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

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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

Women with:

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

↑ Risk of Recurrent Falls and Fractures
Biological Plausibility: Sleep, Fracture & Falls

• Diurnal rhythm of bone turnover: Poor sleep may interrupt these patterns and influence bone metabolism

• Direct effects of sleep
  – Hypoxemia
  – Inflammation
  – Alterations in melatonic
  – Vitamin D deficiency
  – Insulin resistance
  – Hypogonadism

• Indirect effects of sleep
  – Physical function impairment
  – Depression
  – Comorbidity
  – Obesity
  – Cognitive impairments
Study Population

- 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

• 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

• Recurrent falls
  – Annual reporting of falling ≥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

- Falls: recurrent falls (≥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

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>≤5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>≥10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td>63.2</td>
<td>63.1</td>
<td>63.0</td>
<td>63.5</td>
<td>64.0</td>
<td>63.2</td>
</tr>
<tr>
<td>Non-White (%)</td>
<td>33.2</td>
<td>2.15</td>
<td>13.2</td>
<td>11.1</td>
<td>12.6</td>
<td>34.4</td>
</tr>
<tr>
<td>High School or less (%)</td>
<td>29.6</td>
<td>23.4</td>
<td>20.5</td>
<td>21.2</td>
<td>22.9</td>
<td>32.7</td>
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<tr>
<td>Physical Activity</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>(≥12 MET hrs/week) (%)</td>
<td>32.5</td>
<td>37.8</td>
<td>41.1</td>
<td>41.5</td>
<td>37.8</td>
<td>30.8</td>
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<tr>
<td>Depressive Symptoms (%)</td>
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<tr>
<td>(≥0.06)</td>
<td>25.0</td>
<td>13.4</td>
<td>8.2</td>
<td>7.2</td>
<td>10.6</td>
<td>23.9</td>
</tr>
<tr>
<td>Fair/Poor Health Status (%)</td>
<td>19.8</td>
<td>9.9</td>
<td>6.7</td>
<td>6.8</td>
<td>10.3</td>
<td>25.3</td>
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<tr>
<td>Diabetes (%)</td>
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<tr>
<td></td>
<td>7.4</td>
<td>4.7</td>
<td>307</td>
<td>3.7</td>
<td>4.9</td>
<td>7.0</td>
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<tr>
<td>Current HT (%)</td>
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<tr>
<td></td>
<td>33.0</td>
<td>38.8</td>
<td>42.3</td>
<td>42.0</td>
<td>40.2</td>
<td>34.9</td>
</tr>
<tr>
<td>Sleep Quality</td>
<td>Ann %</td>
<td>Model 1</td>
<td>Model 2 (+ meds)</td>
<td>Model 3 (+ PF)</td>
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<tr>
<td>Very restless</td>
<td>13.0</td>
<td>1.31 (1.22, 1.40)</td>
<td>1.29 (1.20, 1.38)</td>
<td>1.22 (1.14, 1.31)</td>
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<tr>
<td>Restless</td>
<td>19.3</td>
<td>1.14 (1.10, 1.18)</td>
<td>1.13 (1.10, 1.17)</td>
<td>1.11 (1.07, 1.15)</td>
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<tr>
<td>Average quality</td>
<td>8.1</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sound or restful</td>
<td>6.9</td>
<td>0.95 (0.92, 0.97)</td>
<td>0.95 (0.93, 0.98)</td>
<td>0.96 (0.94, 0.99)</td>
<td></td>
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<tr>
<td>Very Sound or restful</td>
<td>6.2</td>
<td>0.90 (0.86, 0.94)</td>
<td>0.90 (0.87, 0.94)</td>
<td>0.92 (0.88, 0.86)</td>
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P linear: <0.001 <0.001 <0.001
## Baseline Characteristics by Sleep Duration

<table>
<thead>
<tr>
<th>Medications (%)</th>
<th>≤5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>≥10</th>
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</thead>
<tbody>
<tr>
<td>Anti-depressants</td>
<td>7.0</td>
<td>6.2</td>
<td>6.3</td>
<td>8.1</td>
<td>13.8</td>
<td>21.2</td>
</tr>
<tr>
<td>Anti-anxiety</td>
<td>4.6</td>
<td>3.4</td>
<td>2.8</td>
<td>2.9</td>
<td>3.9</td>
<td>4.2</td>
</tr>
<tr>
<td>Hypnotics/sleep</td>
<td>4.4</td>
<td>3.3</td>
<td>2.4</td>
<td>2.2</td>
<td>2.4</td>
<td>2.7</td>
</tr>
<tr>
<td>Analgesics/narcotics</td>
<td>3.9</td>
<td>2.0</td>
<td>1.6</td>
<td>1.7</td>
<td>2.5</td>
<td>4.1</td>
</tr>
<tr>
<td>Sleep Variable (%)</td>
<td>≤5</td>
<td>6</td>
<td>7</td>
<td>8</td>
<td>9</td>
<td>≥10</td>
</tr>
<tr>
<td>-------------------------</td>
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<td>----</td>
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</tr>
<tr>
<td>Disturbance construct</td>
<td>11.3</td>
<td>7.8</td>
<td>5.9</td>
<td>5.1</td>
<td>5.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Disturbance level (≥11)</td>
<td>59.0</td>
<td>28.8</td>
<td>12.7</td>
<td>7.7</td>
<td>7.2</td>
<td>14.9</td>
</tr>
<tr>
<td>Insomnia (≥9)</td>
<td>69.5</td>
<td>42.3</td>
<td>24.4</td>
<td>16.2</td>
<td>15.3</td>
<td>25.7</td>
</tr>
</tbody>
</table>
# Association of Sleep Duration and Recurrent Falls: Annualized Percent and OR (95% CI)

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

Quadratic p-values: <0.001 <0.001 <0.001
## Sleep Disturbance Level and Recurrent Falls: Annualized % Events and OR (95% CI)

<table>
<thead>
<tr>
<th>Sleep Disturbance Level</th>
<th>Ann %</th>
<th>Model 1</th>
<th>Model 2 (+ meds)</th>
<th>Model 3 (+ PF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>5.9</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
</tr>
<tr>
<td>4-6</td>
<td>7.4</td>
<td>1.17 (1.13, 1.21)</td>
<td>1.17 (1.13, 1.21)</td>
<td>1.15 (1.11, 1.19)</td>
</tr>
<tr>
<td>7-10</td>
<td>8.6</td>
<td>1.28 (1.24, 1.33)</td>
<td>1.28 (1.24, 1.32)</td>
<td>1.24 (1.20, 1.28)</td>
</tr>
<tr>
<td>≥11</td>
<td>10.5</td>
<td>1.43 (1.38, 1.48)</td>
<td>1.41 (1.36, 1.46)</td>
<td>1.35 (1.30, 1.40)</td>
</tr>
<tr>
<td>P linear</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Insomnia, yes</td>
<td>10.0</td>
<td>1.23 (1.20, 1.26)</td>
<td>1.22 (1.19, 1.25)</td>
<td>1.19 (1.16, 1.22)</td>
</tr>
</tbody>
</table>
## Association of Sleep Duration and All Incident Fractures: Annualized Percent and OR (95% CI)

<table>
<thead>
<tr>
<th>Sleep Duration</th>
<th>Ann %</th>
<th>Model 1</th>
<th>Model 2 (+ meds)</th>
<th>Model 3 (+ PF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤5</td>
<td>2.8</td>
<td>1.10 (1.06, 1.14)</td>
<td>1.11 (1.07, 1.15)</td>
<td>1.10 (1.06, 1.14)</td>
</tr>
<tr>
<td>6</td>
<td>2.7</td>
<td>1.04 (1.02, 1.07)</td>
<td>1.05 (1.02, 1.07)</td>
<td>1.05 (1.02, 1.07)</td>
</tr>
<tr>
<td>7</td>
<td>2.6</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
</tr>
<tr>
<td>8</td>
<td>2.6</td>
<td>0.96 (0.93, 0.98)</td>
<td>0.95 (0.93, 0.98)</td>
<td>0.95 (0.93, 0.97)</td>
</tr>
<tr>
<td>9</td>
<td>2.8</td>
<td>0.97 (0.92, 1.02)</td>
<td>0.95 (0.91, 1.00)</td>
<td>0.95 (0.90, 0.99)</td>
</tr>
<tr>
<td>≥10</td>
<td>2.5</td>
<td>1.01 (0.88, 1.17)</td>
<td>0.98 (0.85, 1.13)</td>
<td>0.97 (0.84, 1.11)</td>
</tr>
</tbody>
</table>
# Sleep Disturbance Level and All Incident Fractures: Annualized % Events and OR (95% CI)

<table>
<thead>
<tr>
<th>Sleep Disturbance Level</th>
<th>Ann %</th>
<th>Model 1</th>
<th>Model 2 (+ meds)</th>
<th>Model 3 (+ PF)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-3</td>
<td>2.4</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
<td>1 (ref)</td>
</tr>
<tr>
<td>4-6</td>
<td>2.6</td>
<td>1.04 (1.01, 1.07)</td>
<td>1.04 (1.02, 1.07)</td>
<td>1.04 (1.01, 1.06)</td>
</tr>
<tr>
<td>7-10</td>
<td>2.8</td>
<td>1.04 (1.02, 1.07)</td>
<td>1.04 (1.02, 1.07)</td>
<td>1.04 (1.01, 1.06)</td>
</tr>
<tr>
<td>≥11</td>
<td>3.0</td>
<td>1.09 (1.06, 1.12)</td>
<td>1.09 (1.06, 1.12)</td>
<td>1.08 (1.05, 1.06)</td>
</tr>
</tbody>
</table>
## Results Specific types of Fractures

<table>
<thead>
<tr>
<th>Fracture Type</th>
<th>No association with sleep</th>
<th>Sleep Duration</th>
<th>HR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hip Fracture</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Upper Limb Fractures</strong></td>
<td></td>
<td>≤5 hours</td>
<td>1.11 (1.04, 1.18)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6 hours</td>
<td>1.05 (1.01, 1.09)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insomnia</td>
<td>1.04 (1.01, 1.07)</td>
</tr>
<tr>
<td><strong>Lower Limb Fractures</strong></td>
<td></td>
<td>≤5 hours</td>
<td>1.14 (1.07, 1.21)</td>
</tr>
<tr>
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<td></td>
<td>6 hours</td>
<td>1.06 (1.02, 1.10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insomnia</td>
<td>1.04 (1.01, 1.08)</td>
</tr>
<tr>
<td><strong>Central Fractures</strong></td>
<td></td>
<td>≤5 hours</td>
<td>1.14 (1.07, 1.22)</td>
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<tr>
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<td></td>
<td>6 hours</td>
<td>1.05 (1.01, 1.10)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Insomnia</td>
<td>1.07 (1.03, 1.11)</td>
</tr>
<tr>
<td>HR all estimated from Model (MV)</td>
<td></td>
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<td></td>
</tr>
</tbody>
</table>
Summary of Sleep and Falls

• 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

• 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

• 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!