Characteristics of Self-Reported Sleep and the Risk of Falls and Fractures: The Women’s Health Initiative (WHI)

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ABSTRACT
Sleep disturbances are common and may influence falls and fracture directly by influencing bone turnover and muscle strength or indirectly through high comorbidity or poor physical function. To investigate the association between self-reported sleep and falls and fractures, we prospectively studied 157,306 women in the Women’s Health Initiative (WHI) using information on sleep quality, sleep duration, and insomnia from questionnaires. Annual self-report of falling two or more times (ie, “recurrent falling”) during each year of follow-up was modeled with repeated measures logistic regression models fit by generalized estimating equations. Cox proportional hazards models were used to investigate sleep disturbance and time to first fracture. We examined the risks of recurrent falls and fracture by sleep duration with 7 hours as referent. We examined the risks across categories of sleep disturbance, insomnia status, and sleep quality. The average follow-up time was 7.6 years for falls and 12.0 years for fractures. In multivariable adjusted models, including adjustment for comorbidity, medications, and physical function, women who were short (<5 hours) and long (>10 hours) sleepers had increased odds of recurrent falls (odds ratio [OR] 1.28; 95% confidence interval [CI], 1.23 to 1.34 and OR 1.25; 95% CI, 1.09 to 1.43, respectively). Poor sleep quality, insomnia, and more sleep disturbances were also associated with an increased odds of recurrent falls. Short sleep was associated with an increased risk of all fractures, and upper limb, lower limb, and central body fractures, but not hip fractures, with hazard ratios ranging from 1.10 to 1.13 (p < 0.05). There was little association between other sleep characteristics and fracture. In conclusion, short and long sleep duration and poor sleep quality were independently associated with increased odds of recurrent falls. Short sleep was associated with modest increase in fractures. Future long-term trials of sleep interventions should include falls and fractures as endpoints. © 2018 American Society for Bone and Mineral Research.

KEY WORDS: EPIDEMIOLOGY; GENERAL POPULATION STUDIES; FRACTURE PREVENTION; FALLS
SLEEP, RECURRENT FALLS AND FRACTURES

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Subjects and Methods

Study population

The study population includes all women enrolled in the Women’s Health Initiative (WHI). The WHI, carried out at 40 US clinical centers, is a study of postmenopausal women aged 50 to 79 years and free of serious medical conditions at baseline (1993 to 1998)(23–26). The current analysis used data from participants in the WHI Observational Study (WHI-OS) and WHI Clinical Trials (WHI-CT). The WHI-OS was designed to examine important causes of morbidity and mortality in postmenopausal women.(24) The WHI-CTs examined the effects of menopausal hormone therapy (HT) (WHI Hormone Therapy Trials), calcium and vitamin D supplementation (WHI CaD Trial), and a low-fat eating pattern (WHI Dietary Modification Trial). (25) The WHI-OS and WHI-CT main studies were conducted between 1993 and 2005. Of 150,076 participants who were in active follow-up at the end of the main studies, 76.9% consented to participate in an extension study conducted between 2005 and 2010 and 86.9% of those eligible in Extension Study 2 (2010 to 2020).

Of the 93,676 WHI-OS participants and 68,132 WHI-CT participants enrolled, we excluded data from 878 participants who provided no follow-up information, 948 with no fall data, and 605 participants who provided no information on sleep, resulting in an analytic sample of 157,306 participants.

Assessment of self-reported sleep characteristics

All self-reported sleep characteristics including information on sleep duration, sleep quality, sleep disturbance level, and insomnia were collected on baseline questionnaires. Participants were asked: “About how many hours of sleep did you get on a typical night during the last 4 weeks?” Item response choices were 5 or less hours, 6 hours, 7 hours, 8 hours, 9 hours, or 10 or more hours.

A sleep disturbance construct was developed using the WHI Insomnia Rating Scale (WHIIRS). (27,28) The five-item sleep disturbance scale included questions on whether participants over the past 4 weeks had trouble falling asleep, woke up several times at night, woke up earlier than planned, and had trouble getting back to sleep after awakening early. Response categories were as follows: (0) no, not in the past 4 weeks; (1) yes, less than once per week; (2) yes, 1 to 2 times per week; (3) yes, 3 or 4 times per week; and (4) yes, 5 or more times per week. The sleep disturbance construct also included overall sleep quality: (0), very sound or restful; (1), sound or restful; (2), average quality; (3), restless; or (4), very restless. Possible scores on the WHIIRS ranged from 0 to 20, with scores >9 indicating high risk for insomnia. (27) This sleep disturbance scale was also categorized in quartiles: 0 to 3; 4 to 6; 7 to 10; and >11. The WHIIRS consisting of the questions on sleep disturbances and overall sleep quality has been validated. (27,28) Reliability of the WHIIRS was estimated using a resampling approach; the mean alpha coefficient was 0.78. Test reliability coefficients were 0.96 for same day administration. A between group difference of approximately 0.5 for a standard deviation on the WHIIRS may be clinically meaningful. (27)

Falls

Women were asked on annual self-reported health updates, “How many times did you fall and land on the floor or ground (do not include falls due to sports activities such as snow
water skiing or horseback riding)." The falls outcome was defined as annually repeated assessment of self-report of falling two or more times in the past year (recurrent falls), similar to a previous WHI report.\(^\text{29}\) Self-reporting of two or more falls in a given year was considered an event. Self-report of falls was discontinued during the extension phase, limiting the average follow-up for falls to 7.6 years.

**Outcomes: fracture**

Information regarding incident fractures was obtained semianually for the WHI-CT and annually for the WHI-OS. At each assessment, questionnaires asked whether participants had experienced a first fracture event since the previous visit: "Has a doctor told you for the first time that you have a new broken, fractured, or crushed bone? Which bone(s) did you break, fracture, or crush?" Response choices included: hip, upper leg (not hip), pelvis, knee (patella), lower leg or ankle, foot (not toe), tailbone (coccyx), spine or back (vertebra), upper arm or shoulder, elbow, lower arm or wrist, hand (not finger), jaw, nose, face, and/or skull, ribs and/or chest or breast bone, and "other".

All hip fractures were adjudicated by trained staff using medical record review for both WHI-OS and WHI-CTs during the main study and Extension 1. Adjudication of non-hip fractures was limited to a subset of participants during the main WHI study,\(^\text{30}\) including (i) fractures among participants of the WHI Clinical Trials and (ii) fractures among participants in the WHI Bone Mineral Density (BMD) Cohort. Any fractures that occurred during the WHI Extension 2 phase in the WHI-OS and WHI-CTs were self-reported.

All fractures reported up to September 30, 2015, were included in these analyses for an average follow-up of 12.0 years. We studied all fractures (any fractures except those of the fingers, toes, ribs, coccyx, face, skull, and sternum), hip fractures, upper limb fractures (elbow, hand except fingers, lower arm/wrist, upper arm/humerus or shoulder), lower limb fracture (foot except toes, knee/patella, upper leg except hip, lower leg/ankle), and central body fractures (hip, pelvis, spine).

**Other measurements**

Demographic characteristics, medical history, lifestyle factors (alcohol, smoking), and health status were collected using standardized questionnaires at the baseline examination. Weight was measured on a balanced beam scale while wearing indoor clothing. Height was measured with a fixed stadiometer. Weight and height were used to calculate the body mass index (BMI): weight in kilograms divided by height in meters squared. Calcium intake was defined as the dietary calcium intake assessed by food-frequency questionnaires developed and validated by the Fred Hutchinson Cancer Research Center (Seattle, WA, USA).\(^\text{31}\) Information was also obtained about intake of calcium from supplements in the previous 2 weeks. Total vitamin D intake was similarly determined. Caffeine intake was also assessed by the food frequency questionnaire. Physical activity was assessed by a detailed questionnaire on the frequency and duration of walking and mild, moderate, and strenuous activities in the prior week. Walking was assessed by a series of questions about the frequency of walks outside the home for more than 10 min without stopping, the average duration of each walk, and the usual walking pace. Vigorous exercise was defined as that in which "you work up a sweat and your heart beats fast," and examples included aerobics, aerobic dancing, jogging, tennis, and swimming laps. Moderate exercise was defined as that which was "not exhausting," and examples included biking outdoors, using an exercise machine (such as a stationary bicycle or a treadmill), calisthenics, easy swimming, and popular or folk dancing. Examples of mild exercise were slow dancing, bowling, and golf. Total weekly kilocalories of energy expended were calculated (metabolic equivalent [MET]).\(^\text{32}\) Assessment of depression was done with baseline questions drawn from the Center for Epidemiologic Studies–Depression Scale (CES-D).\(^\text{33}\)

Information regarding current use of menopausal HT, daily oral corticosteroid use, baseline use of drugs for osteoporosis (bisphosphonates, selective estrogen receptor modulators [SERMs], calcitonin, parathyroid hormone), use of oral or injectable drugs for the treatment of diabetes (eg, thiazolidinediones, dipeptidyl peptidase-4 inhibitors, meglitinides, glucagon-like peptide-1 agonists, insulin injection, amylin analog, sulfonylureas, biguanides, and alpha-glucosidase inhibitors), sleep medications (over-the-counter sleep aids; eg, Tylenol PM, Ambien, temazepam), analgesic narcotics (narcotic agonists, narcotic antagonists, codeine combinations, dihydrocodeine combinations, fentanyl combinations, hydrocodone combinations, hydromorphone combinations, propoxyphene combinations, meperidine combinations, pentazocine combinations, tramadol combinations), antidepressants (Alpha-2 receptor antagonists [tetracyclic antidepressants], monoamine oxidase [MAO] inhibitors, modified cyclerics, selective serotonin reuptake inhibitors [SSRIs], tricyclic agents), and hypnotics (barbiturates, benzodiazepines, selective alpha-2 adrenoreceptor agonist sedative, antihistamine hypnotics) was obtained. Participants were asked to bring medications they were regularly taking to the clinic visit, medication name, strength, and duration of use were recorded. Physical function was measured by the 10-item Rand-36 physical function score.\(^\text{34}\)

**Statistical analyses**

We used chi-square tests and ANOVA to compare characteristics of women by self-reported duration of sleep. For the analysis of recurrent falls (falling two or more times per year), we used the generalized estimating equation (GEE) approach for repeated measures logistic regression models with independence working covariance mixture. We used Cox proportional hazard regression to estimate the association between self-reported sleep and time to first fracture, using separate regression models for total fractures and for each anatomical fracture location: hip, lower limb, upper limb, and central. Among women who experienced a fracture, duration of follow-up was defined as time to first fracture. Among women who did not experience a fracture during follow-up, duration of follow-up was defined as time until last follow-up visit or death, whichever came first. The proportional hazard assumption of the main exposure variables (sleep) variables was tested by using sleep × log (time) was interaction variables and plots of Schoenfeld residuals were evaluated. No gross violations were observed. We tested for a quadratic or linear trend, as appropriate. We examined the risk of fracture over the full follow-up and truncating follow-up to 5 years after baseline.

We examined the recurrent risk of falls and fractures across self-reported sleep duration with 7 hours per night as the referent group because the highest percentage of women reported 7 hours of sleep per day. Other self-reported sleep characteristics examined were sleep quality (average quality as...
Among short sleepers (<5 hours per night), sleep disturbance level (0 to 3 as referent), and insomnia symptoms (<9 as referent) all covariates were measured at baseline. We adjusted models for risk factors for falls and fractures including age, region, ethnicity/race, weight, height, treated diabetes, smoking status, general health status, HT, total calcium and vitamin D intake, physical activity, alcohol intake, depressive symptoms score, caffeine intake, HT trial arm and Diet Modification trial arm, medications (hypnotics, anti-anxiety, antidepressants, and analgesic narcotics), physical functioning and number of comorbidities (stroke, myocardial infarction [MI], congestive heart failure [CHF], Parkinson’s disease, chronic obstructive pulmonary disease [COPD], asthma, and any prevalent cancer). Fracture models were additionally adjusted for parental history of hip fracture, oral glucocorticoid use, and previous fracture. Missing data on categorical covariates were recoded as unknown and included in our modeling. All analyses were completed in SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Baseline characteristics of women by self-reported duration of sleep are shown in Table 1. The majority of women reported sleeping on average 7 hours per night (37%); 8.3%, slept 5 hours and 4.4% reporting ≥9 hours per night. Women who reported sleeping 8 to 9 hours per night tended to be slightly older than short sleepers (<5 hours). Asian and African American women and women with a high school degree or less tended to be short sleepers. Many of the characteristics of women across self-reported sleep duration were statistically significant but absolute differences were small. However, large differences were observed for depressive symptoms, use of antidepressants and self-reported health status. Both short (<5 hours) and long sleepers (≥10 hours) were more likely to report a higher number of depressive symptoms with approximately 21% of women who reported ≥10 hours of sleep reporting use of an antidepressant compared with 6% of those reporting sleeping 7 hours per night. Use of hypnotics, anti-anxiety, and analgesic narcotic medications was low with slightly greater prevalence among the very short and very long sleepers. Twenty percent of short sleepers and 25% of long sleepers reported fair/poor health status compared to 7% of the referent group. Use of diabetes medication was also highest among short and long sleepers. Long sleepers weighed on average 2 kg more than short sleepers. A history of falling in the past 12 months was almost double among both short and long sleepers compared to those sleeping 7 hours per night.

Self-reported sleep characteristics by hours of sleep duration are shown in Supplemental Table 1. Women who reported sleeping ≤5 hours per night were more likely to report restless sleep, trouble falling asleep, waking up during the night, waking up earlier than planned, and having trouble falling back to sleep. Among short sleepers (≤5 hours per night), almost 60% had the highest sleep disturbance level and 70% had insomnia.

Falls

The annualized rate of recurrent fall events was 10.6% among women reporting ≤5 hours of sleep per night, lowest (about 7.0%) among women sleeping 7 to 8 hours per night and highest among women sleeping ≥10 hours per night (11.8%) (Table 2). Women who reported ≤5 hours of sleep were 27% more likely to experience recurrent falls in the multivariable (MV) model (odds ratio [OR] 1.27; 95% confidence interval [CI], 1.22 to 1.33) compared to women reporting ≥10 hours of sleep per night. Women reporting ≥10 hours of sleep per night were 24% more likely to experience recurrent falls in the MV adjusted model (OR 1.24; 95% CI, 1.08 to 1.42). The model fit a significant quadratic pattern.

The annualized rate of recurrent falls was greatest among women who self-reported very restless sleep. Women with very restless sleep and restless sleep were 21% and 11%, respectively, more likely to experience recurrent falls compared to women who self-reported average sleep quality in MV models. In contrast, women who reported sound or very sound or restful sleep had the lowest annualized rate of recurrent falls and were about 4% to 8% less likely to experience recurrent falls, an association that remained after MV adjustment. The risk of recurrent falls increased with increasing sleep disturbance levels in MV models, p linear trend, p < 0.0001. Women with the greatest sleep disturbance were 34% more likely to experience recurrent falls compared to women with the lowest sleep disturbance levels in MV models. Women with insomnia had an annualized rate of recurrent falls of 10% and were 18% (OR 1.18; 95% CI, 1.15 to 1.21) more likely to experience recurrent falls.

Fractures

Generally, the annualized (%) incidence of fracture was greatest among self-reported short and long sleepers, those with very restless sleep, the highest sleep disturbance level, and insomnia (Table 3). There was a modest association between short sleep duration (<5 hours) and an increased risk of any fracture, upper limb fracture, lower limb fracture, and central fracture but no association with hip fractures alone. The hazard ratios (HRs) showed a significant 10% to 13% increased risk of fracture among self-reported short sleepers compared to women who slept 7 hours per night, an association that was independent of established risk factors for fracture. There was no association between long duration of sleep and fracture at any site. In unadjusted models, women who self-reported the greatest sleep disturbance had a 22% to 36% increased risk of any fracture, upper and lower limb fracture, and central body fracture compared to women with the lowest sleep disturbance. Adjustment for established risk factors for fracture attenuated the magnitude of the association to about a 5% to 11% increased risk of total, upper body, lower limb, and central fractures among women with the greatest sleep disturbance level but the HR remained statistically significant. There was little association between overall sleep quality and fracture at any site in the MV models. Women with insomnia had a modest elevated risk of all fractures except hip in the MV adjusted model (3% to 5%).

Discussion

Women who reported short (<5 hours) and long (≥10 hours) sleep had about a 27% and 24%, respectively, increased odds of recurrent falls (>2 falls/year) during any year of follow-up in MV models. This U-shaped relationship between self-reported sleep duration and recurrent falls was independent of established risk factors for falls including use of central nervous system (CNS)-active medications, physical function, and comorbidity. In addition, women reporting restless and very restless sleep had a 11% to 21% increased odds of recurrent falls, while women reporting sound, restful, very sound, or very restful sleep had
Table 1. Baseline Characteristics by Hours of Sleep Excluding Those With No Following or Missing Exposure or Falls Data

| Hours of sleep | 5 or less | 6 | 7 | 8 | 9 | 10 or more | p (test of trend) |
|---------------|-----------|---|---|---|---|------------|------------------|
| n (%)         | 13,119 (8.3) | 43,306 (27.5) | 58,962 (37.4) | 35,029 (22.2) | 6,080 (3.9) | 810 (0.5) | <0.001 |
| Age (years), mean ± SD | 63.2 (7.6) | 63.1 (7.4) | 63.0 (7.2) | 63.5 (7.0) | 64.0 (7.1) | 63.2 (7.4) | <0.001 |
| Race/ethnicity, n (%) | 107 (0.8) | 190 (0.4) | 209 (0.4) | 140 (0.4) | 26 (0.4) | 4 (0.5) | <0.001 |
| American Indian or Alaskan Native | 628 (4.8) | 1,614 (3.7) | 1,305 (2.2) | 464 (1.3) | 69 (1.1) | 10 (1.2) | <0.001 |
| Asian or Pacific Islander | 2,580 (19.7) | 5,086 (11.8) | 3,754 (6.4) | 1,849 (5.3) | 410 (6.8) | 152 (18.8) | <0.001 |
| Black or African-American | 794 (6.1) | 1,806 (4.2) | 1,944 (3.3) | 1,105 (3.2) | 206 (3.4) | 107 (13.2) | <0.001 |
| Hispanic/Latino | 8,735 (66.8) | 33,225 (78.5) | 51,042 (86.8) | 31,047 (88.9) | 5,303 (87.4) | 531 (65.6) | <0.001 |
| White (not of Hispanic origin) | 239 (1.8) | 573 (1.3) | 573 (1.0) | 331 (0.9) | 53 (0.9) | 5 (0.6) | <0.001 |
| Education, n (%) | 3,847 (29.6) | 10,038 (23.4) | 11,986 (20.5) | 7,383 (21.2) | 1,381 (22.9) | 262 (32.7) | <0.001 |
| High school or less | 1,594 (12.7) | 4,836 (11.7) | 6,104 (10.9) | 3,748 (11.2) | 666 (11.5) | 100 (13.0) | <0.001 |
| College grad or more | 4,095 (32.5) | 15,676 (37.8) | 23,128 (41.1) | 13,847 (41.5) | 2,190 (37.8) | 238 (30.8) | <0.001 |
| Physical activity (MET hours/week), n (%) | 12,746 (97.4) | 41,829 (96.8) | 56,586 (96.3) | 33,203 (95.1) | 5,641 (93.2) | 756 (93.8) | <0.001 |
| Alcohol intake, n (%) | 338 (2.6) | 1,365 (3.2) | 2,191 (3.7) | 1,725 (4.9) | 414 (6.8) | 50 (6.2) | <0.001 |
| Smoking status, n (%) | 6,758 (52.1) | 21,768 (50.9) | 29,890 (51.3) | 17,533 (50.6) | 2,896 (48.2) | 367 (45.9) | <0.001 |
| Never smoked | 5,063 (39.1) | 17,788 (41.6) | 24,604 (42.2) | 14,969 (43.2) | 2,702 (45.0) | 351 (43.9) | <0.001 |
| Current smoker | 1,138 (8.8) | 3,245 (7.6) | 3,802 (6.5) | 2,122 (6.1) | 409 (6.8) | 282 (34.9) | <0.001 |
| Hormone therapy, n (%) | 922 (7.0) | 2,675 (6.2) | 3,710 (6.3) | 2,820 (8.1) | 414 (6.8) | 81 (10.1) | <0.001 |
| Never used | 338 (2.6) | 1,365 (3.2) | 2,191 (3.7) | 1,725 (4.9) | 414 (6.8) | 50 (6.2) | <0.001 |
| Past user | 4,326 (33.0) | 16,795 (38.8) | 24,907 (42.3) | 14,706 (42.0) | 2,439 (40.2) | 282 (34.9) | <0.001 |
| Current user | 5,063 (39.1) | 17,788 (41.6) | 24,604 (42.2) | 14,969 (43.2) | 2,702 (45.0) | 351 (43.9) | <0.001 |
| Depressive symptoms (CESD >0.06), n (%) | 9,514 (75.0) | 36,628 (86.6) | 53,040 (91.8) | 31,901 (92.8) | 5,298 (89.4) | 597 (76.1) | <0.001 |
| No | 3,173 (25.0) | 5,644 (13.4) | 4,768 (8.2) | 2,461 (7.2) | 625 (10.6) | 188 (23.9) | <0.001 |
| Yes | 1059 (705) | 1137 (710) | 1200 (708) | 1201 (705) | 1195 (725) | 1108 (752) | <0.001 |
| Total calcium (mg/day), mean ± SD | 164.7 (137.3) | 169.7 (133.4) | 168.6 (131.2) | 166.9 (137.1) | 146.6 (142.3) | <0.001 |
| Antidepressants (yes), n (%) | 922 (7.0) | 2,675 (6.2) | 3,710 (6.3) | 2,820 (8.1) | 836 (13.8) | 172 (21.2) | <0.001 |
| Anti-anxiety pills (yes), n (%) | 607 (4.6) | 1,481 (3.4) | 1,645 (2.4) | 1,003 (2.9) | 237 (3.9) | 34 (4.2) | <0.001 |
| Hypnotics (yes), n (%) | 576 (4.4) | 1,449 (3.3) | 1,435 (2.4) | 757 (2.2) | 146 (2.4) | 22 (2.7) | <0.001 |
| Analgesic narcotics (yes), n (%) | 517 (3.9) | 878 (2.0) | 957 (1.6) | 582 (1.7) | 150 (2.5) | 33 (4.1) | <0.001 |
| Oral glucocorticosteroid (yes), n (%) | 140 (1.1) | 326 (0.8) | 322 (0.6) | 225 (0.6) | 45 (0.7) | 8 (1.0) | <0.001 |
| Fracture (age ≥55 years), (yes), n (%) | 1,705 (17.4) | 5,488 (16.7) | 7,140 (15.9) | 4,415 (16.2) | 843 (17.7) | 96 (15.9) | <0.001 |
Table 1. (Continued)

| Hours of sleep | 5 or less | 6 | 7 | 8 | 9 | 10 or more | p (test of trend) |
|----------------|-----------|---|---|---|---|-------------|------------------|
| Parental history of broken bone (age >40 years) (yes), n (%) | 4,397 (37.7) | 15,630 (39.4) | 22,280 (40.6) | 13,028 (39.8) | 2,225 (39.5) | 242 (33.4) | <0.001 |
| Parental history of broken hip (yes), n (%) | 1,488 (12.7) | 5,429 (13.7) | 7,267 (14.1) | 4,715 (14.4) | 805 (14.3) | 85 (11.7) | <0.001 |
| Weight (kg), mean ± SD | 75.8 (18.6) | 73.9 (17.2) | 72.7 (16.4) | 73.3 (16.4) | 74.6 (17.2) | 77.8 (19.3) | <0.001 |
| Height (cm), mean ± SD | 160.7 (6.8) | 161.4 (6.7) | 162.0 (6.6) | 162.2 (6.6) | 162.4 (6.4) | 161.2 (7.1) | <0.001 |
| Diabetes treated (pills or shots) (yes), n (%) | 976 (7.4) | 2,039 (4.7) | 2,174 (3.7) | 1,290 (3.7) | 299 (4.9) | 57 (7.0) | <0.001 |
| In general, health is fair/poor, n (%) | 2586 (19.8) | 4305 (9.9) | 3950 (6.7) | 3798 (6.8) | 633 (10.3) | 203 (25.3) | <0.001 |
| Times fell down last 12 months, n (%) | 3 843 (6.7) | 1,812 (4.3) | 2,052 (3.6) | 1,240 (3.7) | 261 (4.5) | 59 (7.6) | <0.001 |

| Physical function score, mean ± SD* | 73.9 (24.1) | 80.4 (20.3) | 83.1 (18.4) | 82.3 (19.1) | 78.4 (21.7) | 69.5 (25.8) | <0.001 |

*Rand-36 physical function score (34).
Table 2. Association of Hours of Sleep, Sleep Quality, and Sleep Disturbance With Risk of Two or More Falls in the Past Year

| Total events, n (%) | Events n (%) | Crude OR (95% CI) | Multivariable model<sup>a</sup> OR (95% CI) |
|---------------------|-------------|-------------------|--------------------------------------------|
| <5 hours            | 10,548 (10.6) | 1.54 (1.48–1.60) | 1.27 (1.22–1.33)                          |
| 6 hours             | 28,350 (8.4)  | 1.17 (1.14–1.21) | 1.13 (1.10–1.16)                          |
| 7 hours             | 33,877 (7.3)  | 1 (Ref)           | 1 (Ref)                                   |
| 8 hours             | 19,446 (7.1)  | 0.97 (0.94–1.00) | 0.92 (0.90–0.95)                          |
| 9 hours             | 4,041 (8.6)   | 1.19 (1.13–1.26) | 0.99 (0.94–1.05)                          |
| >10 hours           | 719 (11.8)    | 1.80 (1.57–2.05) | 1.24 (1.08–1.42)                          |
| Quadratic p value   | <0.001       |                   | <0.001                                    |
| Overall sleep quality |            |                   |                                           |
| Very restless       | 3,524 (13.0)  | 1.75 (1.64–1.87) | 1.21 (1.13–1.30)                          |
| Restless            | 17,641 (10.3) | 1.32 (1.28–1.36) | 1.11 (1.07–1.14)                          |
| Average quality     | 41,475 (8.1)  | 1 (Ref)           | 1 (Ref)                                   |
| Sound or restful    | 24,501 (6.9)  | 0.84 (0.82–0.87) | 0.96 (0.94–0.99)                          |
| Very sound or restful| 9,840 (6.2)  | 0.75 (0.73–0.78) | 0.92 (0.88–0.96)                          |
| p value             | <0.001       |                   | <0.001                                    |
| Sleep disturbance level |            |                   |                                           |
| 0–3                 | 19,902 (5.9)  | 1 (Ref)           | 1 (Ref)                                   |
| 4–6                 | 24,820 (7.4)  | 1.27 (1.23–1.31) | 1.15 (1.11–1.19)                          |
| 7–10                | 27,175 (8.6)  | 1.51 (1.46–1.56) | 1.24 (1.20–1.28)                          |
| ≥11                 | 25,084 (10.5) | 1.88 (1.83–1.95) | 1.34 (1.30–1.39)                          |
| Linear p value      | <0.001       |                   | <0.001                                    |
| Insomnia scale      |             |                   |                                           |
| No                  | 59,364 (7.0)  | 1 (Ref)           | 1 (Ref)                                   |
| Yes (sleep disturbance ≥9) | 37,617 (10.0) | 1.49 (1.45–1.52) | 1.18 (1.15–1.21)                          |
| p value             | <0.001       |                   | <0.001                                    |

Value of p represents chi-square Wald statistic. Event is defined as 2 or more falls in the past year. % = annualized percent. ORs are estimated from repeated logistic models.

<sup>a</sup>Multivariable model: age, weight, height, treated diabetes, ethnicity/race, region, smoking status, general health status, current HT use, total vitamin D intake, physical activity, alcohol intake, depressive symptom score, caffeine intake, HT trial arm, diet modification trial arm, hypnotics medication use, anti-anxiety medication use, antidepressant medication use, analgesic narcotic medication use, physical function score and number of chronic conditions (stroke, MI, CHF, diabetes, Parkinson’s disease, COPD, asthma, any cancer).

of fracture.<sup>10</sup> In the Malmo study, premature awakening was associated with hip fractures, but in men only.<sup>11</sup> Thus, there are several suggestive findings of an association between sleep characteristics and fractures that are consistent with our modest associations. Given the widespread prevalence of sleep disorders in the population, more information is needed on whether sleep influences the risk of fracture. These studies should be carried out with objective assessments of sleep duration and quality.

There are a number of strengths to our study. We prospectively evaluated associations with recurrent falls and a number of fracture outcomes in a large cohort of women over an average follow-up of 12 years. We also adjusted for important risk factors for falls and fractures. We used validated measures of sleep disturbances and insomnia but we were limited to self-reported sleep characteristics. Associations between sleep duration and poor health outcomes have been shown to vary by how sleep was measured.<sup>35</sup> For example, long sleep (>9 hours) was associated with poor health status only if self-report was used. In our study, adjusting the association between long sleep and recurrent falls was attenuated to a greater degree after MV adjustment than associations between short sleep and recurrent falls. Self-reported total sleep time associations with poor health may be due principally to confounding or reverse causality whereby sicker people spend more time in bed or need more sleep precisely because they are sick. Long sleep could reflect the presence of other sleep disorders; eg, sleep-disordered breathing. Future studies should rely on objective measures of sleep using actigraphy and polysomnography because certain sleep characteristics, such as sleep duration, may not be accurately reported, especially in older adults.

Despite the strengths to our study, there are several limitations. In addition to reliance on self-report of sleep characteristics, we relied on self-report of non-hip fractures in women enrolled in WHI-OS and during Extension 2, but we previously showed that 76% of all self-reported fractures were confirmed by radiographic report.<sup>30</sup> Although monthly fall calendars are the gold standard, the annual self-report assessment of falls used in our study was standardized, allowing the study of an association with sleep patterns. Given our sample size, we could detect small effects and it is uncertain whether these effects are clinically significant. BMD was measured at only three WHI clinics and thus we could not adjust for BMD. We had no information on bone turnover makers. We assessed sleep only once at baseline. We adjusted for many covariates in our models, but relied only on baseline measures. Our study was observational and residual confounding by unmeasured factors is an inherent limitation.

In conclusion, both self-reported short sleep (<5 hours) and long sleep (≥10 hours), poor sleep quality, greater sleep disturbances, and insomnia were each associated with recurrent falls, independent of traditional risk factors. Modest but
### Table 3. Association of Hours of Sleep, Sleep Quality, and Sleep Disturbance With Risk of Fracture

| Fracture site  | Events n (%) | Crude (n = 157,306) HR (95% CI) | Multivariable modelc (n = 141,079) HR (95% CI) | Multivariable modelc (5-year follow-up) (n = 141,079) HR (95% CI) |
|----------------|--------------|----------------------------------|-----------------------------------------------|-------------------------------------------------|
| **Total fracture** | | | | |
| How many hours of sleep | | | | |
| 5 or less hours | 4,052 (2.8) | 1.11 (1.07–1.15) | 1.10 (1.06–1.14) | 1.12 (1.05–1.20) |
| 6 hours | 13,904 (2.7) | 1.04 (1.02–1.07) | 1.05 (1.02–1.07) | 1.07 (1.03–1.12) |
| 7 hours | 19,306 (2.6) | 1 (Ref) | 1 (Ref) | 1 (Ref) |
| 8 hours | 11,149 (2.6) | 0.98 (0.96–1.00) | 0.95 (0.93–0.97) | 0.96 (0.91–1.00) |
| 9 hours | 1,975 (2.8) | 1.06 (1.01–1.11) | 0.95 (0.90–0.99) | 0.94 (0.86–1.03) |
| 10 or more hours | 215 (2.5) | 1.01 (0.88–1.16) | 0.96 (0.83–1.11) | 0.99 (0.77–1.26) |
| Overall sleep quality | | | | |
| Very restless | 1,145 (2.9) | 1.09 (1.03–1.16) | 0.99 (0.93–1.06) | 1.04 (0.93–1.17) |
| Restless | 7,593 (2.9) | 1.10 (1.07–1.13) | 1.04 (1.01–1.07) | 1.09 (1.04–1.15) |
| Average quality | 21,362 (2.7) | 1 (Ref) | 1 (Ref) | 1 (Ref) |
| Sound or restful | 14,338 (2.6) | 0.94 (0.92–0.96) | 0.98 (0.96–1.01) | 1.03 (0.99–1.08) |
| Very sound or restful | 6,163 (2.5) | 0.89 (0.87–0.92) | 0.97 (0.94–1.00) | 1.02 (0.96–1.08) |
| Insomnia scale | | | | |
| No | 34,156 (2.6) | 1 (Ref) | 1 (Ref) | 1 (Ref) |
| Yes (sleep disturbance ≥9) | 16,445 (2.9) | 1.15 (1.13–1.17) | 1.03 (1.01–1.06) | 1.00 (0.96–1.04) |
| **Hip fracture** | | | | |
| How many hours of sleep | | | | |
| 5 or less hours | 439 (0.26) | 1.08 (0.97–1.19) | 1.01 (0.91–1.14) | 0.82 (0.61–1.09) |
| 6 hours | 1,506 (0.25) | 1.00 (0.94–1.07) | 1.00 (0.93–1.07) | 0.94 (0.79–1.13) |
| 7 hours | 2,177 (0.26) | 1 (Ref) | 1 (Ref) | 1 (Ref) |
| 8 hours | 1,287 (0.26) | 1.01 (0.94–1.08) | 0.93 (0.87–1.00) | 0.88 (0.72–1.06) |
| 9 hours | 234 (0.28) | 1.12 (0.98–1.28) | 0.93 (0.81–1.07) | 1.07 (0.77–1.50) |
| 10 or more hours | 27 (0.28) | 1.19 (0.81–1.74) | 1.06 (0.71–1.59) | 1.46 (0.69–3.11) |
| Overall sleep quality | | | | |
| Very restless | 109 (0.23) | 0.90 (0.74–1.08) | 0.96 (0.78–1.18) | 0.90 (0.52–1.55) |
| Restless | 794 (0.26) | 0.97 (0.90–1.05) | 0.98 (0.90–1.06) | 1.01 (0.81–1.27) |
| Average quality | 2,478 (0.27) | 1 (Ref) | 1 (Ref) | 1 (Ref) |
| Sound or restful | 1,652 (0.25) | 0.93 (0.88–0.99) | 1.01 (0.94–1.08) | 1.29 (1.08–1.53) |
| Very sound or restful | 637 (0.22) | 0.80 (0.73–0.87) | 0.96 (0.87–1.05) | 1.41 (1.12–1.77) |
| Sleep disturbance level | | | | |
| 0–3 | 1,396 (0.23) | 1 (Ref) | 1 (Ref) | 1 (Ref) |
| 4–6 | 1,502 (0.25) | 1.10 (1.02–1.18) | 0.97 (0.89–1.04) | 0.90 (0.74–1.10) |
| 7–10 | 1,574 (0.28) | 1.25 (1.16–1.34) | 1.00 (0.92–1.08) | 0.88 (0.72–1.07) |
| ≥11 | 1,198 (0.28) | 1.30 (1.20–1.41) | 0.98 (0.90–1.07) | 0.79 (0.63–0.98) |
| Insomnia scale | | | | |
| No | 3,777 (0.24) | 1 (Ref) | 1 (Ref) | 1 (Ref) |
| Yes (sleep disturbance ≥9) | 1,893 (0.28) | 1.19 (1.12–1.25) | 1.00 (0.94–1.06) | 0.87 (0.74–1.02) |
| **Upper limb fracture** | | | | |
| How many hours of sleep | | | | |
| 5 or less hours | 1,580 (0.98) | 1.10 (1.04–1.16) | 1.10 (1.04–1.17) | 1.11 (1.00–1.23) |
| 6 hours | 5,383 (0.94) | 1.04 (1.01–1.08) | 1.05 (1.01–1.09) | 1.06 (0.99–1.14) |
| 7 hours | 7,428 (0.92) | 1 (Ref) | 1 (Ref) | 1 (Ref) |
| 8 hours | 4,235 (0.89) | 0.97 (0.93–1.01) | 0.94 (0.91–0.98) | 0.95 (0.88–1.03) |
| 9 hours | 780 (0.98) | 1.09 (1.01–1.17) | 1.00 (0.93–1.08) | 0.99 (0.85–1.15) |
| 10 or more hours | 80 (0.86) | 0.98 (0.79–1.22) | 0.97 (0.76–1.22) | 0.93 (0.61–1.41) |
| Overall sleep quality | | | | |
| Very restless | 434 (0.98) | 1.05 (0.96–1.16) | 0.97 (0.87–1.08) | 1.00 (0.83–1.22) |
| Restless | 2,912 (1.0) | 1.07 (1.02–1.11) | 1.02 (0.97–1.06) | 1.10 (1.01–1.19) | continued
| Fracture site<sup>a</sup> | Events n (%)<sup>b</sup> | Crude (n = 157,306) | Multivariable model<sup>c</sup> (n = 141,079) | Multivariable model<sup>d</sup> (5-year follow-up) (n = 141,079) |
|---------------------------|--------------------------|---------------------|---------------------------------|---------------------------------|
|                           |                           | HR (95% CI)         | HR (95% CI)                     | HR (95% CI)                     |
| **Central fracture**      |                           |                     |                                 |                                 |
| How many hours of sleep   |                           |                     |                                 |                                 |
| 5 or less hours           | 1,632 (1.0)               | 1.16 (1.10–1.22)    | 1.13 (1.07–1.20)                | 1.16 (1.05–1.29)                |
| 6 hours                   | 5,421 (0.95)              | 1.06 (1.03–1.10)    | 1.06 (1.02–1.10)                | 1.10 (1.02–1.17)                |
| 7 hours                   | 7,332 (0.90)              | 1.00 (Ref)          | 1.00 (Ref)                      | 1.00 (Ref)                      |
| 8 hours                   | 4,223 (0.89)              | 0.98 (0.94–1.02)    | 0.96 (0.93–1.00)                | 1.00 (0.93–1.07)                |
| 9 hours                   | 737 (0.93)                | 1.03 (0.96–1.12)    | 0.96 (0.88–1.04)                | 0.93 (0.80–1.08)                |
| 10 or more hours          | 88 (0.95)                 | 1.10 (0.88–1.35)    | 1.01 (0.80–1.26)                | 0.88 (0.58–1.33)                |
| **Overall sleep quality** |                           |                     |                                 |                                 |
| Very restless             | 465 (1.1)                 | 1.16 (1.06–1.28)    | 1.01 (0.91–1.12)                | 1.04 (0.87–1.25)                |
| Restless                  | 3,032 (1.1)               | 1.14 (1.10–1.19)    | 1.07 (1.02–1.12)                | 1.06 (0.98–1.15)                |
| Average quality           | 8,086 (0.92)              | 1.12 (1.09–1.15)    | 1.00 (Ref)                      | 1.00 (Ref)                      |
| Sound or restless         | 5,474 (0.88)              | 0.95 (0.92–0.99)    | 1.00 (0.96–1.04)                | 1.01 (0.95–1.08)                |
| Very sound or restless    | 2,376 (0.86)              | 0.92 (0.88–0.97)    | 0.99 (0.94–1.04)                | 1.05 (0.96–1.15)                |
| **Sleep disturbance level**|                           |                     |                                 |                                 |
| 0–3                       | 5,004 (0.85)              | 1.13 (1.07–1.20)    | 1.01 (0.97–1.06)                | 1.00 (0.93–1.08)                |
| 4–6                       | 5,202 (0.90)              | 1.06 (1.02–1.10)    | 1.01 (0.97–1.06)                | 1.00 (0.93–1.08)                |
| 7–10                      | 5,143 (0.96)              | 1.13 (1.09–1.18)    | 1.03 (0.99–1.08)                | 0.99 (0.92–1.07)                |
| 11                        | 4,084 (1.0)               | 1.22 (1.18–1.28)    | 1.07 (1.02–1.12)                | 1.03 (0.94–1.12)                |
| **Insomnia scale**        |                           |                     |                                 |                                 |
| No                        | 13,105 (0.89)             | 1.11 (1.09–1.17)    | 1.04 (1.00–1.07)                | 0.99 (0.93–1.05)                |
| Yes (sleep disturbance ≥9)| 6,328 (1.00)              | 1.13 (1.10–1.17)    | 1.04 (1.00–1.07)                | 0.99 (0.93–1.05)                |
| **Central fracture**      |                           |                     |                                 |                                 |
| How many hours of sleep   |                           |                     |                                 |                                 |
| 5 or less hours           | 1,234 (0.75)              | 1.16 (1.09–1.24)    | 1.13 (1.05–1.20)                | 0.94 (0.80–1.10)                |
| 6 hours                   | 4,100 (0.70)              | 1.05 (1.01–1.09)    | 1.05 (1.01–1.10)                | 1.02 (0.92–1.13)                |
| 7 hours                   | 5,683 (0.68)              | 1.13 (1.10–1.19)    | 1.03 (0.99–1.08)                | 0.92 (0.83–1.03)                |
| 8 hours                   | 3,424 (0.70)              | 1.10 (1.01–1.20)    | 0.94 (0.86–1.03)                | 0.95 (0.77–1.17)                |
| 9 hours                   | 601 (0.73)                | 1.08 (0.91–1.46)    | 1.08 (0.84–1.38)                | 1.04 (0.61–1.77)                |
| 10 or more hours          | 69 (0.72)                 | 1.11 (0.99–1.23)    | 1.10 (0.98–1.24)                | 0.94 (0.70–1.25)                |
| **Overall sleep quality** |                           |                     |                                 |                                 |
| Very restless             | 352 (0.78)                | 1.11 (0.99–1.23)    | 1.10 (0.98–1.24)                | 0.94 (0.70–1.25)                |
| Restless                  | 2,289 (0.77)              | 1.07 (1.02–1.12)    | 1.03 (0.98–1.08)                | 1.11 (0.98–1.25)                |
| Average quality           | 6,510 (0.72)              | 1.12 (1.09–1.15)    | 1.03 (0.99–1.08)                | 1.11 (0.98–1.25)                |
| Sound or restless         | 4,246 (0.67)              | 0.91 (0.87–0.94)    | 0.97 (0.93–1.01)                | 1.11 (1.01–1.23)                |
| Very sound or restless    | 1,714 (0.60)              | 0.81 (0.77–0.86)    | 0.94 (0.89–1.00)                | 1.08 (0.94–1.25)                |
| **Sleep disturbance level**|                           |                     |                                 |                                 |
| 0–3                       | 3,565 (0.59)              | 1.16 (1.09–1.20)    | 1.13 (1.05–1.20)                | 0.94 (0.80–1.10)                |
| 4–6                       | 4,070 (0.68)              | 1.17 (1.12–1.23)    | 1.05 (1.00–1.10)                | 0.99 (0.88–1.11)                |
| 7–10                      | 4,141 (0.75)              | 1.29 (1.24–1.35)    | 1.05 (1.00–1.11)                | 0.95 (0.84–1.07)                |
| 11                        | 3,335 (0.81)              | 1.44 (1.37–1.51)    | 1.11 (1.05–1.17)                | 0.99 (0.88–1.13)                |
| **Insomnia scale**        |                           |                     |                                 |                                 |
| No                        | 9,944 (0.65)              | 1.10 (1.09–1.12)    | 1.05 (1.01–1.09)                | 1.00 (0.91–1.09)                |
| Yes (sleep disturbance ≥9)| 5,167 (0.79)              | 1.24 (1.20–1.28)    | 1.05 (1.01–1.09)                | 1.00 (0.91–1.09)                |

Fractures are through end of extension 2 (September 30, 2015). Note: Missing data for history of fracture after age 55 and parental history of broken hip has been recoded as “unknown” and included in the analysis to preserve sample size.
4. Hall MH, Smagula SF, Boudreau RM, et al. Association between sleep duration and mortality is mediated by markers of inflammation and health in older adults: the Health, Aging and Body Composition Study. Sleep. 2015;38(2):189–95.

5. Gottlieb DJ, Punjabi NM, Newman AB, et al. Association of sleep time with diabetes mellitus and impaired glucose tolerance. Arch Intern Med. 2005;165(8):863–7.

6. Shahar E, Whitney CW, Redline S, et al. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med. 2001;163(1):19–25.

7. Christensen AS, Clark A, Salo P, et al. Symptoms of sleep disordered breathing and risk of cancer: a prospective cohort study. Sleep. 2013;36(10):1429–35.

8. Blackwell T, Yaffe K, Laffan A, et al. Associations between sleep-disordered breathing, nocturnal hypoxemia, and subsequent cognitive decline in older community-dwelling men: the Osteoporotic Fractures in Men Sleep Study. J Am Geriatr Soc. 2015;63(3):453–61.

9. St George RJ, Delbaere K, Williams P, Lord SR. Sleep quality and falls in older people living in self- and assisted-care villages. Gerontology. 2009;55(2):162–8.

10. Stone KL, Ewing SK, Lui LY, et al. Self-reported sleep and nap habits and risk of falls and fractures in older women: the study of osteoporotic fractures. J Am Geriatr Soc. 2006;54(8):1177–83.

11. Stone KL, Ancoli-Israel S, Blackwell T, et al. Actigraphy-measured sleep characteristics and risk of falls in older women. Arch Intern Med. 2008;168(16):1768–75.

12. Stone KL, Blackwell TL, Ancoli-Israel S, et al. Sleep disturbances and risk of falls in older community-dwelling men: the outcomes of Sleep Disorders in Older Men (MrOS Sleep) study. J Am Geriatr Soc. 2014;62(2):299–305.

13. Cunningham TD, Dj Pace BS. Is self-reported sleep duration associated with osteoporosis? Data from a 4-year aggregated analysis from the National Health and Nutrition Examination Survey. J Am Geriatr Soc. 2015;63(7):1401–6.

14. Kanis J, Johnell O, Gullberg B, et al. Risk factors for hip fracture in men from southern Europe: the MEDOS study. Mediterranean Osteoporosis Study. Osteoporos Int. 1999;9(1):45–54.

15. Cauley JA, Blackwell TL, Redline S, et al. Hypoxia during sleep and the risk of falls and fractures in older men: the Osteoporotic Fractures in Men Sleep Study. J Am Geriatr Soc. 2014;62(10):1853–9.

16. Holmberg AH, Johnell O, Nilsson PM, Nilsson JA, Berglund G, Akesson K. Risk factors for hip fractures in a middle-aged population: a study of 33,000 men and women. Osteoporos Int. 2005;16(12):2185–94.

17. Holmberg AH, Johnell O, Nilsson PM, Nilsson J, Berglund G, Akesson K. Risk factors for fragility fracture in middle age. A prospective population-based study of 33,000 men and women. Osteoporos Int. 2006;17(11):1065–77.

18. Swanson CM, Shea SA, Stone KL, et al. Obstructive sleep apnea and metabolic bone disease: insights into the relationship between bone and sleep. J Bone Miner Res. 2015;30(2):199–211.

19. Tchalla AE, Wellenius GA, Travison TG, et al. Circulating vascular cell adhesion molecule-1 is associated with cerebral blood flow dysregulation, mobility impairment, and falls in older adults. Hypertension. 2015;66(2):340–6.

20. Barbour KE, Lui LY, McCulloch CE, et al. Trajectories of lower extremity physical performance: effects on fractures and mortality.
in older women. J Gerontol A Biol Sci Med Sci. 2016;71(12):1609–15.

21. Harvey NC, Oden A, Orwoll E, et al. Falls predict fractures independently of FRAX probability: a meta-analysis of the Osteoporotic Fractures in Men (MrOS) Study. J Bone Miner Res. 2018;33(3):510–6.

22. Sibley KM, Voth J, Munce SE, Straus SE, Jaglal SB. Chronic disease and falls in community-dwelling Canadians over 65 years old: a population-based study exploring associations with number and pattern of chronic conditions. BMC Geriatr. 2014;14:22.

23. Design of the Women's Health Initiative clinical trial and observational study. The Women's Health Initiative Study Group. Control Clin Trials. 1998;19(1):61–109.

24. Langer RD, White E, Lewis CE, Kotchen JM, Hendrix SL, Trevisan M. The Women's Health Initiative Observational Study: baseline characteristics of participants and reliability of baseline measures. Ann Epidemiol. 2003;13(9 Suppl): S107–21.

25. Cauley JA, Wampler NS, Barnhart JM, et al. Incidence of fractures compared to cardiovascular disease and breast cancer: the Women's Health Initiative Observational Study. Osteoporos Int. 2008;19(12):1717–23.

26. Anderson GL, Manson J, Wallace R, et al. Implementation of the Women's Health Initiative study design. Ann Epidemiol. 2003;13(9 Suppl): S5–17.

27. Levine DW, Kripke DF, Kaplan RM, et al. Reliability and validity of the Women's Health Initiative Insomnia Rating Scale. Psychol Assess. 2003;15(2):137–48.

28. Levine DW, Kaplan RM, Kripke DF, Bowen DJ, Naughton MJ, Shumaker SA. Factor structure and measurement invariance of the Women's Health Initiative Insomnia Rating Scale. Psychol Assess. 2003;15(2):123–36.

29. Cauley JA, Smagula SF, Hovey KM, et al. Optimism, cynical hostility, falls, and fractures: the Women's Health Initiative Observational Study (WHI-OS). J Bone Miner Res. 2017;32(2):221–9.

30. Chen Z, Kooperberg C, Pettinger MB, et al. Validity of self-report for fractures among a multiethnic cohort of postmenopausal women: results from the Women's Health Initiative observational study and clinical trials. Menopause. 2004;11(3):264–74.

31. Patterson RE, Kristal AR, Tinker LF, Carter RA, Bolton MP, Agurs-Collins T. Measurement characteristics of the Women's Health Initiative food frequency questionnaire. Ann Epidemiol. 1999;9(3):178–87.

32. Manson JE, Greenland P, LaCroix AZ, et al. Walking compared with vigorous exercise for the prevention of cardiovascular events in women. N Engl J Med. 2002;347(10):716–25.

33. Tuunainen A, Langer RD, Klauber MR, Kripke DF. Short version of the CES-D (Burnam screen) for depression in reference to the structured psychiatric interview. Psychiatry Res. 2001;103(2–3):261–70.

34. Hays RD, Sherbourne CD, Mazel RM. The RAND 36-Item Health Survey 1.0. Health Econ. 1993;2(3):217–27.

35. Lauderdale DS, Chen JH, Kurina LM, Waite LJ, Thisted RA. Sleep duration and health among older adults: associations vary by how sleep is measured. J Epidemiol Community Health. 2016;70(4):361–6.