

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 (\geq 10 hrs) sleep duration



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

Country	Year	No. of Survey Participants	Short Sleep Duration		Long Sleep Duration	
			No.	%	No.	%
United Kingdom	1983	1,350	202	15.0	207	15.3
	1995	1,962	169	8.6	618	31.5
	2000	8,688	309	3.6	2,997	34.5
	2005	4,854	490	10.1	1,241	25.6
United States	1985	2,921	343	11.7	768	26.3
	1992	7,514	818	10.9	2,075	27.6
	1994	1,199	176	14.7	265	22.1
	2003	57,114	5,217	9.1	21,952	38.4
	2004	13,318	1,284	9.6	4,769	35.8
	2005	12,419	1,121	9.0	4,631	37.3
	2006	12,200	1,152	9.4	4,644	38.1
	2007	11,606	1,068	9.2	4,355	37.5

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

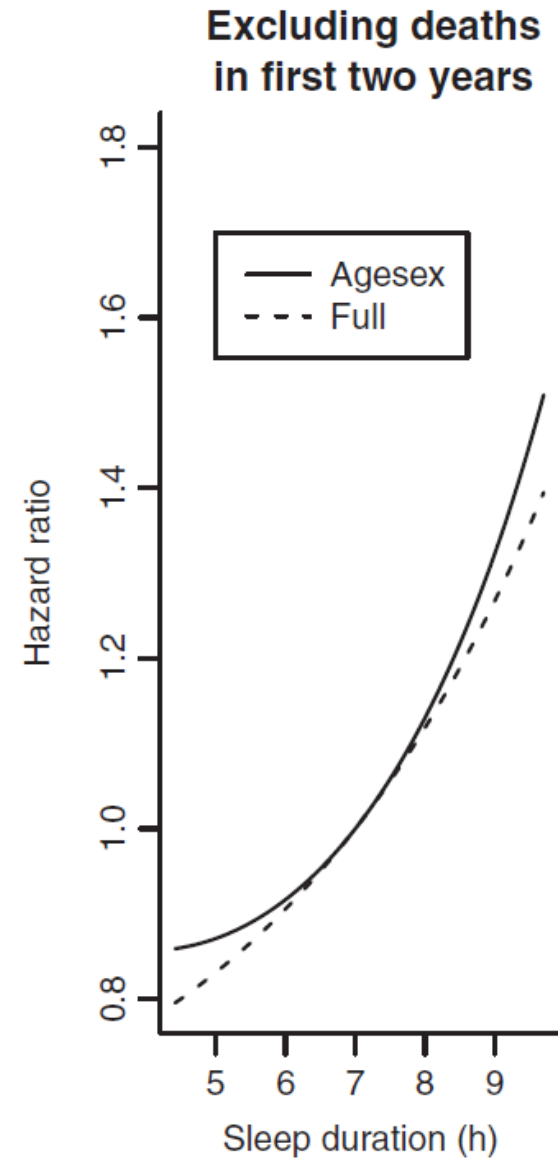
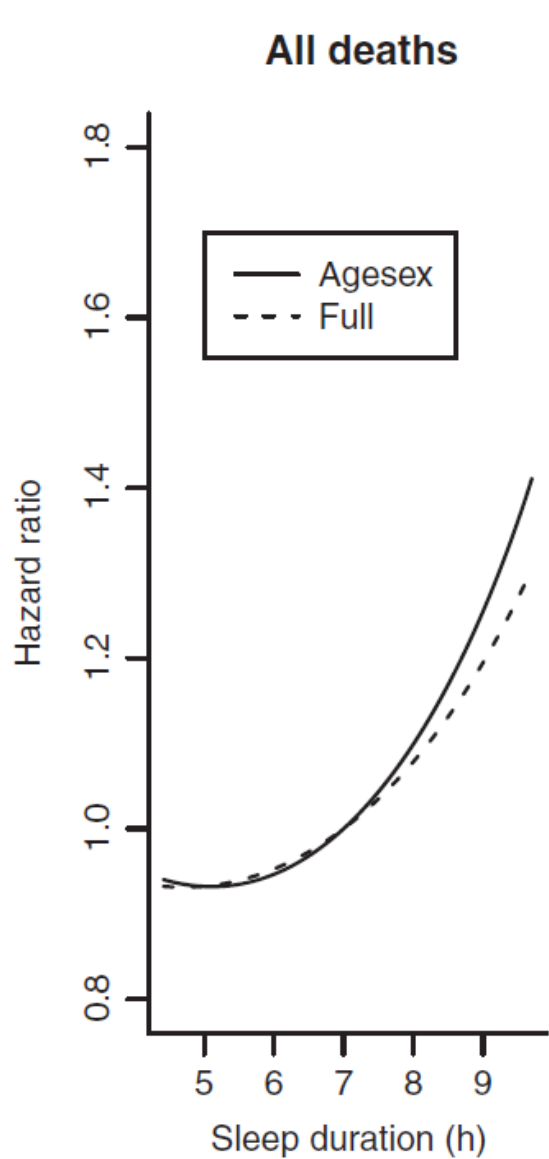
- Millions of subjects worldwide (~ 30 cohorts)
- Across nations
 - US, UK, Japan, Spain, Sweden, Israel, Finland, Taiwan, China, Brazil
- Middle-aged and older adults
- Men and women
- Adjustment for multiple covariates
- Multiple causes of mortality
 - Cardiovascular
 - Cancer
 - Noncardiovascular,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

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

Biological plausibility for the association

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



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

