Reading Center (Cleveland, OH) to be scored by certified research polysomnologists.

Parameters of sleep disordered breathing and nocturnal hypoxemia examined in this analysis included the respiratory disturbance index (RDI) and the percent of time during overnight sleep in which arterial oxygen saturation was below 90% (% of sleep time with SaO₂ <90%). Apnea was defined as complete or near complete cessation of airflow for >10 seconds, and hypopneas were scored if clear reductions in breathing amplitude (at least 30% below baseline breathing) occurred, and lasted >10 seconds.³³ In these analyses, only apneas

and hypopneas that were each associated with a 4% or greater desaturation were included. RDI was calculated as the total number of apneas and hypopneas per hour of sleep.

Leg movements were scored according to AASM criteria³⁴ (>4 consecutive 0.5 to 5 second movements, each separated by 5–90 seconds). The leg movement parameter examined in the analysis was the number of periodic leg movements associated with EEG arousals per hour of sleep (PLMA).¹²

Other Measurements

Participants completed a questionnaire and were interviewed at the baseline and sleep examinations. A selected medical history was obtained (see Table 1 footnote for list of medical conditions). Participants were asked to bring all current medications used within the last 30 days with them to the sleep examination for verification of use. Intention to lose weight (whether or not the participant was trying to lose weight during the past 12 months) was assessed by a mailed interim questionnaire an average of 2.0 (SD $\pm$ 0.4 years) after the baseline examination and 1.4 (SD $\pm$ 0.4 years) prior to the sleep examination. Physical activity was assessed using the Physical Activity Scale for the Elderly (PASE).³⁵ Depressive symptoms including the question, “Do you feel full of energy?”, were evaluated using the 15-item Geriatric Depression Scale.³⁶ Cognitive function was assessed with the Teng Modified Mini-Mental State Exam (3MS).³⁷ To assess functional disability, men were asked whether they had any difficulty performing any of five instrumental activities of daily living (IADL). Tests of physical function included grip strength (using a hand-held Jamar dynamometer) and walk speed (time in seconds to walk 6 meters at usual pace expressed as m/sec). Body weight and height measurements were used to calculate a standard body mass index (BMI) and weight change was calculated by subtracting weight at the baseline examination from weight at the sleep examination and was expressed as a percentage of the baseline value.

Frailty

Frailty status was defined using criteria similar to those proposed by Fried and colleagues¹⁶ using data collected in the CHS study (see Appendix). Frailty was identified by the presence of ≥ 3 of the following components:

1. *Shrinking* as identified by an unintentional weight loss of $\geq 5\%$ between the baseline and sleep examination (mean years between examinations 3.4 ± 0.5);
2. *Weakness* as identified by a grip strength at the sleep examination in the lowest quintile stratified by body mass index (quartiles);
3. *Poor energy* as identified by an answer of “no” to the question “Do you feel full of energy?” from the Geriatric Depression Scale (GDS) administered at the sleep examination;
4. *Slowness* as identified by a walk speed at the sleep examination in the lowest quintile stratified by standing height (median); and
5. *Low physical activity* level at the sleep examination as identified by a PASE score in the lowest quintile.

Measurements or cutpoints used to define these components were similar, but not identical to those used in the original phenotype proposed.¹⁶ Men with none of the above components were considered to be robust and those with 1 or 2 components were considered to be in an intermediate stage.

Statistical Analysis

Differences in characteristics according to frailty status category (robust, intermediate stage, frail) were compared using analysis of variance for normally distributed continuous data, Kruskal-Wallis tests for skewed continuous data, and chi-square tests for categorical data.

For the primary analyses, the sleep parameter predictor variables were expressed as dichotomous variables based on published cutpoints for sleep disturbances, many of which define moderate to severe impairment (PSQI >5 vs. ≤5, ESS >10 vs. ≤10, total sleep time <5 hours vs. ≥5 hours, sleep efficiency <70% vs. ≥70%, sleep latency ≥60 minutes vs. <60 minutes, time awake after sleep onset ≥90 minutes vs. <90 minutes, number of long wake episodes ≥8 vs. <8, RDI ≥15 vs. <15, ≥10% of sleep time with SaO₂ <90% vs. <10% of sleep time with SaO₂ <90%, and PLMA ≥5/hour vs. <5/hour). The prevalence of sleep disturbance as defined by each parameter was compared across the three frailty status categories using the Cochran-Armitage test for trend.

The association between a given sleep disturbance and the ordinal outcome (robust, intermediate stage, frail) was examined using a proportional odds model and the assumption of proportionality was evaluated.³⁸ The assumption of homogeneity of effect of the predictor across levels of the outcome was met for all predictor variables, with the one exception, time awake after sleep onset. Thus, for all other predictors, a single odds ratio summarizing the effect of the predictor over all levels of the outcome was calculated for a base model including terms for age, clinic site, race, body mass index and number of medical conditions. Additional covariates were included in a final multivariable model if they were either known correlates of sleep disturbances and/or were characteristics related to frailty status independent of age. For the variable time awake after sleep onset for which the proportionality assumption was not met, two separate logistic regression models were performed dichotomizing the outcome as robust vs. intermediate stage/frail and robust/intermediate stage vs. frail.

In a secondary analysis to evaluate for evidence of a linear association between each sleep parameter and frailty status, the sleep parameter variables were expressed as continuous variables. Since a substantial portion of participants had 0% of sleep time with SaO₂ <90% and many participants had no PLMA, this secondary analysis did not include these parameters.

We also conducted sensitivity analyses restricting the analytical cohort to the 2860 men with complete data for all predictor and outcome variables including self-reported sleep parameters as assessed by questionnaires, objective sleep parameters as ascertained by actigraphy and PSG, and the CHS frailty index. Since the results from these sensitivity analyses were similar to those of the primary analyses, findings from the primary analyses are presented in this paper.

RESULTS

Characteristics of the Study Population

Of the 3133 men aged 67 years and older at the sleep examination, 1007 (32%) were classified as robust, 1689 (54%) were in the intermediate group, and 437 (14%) were frail. Characteristics of the entire cohort and characteristics by category of frailty status are shown in Table 1.

Compared with the 2481 men from the overall MrOS cohort who were not included in this analysis (did not participate in sleep exam (n=2479) or had incomplete assessment of frailty status (n=2)), the 3133 men included in this analysis were, on average, slightly younger

(73.1 vs. 73.8 years, $p < 0.001$) and more likely to report good to excellent health status (89% vs. 85%, $P < 0.001$). A similar proportion of both groups reported Caucasian race/ethnicity (90% vs. 89%, $p = 0.34$).

Prevalence of Sleep Disturbances According to Frailty Status

In unadjusted analyses, poor sleep quality (PSQI > 5), excessive daytime sleepiness (ESS > 10), short sleep duration (total sleep time ≤ 5 hours), reduced sleep efficiency (sleep efficiency $< 70\%$), prolonged sleep latency (sleep latency ≥ 60 minutes), sleep fragmentation (as manifested by nighttime wakefulness ≥ 90 minutes or ≥ 8 long wake episodes), sleep disordered breathing (RDI ≥ 15), nocturnal hypoxemia ($\geq 10\%$ of sleep time with $\text{SaO}_2 < 90\%$), and frequent PLMA (PLMA ≥ 5 /hour) were increasingly common across frailty status categories (Table 2). The prevalence of each of these sleep disturbances was lowest among robust men, intermediate among men in the intermediate group, and highest among frail men (p -for-trend ≤ 0.002 for all sleep disturbances).

Multivariable Associations between Self-Reported Sleep Disturbances and Frailty Status

After adjustment for age, race, site, number of medical conditions and body mass index (base model), poorer self-reported sleep quality (PSQI > 5) and excessive daytime sleepiness (ESS > 10) were associated with an increased odds of greater frailty status (odds ratio [OR] 2.08, 95% CI 1.80–2.41 for poor sleep quality and 1.59, 95% CI 1.29–1.97 for excessive daytime sleepiness) (Table 3). After further adjustment for multiple correlates of frailty and poor sleep including health status, educational level, social support, alcohol intake, smoking status, antidepressant use, benzodiazepine use, nonbenzodiazepine nonbarbiturate sedative hypnotic use, depressive symptoms, cognitive function, and functional disabilities, both associations were attenuated in magnitude, but the association between poor sleep quality and greater frailty status remained significant (multivariable odds ratio [MOR] 1.28, 95% CI 1.09–1.50).

Multivariable Associations between Disruptions in Sleep-Wake Patterns and Frailty Status

After adjustment for multiple potential confounders, both reduced sleep efficiency (sleep efficiency $< 70\%$) and prolonged sleep latency (sleep latency ≥ 60 minutes) were independently associated with a higher odds of greater frailty status (MOR 1.37, 95% CI 1.12–1.67 for reduced sleep efficiency and 1.42, 95% CI 1.10–1.82 for prolonged sleep latency) (Table 3). Using the base model, short sleep duration (total sleep time < 5 hours) and frequent long wake episodes (≥ 8 long wake episodes) were each associated with an approximate 1.3-fold increase in the odds of greater frailty status (OR 1.27, 95% CI 1.01–1.58 for short sleep duration and 1.27, 95% CI 1.09–1.48 for frequent long wake episodes). However, after further adjustment for additional potential confounders, neither association remained significant. Since the proportionality assumption was not met for the model with time awake after sleep onset, two separate logistic regression models were performed dichotomizing the outcome as robust vs. intermediate stage/frail and robust/intermediate stage vs. frail. After adjustment for multiple potential confounders, nighttime wakefulness ≥ 90 minutes was independently associated with a higher odds of being classified as frail (vs. robust/intermediate stage) (MOR 1.52, 95% CI 1.18–1.96), but there was no evidence of an independent association between nighttime wakefulness and odds of intermediate stage/frail status (vs. robust) (MOR 1.00, 95% CI 0.82–1.24).

Multivariable Associations between Sleep Disordered Breathing, Nocturnal Hypoxemia and Frequent PLMA and Frailty Status

Both sleep disordered breathing (RDI ≥ 15) and nocturnal hypoxemia ($\geq 10\%$ of sleep time with $\text{SaO}_2 < 90\%$) were associated with a 1.3 to 1.4-fold increase in the odds of greater

frailty status (OR for base model 1.37, 95% CI 1.16–1.63 for sleep disordered breathing and 1.31, 95% CI 1.04–1.65 for nocturnal hypoxemia) (Table 3). The association between sleep disordered breathing and odds of greater frailty status remained essentially unchanged despite further adjustment for multiple potential confounders (MOR 1.38, 95% CI 1.15–1.65), while the multivariable association between nocturnal hypoxemia and greater frailty status was attenuated and no longer significant (MOR 1.19, 95% CI 0.93–1.53). Using the base model, there was no evidence that frequent PLMA (PLMA ≥ 5 /hour) was associated with greater frailty status (OR 1.07, 95% CI 0.91–1.27).

Additional Analyses

When sleep parameters were expressed as continuous variables in a secondary analysis, there was evidence of independent linear associations between several parameters and greater frailty status (Table 4). After adjustment for multiple potential confounders, decreasing sleep quality, decreasing total sleep time, decreasing sleep efficiency, increasing sleep latency, increasing time awake after sleep onset, increasing number of long-wake episodes, and increasing RDI were associated in a graded manner with greater frailty status. For example, each one SD decrease in the PSQI was associated with a 1.17-fold increase (95% CI 1.07–1.27) in the odds of greater frailty status.

DISCUSSION

In this cohort of community-dwelling older men, sleep disturbances including self-reported poor sleep quality, objectively measured disruptions in sleep wake parameters, and objective evidence of sleep disordered breathing were all independently associated with greater evidence of frailty.

To the authors' knowledge, this is the first study to examine the association between sleep disorders and frailty status in older people, although prior studies have suggested associations between poor sleep and individual components of frailty. Self-reported sleep disturbances and sleep disordered breathing have been associated with fatigue.^{22–24,39} Greater sleep fragmentation and short sleep duration as measured by actigraphy, and severe sleep disordered breathing and nocturnal hypoxemia as measured by polysomnography, have been independently associated with measures of poor physical performance.^{40–42} Sleep disordered breathing has been associated with reduced levels of physical activity.¹⁰ Finally, although the association between weight change and the incidence, progression or remission of sleep disturbances in older people is not well defined, a prior prospective study examining the association between concurrent changes in weight and RDI in a cohort of 2968 middle-aged and older adults reported that individuals with weight gain compared with those with stable weight were more likely to have increases rather than decreases in RDI, while individuals with weight loss had more frequent increases and decreases in RDI.⁴³ Although weight loss might be expected to reduce the progression of sleep disordered breathing, it is possible that weight loss results in general laxity of muscle tone that could increase airway collapsibility.

The findings from this study indicate that the prevalence of sleep disturbances (poor sleep quality, excessive daytime sleepiness, short sleep duration, reduced sleep efficiency, prolonged sleep latency, sleep fragmentation (as manifested by greater nighttime wakefulness and multiple long wake episodes), sleep disordered breathing, nocturnal hypoxemia, and frequent periodic leg movements) increased in a graded manner with greater evidence of frailty status. With the exception of frequent PLMA, the associations between each of these sleep disorders and greater frailty status persisted despite adjustment for age, race, co-morbidities and body size. While further consideration of multiple other potential confounders attenuated a number of the associations (excessive daytime sleepiness, short

sleep duration, multiple long wake episodes, nocturnal hypoxemia) which no longer reached the level of significance, the relationships between four disturbances (poor sleep quality, reduced sleep efficiency, prolonged sleep latency; and sleep disordered breathing) and greater frailty status remained. In addition, greater nighttime wakefulness was independently associated with an increased likelihood of being frail. There was also evidence of linear independent associations between several continuous parameters of sleep (decreasing sleep quality, decreasing total sleep time, decreasing sleep efficiency, increasing sleep latency, increasing time awake after sleep onset, increasing number of long-wake episodes, and increasing respiratory disturbance index) and greater frailty status. If these cross-sectional results were confirmed in prospective studies indicating that sleep disturbances were associated with a greater odds of incident frailty, studies evaluating the effectiveness of treatments for specific sleep disturbances (such as continuous positive airway pressure for sleep apnea) in reducing the incidence and progression of frailty in older adults would be warranted.

The associations between sleep disturbances and greater frailty status might be mediated through a number of mechanisms. Sleep disorders may be a marker of a number of conditions including poor health, co-morbidities such as cardiovascular disease, depressive symptoms, cognitive dysfunction, and functional disabilities, which by themselves impair sleep and increase the likelihood of greater frailty status. However, these factors and other potential confounders explained some, but not all, of the associations between sleep disturbances and frailty status. In addition, sleep disturbances and frailty or its components have both been linked to alterations in biochemical pathways including lower endogenous testosterone levels^{44,45}, reduced renal function^{46,47}, and elevations in pro-inflammatory cytokines.^{48,49} Any or a combination of these changes might mediate the increased likelihood of greater frailty status observed among men with sleep disturbances.

This study has several strengths, including enrollment of community-dwelling older men not selected on the basis of sleep disturbances or frailty status and comprehensive validated measures of subjective and objective sleep parameters and frailty components. Adjustments for multiple potential confounding factors were made. Objective parameters of sleep-wake patterns were measured over multiple nights, resulting in more stable measures.

This study also had several limitations. The participants were older men living in the community, and findings might not apply to other population groups. Measures used to define some frailty components were similar, but not identical to those used in the original definition.¹⁶ Causality cannot be established due to the cross-sectional study design. Since the association between sleep disorders and frailty status may be bi-directional in nature, future research should examine whether sleep disturbances are independently associated with higher likelihood of incident frailty. Finally, sleep disturbances may be a marker of unknown factors that increased the likelihood of greater frailty status. Several covariates were controlled for, but factors that were not measured may have confounded the results.

Sleep disorders including self-reported poor sleep quality, objectively measured disruptions in sleep wake patterns, and objective evidence of sleep disordered breathing were all independently associated with greater evidence of frailty in older men. Future research is warranted to address the directionality of these associations and to determine whether interventions to treat specific sleep disturbances lower incidence and delay progression of frailty in older adults.

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Table 1
Characteristics of 3133 Participants for Overall Cohort and by Category of Frailty Status

Characteristic	Overall Cohort (n=3133)	Category of Frailty Status			P-value
		Robust (n=1007)	Intermediate (n=1689)	Frail (n=437)	
Age, years, mean $\pm$ SD	76.4 $\pm$ 5.6	74.4 $\pm$ 4.6	76.6 $\pm$ 5.4	80.4 $\pm$ 5.9	<0.001
Race/Ethnicity, n (%)					0.98
Caucasian	2814 (90)	908 (90)	1517 (90)	389 (89)	
African American	121 (4)	37 (4)	66 (4)	18 (4)	
Other	198 (6)	62 (6)	106 (6)	30 (7)	
Self-reported health status, n (%)					<0.001
Excellent or good	2713 (87)	970 (97)	1436 (85)	307 (70)	
Fair, poor, or very poor	417 (13)	35 (3)	253 (15)	129 (30)	
Education, n (%)					<0.001
Less than high school	168 (5)	39 (4)	91 (5)	38 (9)	
High school diploma	498 (16)	146 (14)	264 (16)	88 (20)	
College/Graduate school	2467 (79)	822 (82)	1334 (79)	311 (71)	
Lives alone, n (%)	423 (14)	103 (10)	237 (14)	83 (19)	<0.001
Alcohol intake, drinks/week, n (%)					<0.001
0–2 drinks/week	1849 (59)	520 (52)	1022 (61)	307 (71)	
3–13 drinks/week	1093 (35)	419 (42)	568 (34)	106 (24)	
≥ 14 drinks/week	174 (6)	62 (6)	90 (5)	22 (5)	
Smoking, n (%)					0.36
Never	1236 (39)	411 (41)	668 (40)	157 (36)	
Past	1832 (59)	579 (57)	985 (58)	268 (61)	
Current	65 (2)	17 (2)	36 (2)	12 (3)	
Current antidepressant use, n (%)	247 (8)	34 (3)	138 (8)	75 (17)	<0.001
Current benzodiazepine use, n (%)	139 (4)	23 (2)	76 (4)	40 (9)	<0.001
Current non-benzodiazepine anxiolytic/hypnotic use, n (%)	62 (2)	8 (1)	38 (2)	16 (4)	<0.001
Selected medical conditions [*] , n (%)					<0.001
0–1	1184 (38)	515 (51)	577 (34)	92 (21)	
2–3	1378 (44)	402 (40)	782 (46)	194 (45)	

Characteristic	Overall Cohort (n=3133)	Category of Frailty Status		P-value
		Robust (n=1007)	Intermediate (n=1689)	
≥4	564 (18)	88 (9)	327 (19)	149 (34)
GDS score (range 0–15), mean ± SD	1.8 ± 2.2	0.6 ± 0.8	2.1 ± 2.2	3.6 ± 2.7
Teng 3MS score (range 0–100), mean ± SD	92.6 ± 6.4	93.8 ± 4.9	92.7 ± 6.1	89.5 ± 8.9
IADL impairments (range 0–5), mean ± SD	0.4 ± 0.9	0.1 ± 0.4	0.3 ± 0.7	1.2 ± 1.4
Body mass index, kg/m ² , mean ± SD	27.2 ± 3.9	27.1 ± 3.5	27.3 ± 3.9	26.9 ± 4.4

* History of selected medical conditions including prior fracture since age 50, arthritis, hypo/hyperthyroidism, diabetes mellitus, myocardial infarction, angina, stroke or temporary ischemic attack, claudication, congestive heart failure, chronic obstructive pulmonary disease, non skin cancer, parkinsonism, chronic kidney disease or kidney failure, liver disease and hypertension

Note: All characteristics were assessed at the sleep examination with the exception of race/ethnicity, education level, and living arrangement; these were assessed at the baseline examination.

Abbreviations: GDS, Geriatric Depression Scale; 3MS, Modified Mini-Mental State Exam; IADL, instrumental activities of daily living

Table 2

Prevalence of Sleep Disturbances by Category of Frailty Status

Sleep Disturbance	Category of Frailty Status			P-value*
	Robust (n=1007)	Intermediate (n=1689)	Frail (n=437)	
Pittsburgh Sleep Quality Index >5, n (%)	312 (31)	804 (48)	267 (61)	<0.001
Epworth Sleepiness Scale >10, n (%)	97 (10)	223 (13)	85 (19)	<0.001
Total sleep time ≤5 hours, n (%)	98 (10)	199 (12)	78 (18)	<0.001
Sleep efficiency <70%, n (%)	136 (14)	311 (19)	134 (32)	<0.001
Sleep latency ≥60 min, n (%)	67 (7)	179 (11)	72 (17)	<0.001
Awake after sleep onset ≥90 min, n (%)	263 (27)	520 (32)	196 (46)	<0.001
≥8 long wake episodes, n (%)	271 (28)	547 (33)	188 (44)	<0.001
Respiratory Disturbance Index ≥15, n (%)	190 (20)	436 (28)	140 (35)	<0.001
≥10% of sleep time with SaO ₂ <90%, n (%)	82 (9)	210 (13)	68 (17)	<0.001
PLMA ≥5/hour, n (%)	230 (24)	432 (28)	130 (33)	0.002

* P-values calculated using the Cochran-Armitage test for trend

Abbreviations: min, minutes; SaO₂, arterial oxygen saturation; PLMA, periodic leg movements causing arousal/hour of sleep

Table 3

Multivariable Association between Sleep Disturbance and Odds of Greater Frailty Status

Sleep Disturbance	Proportional Odds Ratio (95% Confidence Interval)	
	Base Model [*]	Final Multivariable Model [†]
Pittsburgh Sleep Quality Index >5	2.08 (1.80–2.41)	1.28 (1.09–1.50)
Epworth Sleepiness Scale >10	1.59 (1.29–1.97)	1.12 (0.89–1.41)
Total sleep time ≤5 hrs	1.27 (1.01–1.58)	1.21 (0.96–1.54)
Sleep efficiency <70%	1.60 (1.32–1.92)	1.37 (1.12–1.67)
Sleep latency ≥60 minutes	1.72 (1.36–2.18)	1.42 (1.10–1.82)
≥8 Long wake episodes	1.27 (1.09–1.48)	1.08 (0.91–1.27)
Respiratory Disturbance Index ≥15	1.37 (1.16–1.63)	1.38 (1.15–1.65)
≥10% of sleep time with SaO ₂ <90%	1.31 (1.04–1.65)	1.19 (0.93–1.53)
PLMA ≥5/hour	1.07 (0.91–1.27)	1.05 (0.88–1.25)

^{*} Adjusted for age, race, site, number of selected medical conditions, body mass index

[†] Adjusted for age, race, site, health status, educational level, social support, alcohol intake, smoking status, antidepressant use, benzodiazepine use, nonbenzodiazepine nonbarbiturate sedative hypnotic use, number of selected medical conditions, depressive symptoms, cognitive function, functional disabilities, and body mass index

Abbreviations: SaO₂, arterial oxygen saturation; PLMA, periodic leg movements causing arousal/hour of sleep

Table 4
Association between Sleep Parameters Expressed as Continuous Variables and Odds of Greater Frailty Status

Sleep Parameter	Unit	Proportional Odds Ratio (95% CI)	
		Base Model [*]	Final Multivariable Model [†]
Pittsburgh Sleep Quality Index	1 SD decrease	1.58 (1.47, 1.71)	1.17 (1.07, 1.27)
Epworth Sleepiness Scale	1 SD increase	1.21 (1.12, 1.29)	1.06 (0.98, 1.14)
Total sleep time	30 min decrease	1.03 (1.00, 1.06)	1.04 (1.00, 1.07)
Sleep efficiency	1 SD decrease	1.25 (1.16, 1.34)	1.16 (1.07, 1.26)
Sleep latency	30 min increase	1.18 (1.10, 1.26)	1.11 (1.03, 1.19)
Time awake after sleep onset	30 min increase	1.15 (1.10, 1.21)	1.08 (1.03, 1.15)
Long wake episodes	1 episode increase	1.06 (1.03, 1.08)	1.03 (1.00, 1.05)
Respiratory Disturbance Index	5 unit increase	1.04 (1.01, 1.07)	1.04 (1.01, 1.07)

^{*} Adjusted for age, race, site, number of selected medical conditions, body mass index

[†] Adjusted for age, race, site, health status, educational level, social support, alcohol intake, smoking status, antidepressant use, benzodiazepine use, nonbenzodiazepine nonbarbiturate sedative hypnotic use, number of selected medical conditions, depressive symptoms, cognitive function, functional disabilities, and body mass index

Appendix

Comparison of Frailty Components for Men in the Cardiovascular Health Study (CHS) and Men in the Outcomes of Sleep Disorders in Older Men (MrOS Sleep) Study

Frailty Component	CHS Definition (n=2233)	MrOS Definition (n=3133)
Shrinking / weight loss	Self-report of >10 pounds lost unintentionally in previous year or documented unintentional weight loss of ≥5% in previous year	Documented unintentional weight loss of ≥5% between baseline and sleep exam (mean years between exams 3.4 ± 0.5)
Weakness	Lowest quintile in grip strength stratified by BMI quartiles: Strength ≤29 for BMI ≤24.0 Strength ≤30 for BMI 24.1–26.0 Strength ≤30 for BMI 26.1–28.0 Strength ≤32 for BMI >28.0	Lowest quintile in grip strength stratified by BMI quartiles: Strength ≤32 for BMI ≤24.5 Strength ≤34 for BMI 24.6–26.7 Strength ≤34 for BMI 26.8–29.4 Strength ≤34 for BMI >29.4
Poor energy	Positive answer to either of two statements from the CES-D Depression Scale: I felt that everything I did was an effort; (and) I could not get going	Negative response to the question from the GDS self-administered questionnaire: Do you feel full of energy?
Slowness	Lowest quintile of walking time stratified by median height from a 15 foot (4.57m) course Time ≥7 seconds for height ≤173cm Time ≥6 seconds for height >173cm	Lowest quintile of walking time stratified by median height from a 6 meter course Walking speed ≤0.93 m/s or unable for height ≤174cm Walking speed ≤1.00 m/s or unable for height >174cm
Low physical activity	Lowest quintile of kcal/wk based on short version of the MLTA questionnaire (cutpoint <383 kcal/wk)	Lowest quintile of PASE score* (cutpoint ≤85.4, range 0–486)

* Higher scores indicate higher activity level

Abbreviations: BMI, body mass index; CES-D, Center for Epidemiologic Studies-Depression; GDS, Geriatric Depression Scale; MLTA, Minnesota Leisure Time Activity; PASE, Physical Activity Scale for the Elderly