

# Characteristics of Sleep and the Risk of Falls and Fractures: The Women's Health Initiative (WHI)

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# Background

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- Sleep disturbances are common: 36-69%
- Sleep disturbances linked with
  - Reduced QOL
  - Physical impairment
  - Depression
  - Diabetes
  - CVD
  - Cancer
  - Cognitive decline
  - Death
- What about falls and fractures?

# Hypotheses

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Women with:

- Short or long sleep
- Poor sleep quality
- Greater sleep disturbance
- Insomnia

↑ Risk of Recurrent Falls and Fractures

# **Biological Plausibility: Sleep, Fracture & Falls**

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- **Diurnal rhythm of bone turnover: Poor sleep may interrupt these patterns and influence bone metabolism**
- **Direct effects of sleep**
  - Hypoxemia
  - Inflammation
  - Alterations in melatonin
  - Vitamin D deficiency
  - Insulin resistance
  - Hypogonadism
- **Indirect effects of sleep**
  - Physical function impairment
  - Depression
  - Comorbidity
  - Obesity
  - Cognitive impairments

# Study Population

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- 93,767, WHI OS
- 68,132, WHI CT
- Exclusions
  - 878 participants - no follow-up data
  - 948 participants - no fall data
  - 605 participants - no sleep date
- Final sample, N=157,306

# Assessment of Sleep

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- Sleep duration:  $\leq 5, 6, 7, 8, 9, \geq 10$ 
  - Referent: 7 hours
- Insomnia: WHI Validated Insomnia Rating Scale (WHIIRS)
  - Trouble falling a sleep
  - Woke up several times
  - Woke up too early
  - Trouble getting back to sleep after awakening
  - Overall sleep quality (very sound to very restless)
- WHIIRS: Scores (0-20);  $>9$ : “insomnia”
  - Also analyzed, quartiles 0-3, 4-6, 7-10,  $\geq 11$

# Outcomes

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- Recurrent falls
  - Annual reporting of falling  $\geq 2$  in past years, “ One event”
  - Average follow-up: 7.6 years
- Incident fractures
  - Total (except fingers, toes, ribs, coccyx, face, skull & sternum)
  - Upper limb fractures
  - Lower limb fractures
  - Hip fractures
  - Central body (hip, pelvis, spine)
- Fracture follow-up: 12 years

# Statistical Analysis

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- Falls: recurrent falls ( $\geq 2$  in past year)
  - GEE for repeated logistic regression models
- Fractures: Cox Proportional Hazards Regression
- Model 1: age, weight, height, treated diabetes, ethnicity/race, region, smoking, health status, height, total vitamin D intake, physical activity, alcohol, depressive symptom score, caffeine intake, height trial arm, DM trial arm.
- Model 2: Model 1 + medication (hypnotics, sleep, antianxiety, antidepressant, analgesic narcotics).
- Model 3: Model 2 + physical function.



# Baseline Characteristics by Sleep Duration

Characteristic	≤5	6	7	8	9	≥10
Age (y)	63.2	63.1	63.0	63.5	64.0	63.2
Non-White (%)	33.2	2.15	13.2	11.1	12.6	34.4
High School or less (%)	29.6	23.4	20.5	21.2	22.9	32.7
Physical Activity (≥12 MET hrs/week) (%)	32.5	37.8	41.1	41.5	37.8	30.8
Depressive Symptoms (%) (≥0.06)	25.0	13.4	8.2	7.2	10.6	23.9
Fair/Poor Health Status (%)	19.8	9.9	6.7	6.8	10.3	25.3
Diabetes (%)	7.4	4.7	307	3.7	4.9	7.0
Current HT (%)	33.0	38.8	42.3	42.0	40.2	34.9

## **Overall Sleep Quality and Recurrent Falls: Annualized % Events and OR (95% CI)**

<b>Sleep Quality</b>	<b>Ann %</b>	<b>Model 1</b>	<b>Model 2 (+ meds)</b>	<b>Model 3 (+ PF)</b>
<b>Very restless</b>	<b>13.0</b>	<b>1.31 (1.22, 1.40)</b>	<b>1.29 (1.20, 1.38)</b>	<b>1.22 (1.14, 1.31)</b>
<b>Restless</b>	<b>19.3</b>	<b>1.14 (1.10, 1.18)</b>	<b>1.13 (1.10, 1.17)</b>	<b>1.11 (1.07, 1.15)</b>
<b>Average quality</b>	<b>8.1</b>	<b>1 (ref)</b>	<b>1 (ref)</b>	<b>1 (ref)</b>
<b>Sound or restful</b>	<b>6.9</b>	<b>0.95 (0.92, 0.97)</b>	<b>0.95 (0.93, 0.98)</b>	<b>0.96 (0.94, 0.99)</b>
<b>Very Sound or restful</b>	<b>6.2</b>	<b>0.90 (0.86, 0.94)</b>	<b>0.90 (0.87, 0.94)</b>	<b>0.92 (0.88, 0.86)</b>
<b>P linear</b>		<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>

# Baseline Characteristics by Sleep Duration

Medications (%)	≤5	6	7	8	9	≥10
Anti-depressants	7.0	6.2	6.3	8.1	13.8	21.2
Anti-anxiety	4.6	3.4	2.8	2.9	3.9	4.2
Hypnotics/ sleep	4.4	3.3	2.4	2.2	2.4	2.7
Analgesics narcotics	3.9	2.0	1.6	1.7	2.5	4.1

# Baseline Characteristics by Sleep Duration

Sleep Variable (%)	≤5	6	7	8	9	≥10
Disturbance construct	11.3	7.8	5.9	5.1	5.0	6.0
Disturbance level (≥11)	59.0	28.8	12.7	7.7	7.2	14.9
Insomnia (≥9)	69.5	42.3	24.4	16.2	15.3	25.7

# ***Association of Sleep Duration and Recurrent Falls: Annualized Percent and OR (95% CI)***

<b>Sleep Duration</b>	<b>Ann %</b>	<b>Model 1</b>	<b>Model 2 (+ meds)</b>	<b>Model 3 (+ PF)</b>
<b>≤5</b>	<b>10.6</b>	<b>1.31 (1.26, 1.37)</b>	<b>1.32 (1.27, 1.38)</b>	<b>1.28 (1.23, 1.34)</b>
<b>6</b>	<b>8.4</b>	<b>1.13 (1.10, 1.16)</b>	<b>1.14 (1.11, 1.17)</b>	<b>1.13 (1.10, 1.16)</b>
<b>7</b>	<b>7.3</b>	<b>1 (ref)</b>	<b>1 (ref)</b>	<b>1 (ref)</b>
<b>8</b>	<b>7.1</b>	<b>0.95 (0.92, 0.98)</b>	<b>0.93 (0.90, 0.96)</b>	<b>0.92 (0.90, 0.95)</b>
<b>9</b>	<b>8.6</b>	<b>1.09 (1.03, 1.15)</b>	<b>1.02 (0.96, 0.81)</b>	<b>0.99 (0.94, 1.05)</b>
<b>≥10</b>	<b>11.8</b>	<b>1.47 (1.28, 1.68)</b>	<b>1.30 (1.13, 1.49)</b>	<b>1.25 (1.09, 1.43)</b>
<b>Quadratic p-values</b>		<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>

# ***Sleep Disturbance Level and Recurrent Falls: Annualized % Events and OR (95% CI)***

<b>Sleep Disturbance Level</b>	<b>Ann %</b>	<b>Model 1</b>	<b>Model 2 (+ meds)</b>	<b>Model 3 (+ PF)</b>
<b>0-3</b>	<b>5.9</b>	<b>1 (ref)</b>	<b>1 (ref)</b>	<b>1 (ref)</b>
<b>4-6</b>	<b>7.4</b>	<b>1.17 (1.13, 1.21)</b>	<b>1.17 (1.13, 1.21)</b>	<b>1.15 (1.11, 1.19)</b>
<b>7-10</b>	<b>8.6</b>	<b>1.28 (1.24, 1.33)</b>	<b>1.28 (1.24, 1.32)</b>	<b>1.24 (1.20, 1.28)</b>
<b>≥11</b>	<b>10.5</b>	<b>1.43 (1.38, 1.48)</b>	<b>1.41 (1.36, 1.46)</b>	<b>1.35 (1.30, 1.40)</b>
<b>P linear</b>		<b>&lt;0.001</b>	<b>&lt;0.001</b>	<b>&lt;0.001</b>
<b>Insomnia, yes</b>	<b>10.0</b>	<b>1.23 (1.20, 1.26)</b>	<b>1.22 (1.19, 1.25)</b>	<b>1.19 (1.16, 1.22)</b>

# ***Association of Sleep Duration and All Incident Fractures: Annualized Percent and OR (95% CI)***

<b>Sleep Duration</b>	<b>Ann %</b>	<b>Model 1</b>	<b>Model 2 (+ meds)</b>	<b>Model 3 (+ PF)</b>
<b>≤5</b>	<b>2.8</b>	<b>1.10 (1.06, 1.14)</b>	<b>1.11 (1.07, 1.15)</b>	<b>1.10 (1.06, 1.14)</b>
<b>6</b>	<b>2.7</b>	<b>1.04 (1.02, 1.07)</b>	<b>1.05 (1.02, 1.07)</b>	<b>1.05 (1.02, 1.07)</b>
<b>7</b>	<b>2.6</b>	<b>1 (ref)</b>	<b>1 (ref)</b>	<b>1 (ref)</b>
<b>8</b>	<b>2.6</b>	<b>0.96 (0.93, 0.98)</b>	<b>0.95 (0.93, 0.98)</b>	<b>0.95 (0.93, 0.97)</b>
<b>9</b>	<b>2.8</b>	<b>0.97 (0.92, 1.02)</b>	<b>0.95 (0.91, 1.00)</b>	<b>0.95 (0.90, 0.99)</b>
<b>≥10</b>	<b>2.5</b>	<b>1.01 (0.88, 1.17)</b>	<b>0.98 (0.85, 1.13)</b>	<b>0.97, (0.84, 1.11)</b>

# ***Sleep Disturbance Level and All Incident Fractures: Annualized % Events and OR (95% CI)***

<b>Sleep Disturbance Level</b>	<b>Ann %</b>	<b>Model 1</b>	<b>Model 2 (+ meds)</b>	<b>Model 3 (+ PF)</b>
<b>0-3</b>	<b>2.4</b>	<b>1 (ref)</b>	<b>1 (ref)</b>	<b>1 (ref)</b>
<b>4-6</b>	<b>2.6</b>	<b>1.04 (1.01, 1.07)</b>	<b>1.04 (1.02, 1.07)</b>	<b>1.04 (1.01, 1.06)</b>
<b>7-10</b>	<b>2.8</b>	<b>1.04 (1.02, 1.07)</b>	<b>1.04 (1.02, 1.07)</b>	<b>1.04 (1.01, 1.06)</b>
<b>≥11</b>	<b>3.0</b>	<b>1.09 (1.06, 1.12)</b>	<b>1.09 (1.06, 1.12)</b>	<b>1.08 (1.05, 1.06)</b>



# Results Specific types of Fractures

<b>Hip Fracture</b>	<b>No association with sleep</b>
<b>Upper Limb Fractures</b>	
<b>Sleep Duration</b>	
≤5 hours	HR= 1.11 (1.04, 1.18)
6 hours	HR= 1.05 (1.01, 1.09)
<b>Insomnia</b>	HR= 1.04 (1.01, 1.07)
<b>Lower Limb Fractures</b>	
<b>Sleep Duration</b>	
≤5 hours	HR= 1.14 (1.07, 1.21)
6 hours	HR= 1.06 (1.02, 1.10)
<b>Insomnia</b>	HR= 1.04 (1.01, 1.08)
<b>Central Fractures</b>	
<b>Sleep Duration</b>	
≤5 hours	HR= 1.14 (1.07, 1.22)
6 hours	HR= 1.05 (1.01, 1.10)
<b>Insomnia</b>	HR= 1.07 (1.03, 1.11)

HR all estimated from Model (MV)

# Summary of Sleep and Falls

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- Short sleep, long sleep, poor sleep quality, sleep disturbances and insomnia
  - All associated with a 14-47% increased risk of recurrent falls.
  - Independent of CNS meds and physical function
- Consistent with previous studies
  - SOF: greater napping and long duration (not short) of sleep by self-report: ↑ risk of falls.
  - SOF: short sleep by actigraphy: ↑ risk of falls.
  - Correlation: Self-report + actigraphy,  $r=0.26$ .
- What's new
  - Follow-up over 8 years
  - Repeated measures
  - Younger women

# Summary of Sleep and Fractures

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- Modest associations: 10-14% increased risk of fractures among short sleepers.
- Previous literature: 3 prospective studies
  - MrOS: nocturnal hypoxemia ↑ fractures
  - SOF: napping and long duration (self-reported):  
↑ fractures
  - Malmo: Premature awakening and ↑ hip fracture risk: Men only

# Limitations

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- Self-report of sleep
- Self-report of non-hip fractures
  - 76% fractures confirmed by radiographic report
- Unable to adjust for BMD

**Interventions aimed at  
improving sleep quality may  
reduce Falls.**

# Thank You!

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