Long Sleep Duration is Associated with an Increased Risk for Adverse Outcomes in Older Adults

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In the beginning

- Association between sleep duration and mortality first reported > 50 years ago
  - U-shaped duration-mortality association
  - Mortality nadir at 7 hours
  - Increased with short (< 5 hrs) sleep duration
  - Increased with long (≥ 10 hrs) sleep duration

Hammond EC, AJPH 1964
In the beginning

- Large number of prospective epidemiological studies have examined extremes of sleep duration and:
  - Cardiovascular outcomes
  - Metabolic outcomes
  - Cause specific and all cause mortality
The short and long of it

• Focus has been on short sleep duration but…
  – Long sleep duration is more prevalent: 22.7-40.5% vs 0.4-14%
  – Long sleep duration increased in 6 of 10 nations

• Increased percentage of long sleepers in the elderly

Bin YS, AJE 2013; Gangwisch JE 2008
<table>
<thead>
<tr>
<th>Country</th>
<th>Year</th>
<th>No. of Survey Participants</th>
<th>Short Sleep Duration</th>
<th>Long Sleep Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>No.</td>
<td>%</td>
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<tr>
<td>United Kingdom</td>
<td>1983</td>
<td>1,350</td>
<td>202</td>
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<td>1995</td>
<td>1,962</td>
<td>169</td>
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<td>2000</td>
<td>8,688</td>
<td>309</td>
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<td></td>
<td>2005</td>
<td>4,854</td>
<td>490</td>
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<td>United States</td>
<td>1985</td>
<td>2,921</td>
<td>343</td>
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<td>1992</td>
<td>7,514</td>
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<td>1994</td>
<td>1,199</td>
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<td>2003</td>
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<td>2004</td>
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<td>1,121</td>
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<td>2006</td>
<td>12,200</td>
<td>1,152</td>
<td>9.4</td>
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<td>2007</td>
<td>11,606</td>
<td>1,068</td>
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</table>
Demonstrating increased risk: Bradford Hill’s criteria

- Consistency
- Strength of association
- Biological gradient/dose response relationship
- Biological plausibility
- Temporality
- Specificity
- Coherence
- Experimental evidence
Consistency of association

- Millions of subjects worldwide (~30 cohorts)
- Across nations
  - US, UK, Japan, Spain, Sweden, Israel, Finland, Taiwan, China, Brazil
- Middle-aged and older adults
- Men and women
- Adjustment for multiple covariates
- Multiple causes of mortality
  - Cardiovascular
  - Cancer
  - Noncardiovascular, noncancer

Cappuccio FP Sleep 2010; Gallichio Sleep 2009
Strength of association and biological gradient

• Strength of association of long sleep and adverse outcomes:
  – Stroke: 1.40-1.46
  – Cardiovascular: 1.07-1.46
  – Diabetes: 1.29-1.79
  – Mortality: 1.22-1.54

• Biological gradient:
  – > 8 hours: 1.20 (0.91-1.58)
  – ≥ 9 hours: 1.25 (1.20-1.30)
  – ≥ 10 hours: 1.54 (1.39-1.70)

Ge B 2015, Cappuccino 2010; Ayas 2003; Gottlieb 2005, Leng 2015
Biological plausibility for the association

- Sleep fragmentation
- Inflammation (↑ CRP, IL-6, TNF-α)
- Fatigue
- Immune function
- Photoperiodic abnormalities
- Lack of challenge (e.g., lack of physiological challenge)
- Fibrinogen

Grandan 2007; Patel 2009; Hale L 2013
Limitations

- Sleep duration often treated as fixed exposure
- Limited studies adjusting for sleep apnea
- Misclassification: TIB versus time asleep
Change in sleep duration over time

• Heslop:
  – Mortality increased with persistently short duration

• Ferrie:
  – Mortality increased with going to shorter or longer duration

• Hublin:
  – Mortality increased with going to shorter or longer duration

• Leng:
  – Stroke risk increased with persistently long duration or going to long duration
Adjusting for sleep apnea

- Studies adjusting for PSG-determined sleep apnea
  - Gottlieb 2005: Diabetes and impaired glucose tolerance
  - Gottlieb 2006: Hypertension
  - Patel 2009: Inflammatory mediators
- Sleep apnea does not seem to confound the association between sleep duration and adverse outcomes
Addressing limitations

• Dearth of studies combining:
  – Change in sleep duration
  – Adjustment for sleep apnea
  – Mortality
Final thoughts

• **Long sleep duration is associated with an increased risk of adverse outcomes**
  – Convergence of epidemiological evidence
  – Multiple covariates and confounders have been considered