Published in final edited form as:
J Am Geriatr Soc. 2009 November ; 57(11): 2094–2100. doi:10.1111/j.1532-5415.2009.02522.x.

Sleep–Wake Disturbances and Frailty in Community-Living Older Persons

Carlos A. Vaz Fragoso, MD[*,†], **Evelyne A. Gahbauer, MD, MPH**[*], **Peter H. Van Ness, PhD, MPH**[*], and **Thomas M. Gill, MD**[*]

[*]Department of Internal Medicine, School of Medicine, Yale University, New Haven, Connecticut

[†]Clinical Epidemiology Research Center, Veterans Affairs Connecticut, West Haven, Connecticut

Abstract

Objectives—To evaluate the association between sleep–wake disturbances and frailty.

Design—Cross-sectional.

Setting—New Haven, Connecticut.

Participants—Three hundred seventy-four community-living persons aged 78 and older.

Measurements—Frailty was based on the Fried phenotype, and sleep–wake disturbances were defined as daytime drowsiness, based on an Epworth Sleepiness Scale (ESS) score of 10 or greater, and as subthreshold and clinical insomnia, based on Insomnia Severity Index (ISI) scores of 8 to 14 and greater than 14, respectively.

Results—Mean age was 84.3; 87 (23.8%) participants were drowsy, 122 (32.8%) had subthreshold insomnia, 38 (10.2%) had clinical insomnia, and 154 (41.2%) were frail. There was a significant association between drowsiness and frailty, with unadjusted and adjusted odds ratios (ORs) of 3.79 (95% confidence interval (CI) = 2.29–6.29) and 3.67 (95% CI = 2.03–6.61), respectively. In contrast, clinical insomnia was significantly associated with frailty in the unadjusted analysis (OR = 2.77, 95% CI = 1.36–5.67) but not the adjusted analysis (OR = 1.93, 95% CI = 0.81–4.61)), and subthreshold insomnia was not associated with frailty in the unadjusted or adjusted analysis.

Conclusion—In older persons, sleep–wake disturbances that present with daytime drowsiness, but not insomnia, are independently associated with frailty. Because drowsiness is potentially remediable, future studies should determine whether there is a temporal relationship between drowsiness and frailty, with the ultimate goal of informing interventions to reverse or prevent the progression of frailty.

Keywords

frailty; Epworth Sleepiness Scale; Insomnia Severity Index

Frailty is a geriatric syndrome that is commonly defined by three or more of the following features: slow gait speed, low physical activity, exhaustion, reduced grip strength, and weight

Address correspondence to Carlos A. Vaz Fragoso, Clinical Epidemiology Research Center, VA Connecticut Healthcare System, Mailcode 151B, West Haven, CT. carlos.fragoso@yale.edu.

Conflict of Interest: The editor in chief has reviewed the conflict of interest checklist provided by the authors and has determined that the authors have no financial or any other kind of personal conflicts with this paper.

Author Contributions: The manuscript reflects the contributions of all four authors.

Sponsor's Role: The investigators retained full independence in the conduct of this research and report.

loss.[1] In community-living older persons, frailty is highly prevalent and is associated with adverse outcomes. Prevalence rates range from 7% in those aged 65 to 74 to approximately 40% in those aged 85 and older.[1–3] Adverse outcomes include greater risk of falls, disability, institutionalization, and death.[1] Strategies for the prevention and treatment of frailty remain to be elucidated, in part because the underlying pathophysiology of frailty has not been firmly established.[4] Proposed contributing factors include systemic inflammation, overactivation of the hypothalamic–pituitary–adrenal axis, malnutrition, depression, cognitive impairment (neurodegenerative disorders), and cardio- and cerebrovascular disease.[1,4]

Sleep–wake disturbances are generally categorized according to the presenting symptoms of insomnia or hypersomnia (e.g., drowsiness).[5,6] In older persons, these symptoms are highly prevalent and associated with adverse outcomes.[5,6] In the Established Populations for Epidemiologic Studies of the Elderly (EPESE), involving 9,282 community-living persons aged 65 and older, 25% reported napping, and 43% reported insomnia symptoms.[5] Adverse outcomes associated with napping include falls, cardiovascular disease, and death, whereas insomnia symptoms are associated with poorer health, cognitive decline, depression, disability, and institutionalization.[6] Whether sleep–wake disturbances play a role in the pathogenesis of frailty is uncertain.

Because they share some common features (e.g., low physical activity) and predict similar outcomes, it was postulated that sleep–wake disturbances might be associated with frailty. The current study was designed to evaluate the prevalence of frailty according to the presence of sleep–wake disturbances, including daytime drowsiness and insomnia, in a cohort of community-living older persons and to determine whether the association between sleep–wake disturbances and frailty is independent of potential confounders. Because sleep–wake disturbances are potentially remediable,[6] establishing such an association could help to inform subsequent interventions designed to reverse or prevent the progression of frailty.

Methods

Study Population

Participants were members of the Precipitating Events Project (PEP), an ongoing longitudinal study of 754 initially nondisabled community-living persons aged 70 and older.[7] The assembly of the cohort has been described in detail elsewhere.[7] To accomplish the specific aims of the parent study, persons who were physically impaired, as denoted by a timed score of longer than 10 seconds on the rapid gait test (walk back and forth over a 10-ft (3-m) course as quickly as possible), were oversampled.[7–9] This cutpoint delineates a threshold response between rapid gait scores and the development of disability in older persons.[8,9] The PEP participation rate was 75.2%. Participants have since been followed with comprehensive assessments administered at 18-month intervals. The Yale University Human Investigation Committee approved the study protocol, and all participants provided written informed consent.

The analytical sample for the current study included community-living participants who completed the comprehensive assessment at 90 months, including at least one of the two validated sleep questionnaires (described below), which were administered for the first time at 90 months. Of the 754 PEP participants, 286 (37.9%) died before the 90-month assessment, 26 (3.4%) dropped out of the study after a median follow-up of 26.5 months, 53 (7.0%) were nursing home residents, and two (0.3%) refused the 90-month assessment. Of the remaining 387 participants, eight (2.1%) did not complete the frailty assessment, and five (1.3%) others did not complete at least one of the two sleep questionnaires, leaving 374 in the analytical sample. The 13 cohort members with missing data on frailty or sleep were older (88.9 vs 87.4; $P < .001$) and more likely to be cognitively impaired (66.7% vs 15.8%; $P = .001$), as defined below, than these participants, although there were no significant differences according to sex,

race or ethnicity, education, health status, or the number of chronic conditions or medications used.

Data Collection

During the 90-month assessment, trained research nurses collected data on nine self-reported, physician-diagnosed chronic conditions (hypertension, arthritis, diabetes mellitus, myocardial infarction, chronic lung disease, cancer (other than minor skin cancers), hip fracture, stroke, and congestive heart failure), health status, medication use, depressive symptoms, cognitive status, frailty, and sleep–wake disturbances. To assess health status, participants were asked, "Would you say your health in general is excellent, very good, good, fair, or poor?"—with reduced health status defined as a rating of fair to poor. Medications, prescription and over-the-counter, were ascertained according to a review of medication bottles and subsequently categorized according to the total number used and risk for central nervous system (CNS) adverse effects (antihistamines, benzodiazepines, barbiturates, opiates, muscle relaxants, antipsychotics, antidepressants, and anticonvulsants). Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D), with a score of 16 or greater denoting significant depressive symptoms.[10,11] Cognitive impairment was defined as a score less than 24 on the Mini-Mental State Examination (MMSE).[12]

Frailty—As described in an earlier report,[13] frailty was operationalized based on the Fried phenotype[1] but with a few modest modifications in three of the five criteria. Specifically, the modified frailty-related criteria included slow gait speed, as defined above; low physical activity, which was defined as a Physical Activity Scale for the Elderly (PASE) score less than 64 for men and 52 for women (these previously validated cutpoints denote the worst quintile of scores in the first 356 enrolled PEP participants who had been selected randomly from the source population[14,15]); and weight loss, defined answering yes when asked, "In the past year, have you lost more than 10 pounds?" Unintentional weight loss was not distinguished from intentional weight loss.[13] These modified criteria have been validated in a recently published study.[13]

The operational definitions were identical for the remaining two Fried frailty criteria.[1] Specifically, the exhaustion criterion was met if the participant answered much or most of the time when asked, "How often in the last week did you feel this way" to either of the following two statements from the CES-D: "I felt that everything I did was an effort" and "I could not get going."[1] The low grip strength criterion was met if the average of three readings, as measured using a handheld dynamometer (Chatillon 100; Ametek, Inc., Largo, FL) was less than or equal to published sex- and body mass index–specific cutpoints.[1]

Consistent with the Fried definition of frailty, participants were then classified as frail based on the presence of three or more of the above criteria.[1]

Sleep–Wake Disturbances—To address the specific aims of the current study, two sleep questionnaires, which had not been included in the prior comprehensive assessments, were added at 90 months. The first was the Epworth Sleepiness Scale (ESS),[16] which is a validated measure of daytime drowsiness as experienced during eight different types of activity, with scores ranging from 0 to 24 (the higher the score, the greater the drowsiness). Although lacking rigorous validation, two frequently cited diagnostic cutpoints for the ESS are 10 and 11.[16–22] To identify participants with clinically meaningful daytime drowsiness, it was decided to use a score of 10 or higher because the National Sleep Foundation has previously used this[17] and, in older persons, it has been associated with hypertension, stroke, and poor driving capacity.[18–20]

The second sleep questionnaire was the Insomnia Severity Index (ISI),[23] which is a validated instrument with seven items that characterize the symptoms and consequences of insomnia, with scores ranging from 0 to 28. Diagnostically, an ISI score less than 8 indicated no clinically significant insomnia, scores of 8 to 14 denoted subthreshold insomnia, and a score greater than 14 was consistent with clinical insomnia.[23] The contents of the ISI are based on the *Diagnostic and Statistical Manual of Mental Disorders, 4th Edition* (DSM-IV) criteria for insomnia.[23]

Statistical Analysis

Clinical characteristics and sleep questionnaire data of all participants and according to frailty status were first summarized as means and standard deviations or as counts and percentages. Using unadjusted logistic regression models, whether drowsiness (ESS ≥10) and insomnia (ISI of 8) were cross-sectionally associated with frailty was next evaluated. This yielded odds ratios (ORs) that were subsequently adjusted for several established risk factors for sleep–wake disturbances, including age, sex, number of chronic conditions, number of medications, use of a medication with adverse CNS effects, health status, cognitive impairment, and significant depressive symptoms. If covariates were highly nonsignificant at a $P > .50$, they were eliminated from the final model. In the multivariable analyses, possible interactions between covariates and the main predictor of a model and potential problems with collinearity and multicollinearity were evaluated. Model fit was assessed according to residual analysis and goodness-of-fit statistics.

To address the possibility that an association between sleep–wake disturbances and frailty might be due largely to the psychological features (exhaustion and, perhaps, low physical activity),[6,18,24] the above analyses were repeated with slow gait speed as the outcome. Prior work has shown that slow gait speed, an objective measure of physical capacity, is the frailty indicator that is most strongly associated with adverse outcomes.[25]

SAS version 9.1.3 (SAS Institute, Inc., Cary, NC) was used for all analyses, with $P < .05$ (two-sided) denoting statistical significance.

Results

Table 1 lists the characteristics of participants in the analytical sample, overall and according to frailty status. The mean age of all 374 participants was nearly 85, and participants were predominantly female and white. On average, participants had a high school education and more than two chronic conditions and were taking approximately nine prescription and over-the-counter medications, of which one had a risk of adverse CNS effects. The five most common chronic conditions were hypertension, arthritis, cancer, diabetes mellitus, and chronic lung disease. Approximately one-third (33.4%) of participants reported health status as fair to poor, 15.8% were cognitively impaired, and 27.9% had significant depressive symptoms. Approximately one-quarter (23.8%) of participants reported being drowsy, nearly one-third (32.8%) had subthreshold insomnia, 10.2% had clinical insomnia, and 41.2% were frail.

Table 2 provides the prevalence and ORs for frailty according to the ESS and ISI. A higher prevalence of frailty was observed in participants with daytime drowsiness than in those without. In the multivariable analysis, daytime drowsiness was statistically associated with frailty, with an adjusted OR of 3.67 (95% confidence interval (CI) = 2.03–6.61). Self-reported health status modulated this association, yielding an adjusted OR of 8.92 (95% CI = 3.25–24.46) in participants with fair to poor health, versus 2.11 (95% CI = 0.99–4.48) in those with good to excellent health.

Similarly, as shown in Table 2, the prevalence of frailty was higher in participants with clinical insomnia than those with no insomnia. However, although associated with frailty in the

unadjusted analysis, clinical insomnia was not statistically associated with frailty in the adjusted analysis. Subthreshold insomnia was not associated with frailty in the unadjusted or adjusted analysis.

Table 3 provides the prevalence and ORs for slow gait speed according to the ESS and ISI. A higher prevalence of slow gait speed was observed in participants with daytime drowsiness than those without daytime drowsiness. In the multivariable analysis, daytime drowsiness was associated with slow gait speed (adjusted OR = 3.12, 95% CI = 1.72–5.65). In contrast, insomnia was not associated with slow gait speed. Furthermore, self-reported health status did not modulate the association between daytime drowsiness and slow gait speed.

Discussion

The current study of community-living older persons found that sleep–wake disturbances and frailty were highly prevalent and that daytime drowsiness, but not insomnia, was independently associated with frailty. Because drowsiness is potentially remediable,[6] establishing an association between drowsiness and frailty could help to inform subsequent interventions to reverse or prevent the progression of frailty.

To the authors' knowledge, the relationship between sleep–wake disturbances and frailty has not been previously evaluated.[1,4] The current study found that the prevalence of frailty was twice as high in participants who were drowsy as in those who were not. The association between drowsiness and frailty remained strong and statistically significant after adjustment for several potential confounders. Although the cross-sectional design did not permit temporal precedence to be established, it may be that a primary sleep disorder, such as obstructive sleep apnea (OSA), advanced sleep-phase type circadian rhythm disorder, or CNS-based hypersomnia, mediates the association between drowsiness and frailty.[26] These primary sleep disorders are prevalent in older persons and are characterized by biological processes that are similar to those seen in frailty.[6,26–29] For example, OSA is associated with systemic inflammation, cognitive impairment, and incident cardio- and cerebrovascular disease;[26–28] circadian rhythm disorders are associated with chronic conditions and neurodegenerative disorders of the brain (cognitive impairment);[26] and CNS-based hypersomnia is associated with vascular and neurodegenerative disorders of the brain.[26]

The association between drowsiness and frailty was particularly strong in participants who reported poor health. This is consistent with prior work, which has shown health status to be strongly associated with drowsiness as defined by the ESS.[21] Although health status probably reflects the intensity of chronic illness, its modification of the association between drowsiness and frailty might be based on psychological factors.[6,18,24] To address this possibility, the association between drowsiness and slow gait speed, a robust indicator of frailty,[25] was evaluated, and a statistically significant and clinically meaningful relationship was found, suggesting that the association between drowsiness and frailty extends beyond psychological factors. The absence of an interaction between health status and the association between drowsiness and slow gait speed strengthens this supposition.

This study found that clinical insomnia was significantly associated with frailty in the unadjusted analysis but not in the adjusted analysis. One possible explanation, supported by the wide confidence interval, which included an adjusted odds ratio as high as 4.61, is that the power to detect a clinically meaningful difference was inadequate in the adjusted analysis. Another possibility is that secondary insomnia (due to a comorbid condition) is more likely to be associated with frailty than primary insomnia (in the absence of comorbidity). It could be that the association between secondary insomnia and frailty is mediated in at least three ways. First, prior work has shown that insomnia worsens the course of comorbid medical and

psychiatric disease,[26,30] thus increasing vulnerability to developing frailty. Second, insomnia may also occur as a manifestation of an underlying primary sleep disorder, such as central sleep apnea, restless legs syndrome, or periodic limb movement disorder. These primary sleep disorders are often associated with cardio- and cerebrovascular disease and neurodegenerative disorders,[26] all of which are proposed risk factors for frailty.[1,4] Third, insomnia is associated with overactivation of the hypothalamic–pituitary–adrenal axis,[30] a response that may contribute to sarcopenia and osteoporosis and, hence, frailty.[4]

In contrast, clinical insomnia was not statistically associated with slow gait speed, in the unadjusted or adjusted analysis. These results are in contradistinction to prior work, which has shown that polysomnography (PSG)-derived measures of sleep continuity (sleep efficiency and wake time after sleep onset) are associated with slower gait speed.[31] A possible explanation for these seemingly contradictory results is that self-reported insomnia symptoms and laboratory measures are only weakly related (i.e., their association is low to moderate (correlation coefficient of 0.06–0.32)).[32] Insomnia is a clinical diagnosis that is defined according to DSM-IV criteria, which are incorporated into the ISI,[23] and not laboratory-derived (PSG or actigraphy) measures.

The findings of the current study suggest that the more-important sleep–wake correlate of frailty is daytime drowsiness, not insomnia. Because wakefulness is the basis for all other higher brain functions,[33–36] it may be that the final pathway linking sleep–wake disturbances and frailty requires the development of daytime drowsiness. Prior work has shown that drowsiness increases the risk of other adverse outcomes. In OSA, for example, drowsiness confers a risk of cardiovascular events and is a basis for pursuing therapy.[37–39]

The relationship between sleep–wake disturbances and frailty is likely to be bidirectional. For example, the deleterious effects of frailty include loss of physical function and reduced socialization (living alone, being home-bound, or institutionalization).[1,40] These frailty-related outcomes, in turn, can adversely affect important zeitgebers, such as social activities, physical exercise, and outdoor sunlight exposure. These zeitgebers entrain circadian rhythms to a 24-hour cycle length, which promotes normal sleep–wake scheduling.[6,26] The loss of these zeitgebers could thus lead to highly irregular sleep–wake schedules.[6,26] Diagnostically, this is termed irregular sleep–wake type circadian rhythm disorder, and it is particularly prevalent in chronically ill and institutionalized older persons.[26] Prognostically, such marked alterations in sleep–wake rhythms might lead to further reductions in physical capacity and greater mortality.[41,42]

The study population had a high prevalence of sleep–wake disturbances and frailty. This is probably because of the advanced age of the participants and to the presence of multiple comorbidities, including diabetes mellitus, myocardial infarction, congestive heart failure, cognitive impairment, and depressive symptoms. A large proportion of participants also reported poor health. These clinical characteristics are risk factors for sleep–wake disturbances and frailty[1–6] and, on average, were more prevalent in frail than nonfrail participants.

The current study included only a single measure of global cognition (MMSE) and did not include a neurological assessment. Nonetheless, an “abnormal brain” may be an important contributor to the development of sleep–wake disturbances. For example, a lesion that involves wake-promoting neurons in the posterior hypothalamus (histaminergic neurons), by virtue of their neuronal projections to distant sites, may lead to declines in vigilance, performance, and learning.[33,34] Similarly, age-related changes in the diurnal function of wake-promoting neurons of the lateral hypothalamus (hypocretin/orexin neurons), also by virtue of neuronal projections to distant sites, may reduce numerous physiological functions, including sleep and wake states, feeding, neuroendocrine regulation, autonomic control, and locomotor activity.

[35,36] Further research in sleep neurobiology could lead to therapeutic interventions that target wake-promoting neurons, upstream (at the site of the lesion) or downstream (at sites distal to the neuronal projections), resulting in subsequent improvements in daytime drowsiness and frailty.

In addition to its cross-sectional design, this study has several other limitations. First, because of the advanced age of the study population, the results may apply only to the "oldest old." Second, prior studies that validated the ESS and ISI did not specifically involve older persons.[16,23] Nonetheless, it has since been shown that, in older persons, the stated ESS and ISI cutpoints are associated with important clinical measures, such as those related to cardiovascular disease and driving capacity.[18–20] Third, because study participants did not undergo laboratory-based sleep diagnostics such as actigraphy, PSG, and a multiple sleep latency test, the severity of the sleep–wake disturbance could not be objectively confirmed, and whether the underlying cause was a primary sleep disorder could not be determined. Last, the operational definitions for frailty criteria differed modestly from those previously described by Fried et al.[1] Comparable modifications have been successfully implemented in the Women's Health and Aging Studies,[43] and it has previously been shown that each of the modified criteria are independently associated with chronic disability, long-term nursing home stays, and death, providing evidence of their validity.[25] To address these limitations, longitudinal studies are needed that include a broader spectrum of older persons and laboratory-based sleep diagnostics and questionnaires and that evaluate alternative operational definitions of frailty.[4]

Despite these limitations, the current study provides important new information about the relationship between sleep–wake disturbances and frailty. Because drowsiness is potentially remediable, future studies should determine whether there is a temporal relationship between drowsiness and frailty, with the ultimate goal of informing interventions to reverse or prevent the progression of frailty.

Acknowledgments

We thank Denise Shepard, BSN, MBA, Shirley Hannan, RN, Andrea Benjamin, BSN, Martha Oravetz, RN, Alice Kossack, Barbara Foster, Shari Lani, Alice Van Wie, and the late Bernice Hebert, RN, for assistance with data collection; Wanda Carr and Geraldine Hawthorne for assistance with data entry and management; Peter Charpentier, MPH, for development of the participant tracking system; and Joanne McGloin, MDiv, MBA, for leadership and advice as the Project Director.

Dr. Fragoso is currently a recipient of an award from the Hartford/National Institute on Aging (NIA) Internal Medicine Subspecialty Scholar in Aging Program and of career development awards from the Department of Veterans Affairs and the Association of Specialty Professors/CHEST Foundation (Williams Program). Dr. Gill is the recipient of an NIA Midcareer Investigator Award in Patient-Oriented Research (K24AG021507). Dr. Van Ness received support from the Claude D. Pepper Older Americans Independence Center at Yale (2P30AG021342-06). The PEP Study is supported by a grant from the National Institutes of Health (R37AG17560).

References

1. Fried L, Tangen M, Walston J, et al. Frailty in older adults: Evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001;56A:M146–M156. [PubMed: 11253156]
2. Rockwood K, Howlett S, MacKnight C, et al. Prevalence, attributes, and outcomes of fitness and frailty in community-dwelling older adults: Report from the Canadian study of health and aging. J Gerontol A Biol Sci Med Sci 2004;59A:1310–1317. [PubMed: 15699531]
3. Boyd CM, Xue QL, Simpson CF, et al. Frailty, hospitalization, and progression of disability in a cohort of disabled older women. Am J Med 2005;118:1225–1231. [PubMed: 16271906]
4. Bergman H, Ferrucci L, Guralnik J, et al. Frailty: An emerging research and clinical paradigm—issues and controversies. J Gerontol A Biol Sci Med Sci 2007;62A:731–737. [PubMed: 17634320]
5. Foley D, Monjan A, Brown S, et al. Sleep complaints among elderly persons: An epidemiologic study of three communities. Sleep 1995;18:425–432. [PubMed: 7481413]

6. Fragoso C, Gill TM. Sleep complaints in community-living older persons: A multifactorial geriatric syndrome. J Am Geriatr Soc 2007;55:1853–1866. [PubMed: 17916123]
7. Gill T, Desai M, Gahbauer E, et al. Restricted activity among community-living older persons: Incidence, precipitants, and health care utilization. Ann Intern Med 2001;135:313–321. [PubMed: 11529694]
8. Gill T, Williams CS, Tinetti M. Assessing risk for the onset of functional dependence among older adults: The role of physical performance. J Am Geriatr Soc 1995;43:603–609. [PubMed: 7775716]
9. Gill T, Richardson ED, Tinetti M. Evaluating the risk of dependence in activities of daily living among community-living older adults with mild to moderate cognitive impairment. J Gerontol A Biol Sci Med Sci 1995;50:M235–M241. [PubMed: 7671024]
10. Kohout F, Berkman L, Evans D, et al. Two shorter forms of the CES-D depression symptoms index. J Aging Health 1993;5:179–193. [PubMed: 10125443]
11. Radloff L. The CES-D scale: A self-report depression scale for research in the general population. Appl Psychol Meas 1977;1:385–401.
12. Folstein M, Folstein S, McHugh P. "Mini-mental state." A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189–198. [PubMed: 1202204]
13. Gill T, Gahbauer E, Allore H, et al. Transitions between frailty states among community-living older persons. Arch Intern Med 2006;166:418–423. [PubMed: 16505261]
14. Pereira M, Fitzegerald S, Gregg E, et al. A collection of Physical Activity Questionnaires for health-related research. Med Sci Sports Exerc 1997;29:S1–S205. [PubMed: 9243481]
15. Washburn R, Smith K, Jette A, et al. The Physical Activity Scale for the Elderly (PASE): Development and evaluation. J Clin Epidemiol 1993;46:153–162. [PubMed: 8437031]
16. Johns M. Sleepiness in different situations measured by the Epworth Sleepiness Scale. Sleep 1991;14:540–545. [PubMed: 1798888]
17. National Sleep Foundation. Sleep in America Polls (2000 Omnibus Poll). [November 13, 2008]. [on-line]. Available at http://www.sleepfoundation.org/
18. Goldstein IB, Ancoli-Israel S, Shapiro D. Relationship between daytime sleepiness and blood pressure in healthy older adults. Am J Hypertens 2004;17:787–792. [PubMed: 15363821]
19. Davies DP, Rodgers H, Walshaw D, et al. Snoring, daytime sleepiness and stroke: A case-control study of first ever stroke. J Sleep Res 2003;12:313–318. [PubMed: 14633243]
20. Fragoso C, Araujo K, Van Ness P, et al. Prevalence of sleep disturbances in a cohort of older drivers. J Gerontol A Biol Sci Med Sci 2008;63A:715–723.
21. Whitney CW, Enright PL, Newman AB, et al. Correlates of daytime sleepiness in 4578 elderly persons: The Cardiovascular Health Study. Sleep 1998;21:27–36. [PubMed: 9485530]
22. Sanford S, Lichstein K, Durrence H, et al. The influence of age, gender, ethnicity, and insomnia on Epworth sleepiness scores: A normative US population. Sleep Med 2006;7:319–326. [PubMed: 16713340]
23. Bastien C, Vallieres A, Morin C. Validation of the insomnia severity index as an outcome measure for insomnia research. Sleep Med 2001;2:297–307. [PubMed: 11438246]
24. Olson LG, Cole MF, Ambrogetti A. Correlations among Epworth Sleepiness Scale scores, multiple sleep latency tests and psychological symptoms. J Sleep Res 1998;7:248–253. [PubMed: 9844851]
25. Rothman MD, Summers LL, Gill TM. Prognostic significance of potential frailty criteria. J Am Geriatr Soc 2008;56:2211–2216. [PubMed: 19093920]
26. Diagnostic and Coding Manual. 2nd. Westchester, IL: American Academy of Sleep Medicine; 2005. International Classification of Sleep Disorders.
27. Pack A. Advances in sleep-disordered breathing. Am J Respir Crit Care Med 2006;173:7–15. [PubMed: 16284108]
28. Schulz R. The vascular micromilieu in obstructive sleep apnea. Eur Respir J 2005;25:780–782. [PubMed: 15863632]
29. Czeisler CA, Dumont M, Duffy JF, et al. Association of sleep-wake habits in older people with changes in output of circadian pacemaker. Lancet 1992;340:933–936. [PubMed: 1357348]
30. Roth T, Roehrs T, Pies R. Insomnia: Pathophysiology and implications for treatment. Sleep Med Rev 2007;11:71–79. [PubMed: 17175184]

31. Dam TT, Ewing S, Ancoli-Israel S, et al. Association between sleep and physical function in older men: The Osteoporotic Fractures in Men Sleep Study. J Am Geriatr Soc 2008;56:1665–1673. [PubMed: 18759758]
32. Unruh ML, Redline S, An MW, et al. Subjective and objective sleep quality and aging in the Sleep Heart Health Study. J Am Geriatr Soc 2008;56:1218–1227. [PubMed: 18482295]
33. España RA, Scammell TE. Sleep neurobiology for the clinician. Sleep 2004;27:811–820. [PubMed: 15283019]
34. Kim SH, Cairns N, Fountoulakisc M, et al. Decreased brain histamine-releasing factor protein in patients with Down syndrome and Alzheimer's disease. Neurosci Letters 2001;300:41–44.
35. Desarnaud F, Murillo-Rodriguez E, Lin L, et al. The diurnal rhythm of hypocretin in young and old F344 rats. Sleep 2004;27:851–856. [PubMed: 15453542]
36. Marcus, JN.; Elmquist, JK. Orexin projections and localization of orexin receptors. In: Nishino, S.; Sakurai, T., editors. Contemporary Clinical Neuro-science: The Orexin/Hypocretin System: Physiology and Pathophysiology. Totowa, NJ: Humana Press Inc; 2006. p. 21-43.
37. Young T, Palta M, Dempsey J, et al. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328:1230–1235. [PubMed: 8464434]
38. Wright J, Rachel Johns R, Watt I, et al. Health effects of obstructive sleep apnoea and the effectiveness of continuous positive airways pressure: A systematic review of the research evidence. BMJ 1997;314:851–860. [PubMed: 9093094]
39. Kapur VK, Resnick HE, Gottlieb DJ. Sleep disordered breathing and hypertension: Does self-reported sleepiness modify the association. Sleep 2008;31:1127–1132. [PubMed: 18714785]
40. Xue QL, Fried LP, Glass TA, et al. Life-space constriction, development of frailty, and the competing risk of mortality: The Women's Health and Aging Study I. Am J Epidemiol 2008;167:240–248. [PubMed: 17906296]
41. Gehrman P, Marler M, Martin JL, et al. The timing of rest-activity rhythms in patients with demential is related to survival. J Gerontol A Biol Sci Med Sci 2004;59A:1050–1055. [PubMed: 15528777]
42. Mormont MC, Waterhouse J, Bleuzen P, et al. Marked 24-h rest/activity rhythms are associated with better quality of life, better response and longer survival in patients with metastatic colorectal cancer and good performance status. Clin Cancer Res 2000;6:3038–3045. [PubMed: 10955782]
43. Blaum CS, Qian XL, Michelon E, et al. The association between obesity and the frailty syndrome in older women: The Women's Health and Aging Studies. J Am Geriatr Soc 2005;53:927–934. [PubMed: 15935013]

Table 1
Characteristics of Participants in the Analytical Sample

Characteristic	All N = 374	Frail n = 154	Nonfrail n = 220
Age, mean ± SD	84.3 ± 4.5	85.9 ± 4.8	83.2 ± 3.9
Female, n (%)	252 (67.4)	108 (70.1)	144 (65.5)
Non-Hispanic white, n (%)	331 (88.5)	137 (89.0)	194 (88.2)
Education, years, mean ± SD	12.1 ± 2.8	11.6 ± 2.8	12.5 ± 2.7
Chronic conditions, n (%)			
Hypertension	250 (66.8)	95 (61.7)	155 (70.5)
Arthritis	201 (53.7)	92 (59.7)	109 (49.5)
Cancer*	98 (26.2)	42 (27.3)	56 (25.5)
Diabetes mellitus	75 (20.1)	42 (27.3)	33 (15.0)
Chronic lung disease	72 (19.3)	35 (22.7)	37 (16.8)
Myocardial infarction	65 (17.4)	37 (24.0)	28 (12.7)
Stroke	39 (10.4)	18 (11.7)	21 (9.5)
Hip fracture	29 (7.8)	16 (10.4)	13 (5.9)
Congestive heart failure	25 (6.7)	18 (11.7)	7 (3.2)
Total, mean ± SD	2.3 ± 1.2	2.6 ± 1.3	2.1 ± 1.1
Medications, mean ± SD			
Total	9.2 ± 3.8	9.7 ± 3.9	8.8 ± 3.6
With adverse central nervous system effects	0.9 ± 1.0	1.1 ± 1.1	0.8 ± 0.9
Fair to poor self-reported health	125 (33.4)	73 (47.4)	52 (23.6)
Mini-Mental State Examination score <24, n (%)	59 (15.8)	41 (26.6)	18 (8.2)
Center for Epidemiologic Studies Depression Scale score ≥16, n (%)	104 (27.9)	58 (37.7)	46 (20.9)
Epworth Sleepiness Scale score†			
<10 (normal)	279 (76.2)	90 (58.4)	189 (85.9)
≥10 (daytime drowsiness)	87 (23.8)	56 (36.4)	31 (14.1)
Insomnia Severity Index score‡			
<8 (no insomnia)	212 (57.0)	81 (52.6)	131 (59.5)
8–14 (subthreshold insomnia)	122 (32.8)	48 (31.2)	74 (33.6)
>14 (clinical insomnia)	38 (10.2)	24 (15.6)	14 (6.4)

*Other than minor skin cancers.

†Eight missing values.

‡Two missing values.

SD = standard deviation;.

Table 2
Frailty According to the Epworth Sleepiness Scale (ESS) and Insomnia Severity Index (ISI)

		Odds Ratio (95% Confidence Interval)	
Sleep Questionnaire	**n/N (%)**	**Unadjusted**	**Adjusted***
ESS score			
<10 (no drowsiness)	90/279 (32.3)	1.00	
≥10 (daytime drowsiness)	56/87 (64.4)	3.79 (2.29–6.29)	3.67 (2.03–6.61)†
ISI score			
<8 (no insomnia)	81/212 (38.2)	1.00	
8–14 (subthreshold insomnia)	48/122 (39.3)	1.05 (0.66–1.66)	0.89 (0.51–1.55)
>14 (clinical insomnia)	24/38 (63.2)	2.77 (1.36–5.67)	1.93 (0.81–4.61)

*Based on a logistic regression model adjusted for age, sex, cognitive impairment (Mini-Mental State Examination score <24), number of chronic conditions, self-reported health status, depressive symptoms (Center for Epidemiologic Studies Depression Scale score ≥16), and use of a medication with adverse central nervous system effects; a variable for number of medications was entered into the multivariable model but was highly nonsignificant ($P > .50$) and was deleted from the reported model.

†An interaction term crossing the self-reported health status covariate with the ESS main predictor was statistically significant ($P = .02$) in a separate adjusted model; the odds ratio for the ESS predictor for participants with fair to poor health was 8.92 (95% confidence interval (CI) = 3.25–24.46), and for those with good to excellent health, it was 2.11 (95% CI = 0.99–4.48).

Table 3

Slow Gait Speed According to the Epworth Sleepiness Scale (ESS) and Insomnia Severity Index (ISI)

		Odds Ratio (95% Confidence Interval)	
Sleep Questionnaire	**n/N (%)**	**Unadjusted**	**Adjusted***
ESS score			
<10 (no drowsiness)	126/284 (44.4)	1.00	
≥10 (daytime drowsiness)	61/87 (70.1)	2.94 (1.76–4.92)	3.12 (1.72–5.65)†
ISI score			
<8 (no insomnia)	112/216 (51.9)	1.00	
8–14 (subthreshold insomnia)	57/122 (46.7)	0.81 (0.52–1.27)	0.68 (0.39–1.17)‡
>14 (clinical insomnia)	25/39 (64.1)	1.66 (0.82–3.36)	1.01 (0.42–2.44)‡

*Based on a logistic regression model adjusted for age, sex, number of chronic conditions, self-reported health status, number of medications, use of a medication with adverse central nervous system (CNS) effects, cognitive impairment (Mini-Mental State Examination score <24), and significant depressive symptoms (Center for Epidemiologic Studies Depression Scale score ≥16).

†Variables for depressive symptoms and use of a medication with adverse CNS effects were entered into the multivariable model but were highly nonsignificant ($P > .50$) and were deleted from the reported model.

‡Variables for number of medications and for use of a medication with CNS adverse effects were entered into the multivariable model but were highly nonsignificant ($P > .50$) and were deleted from the reported model.