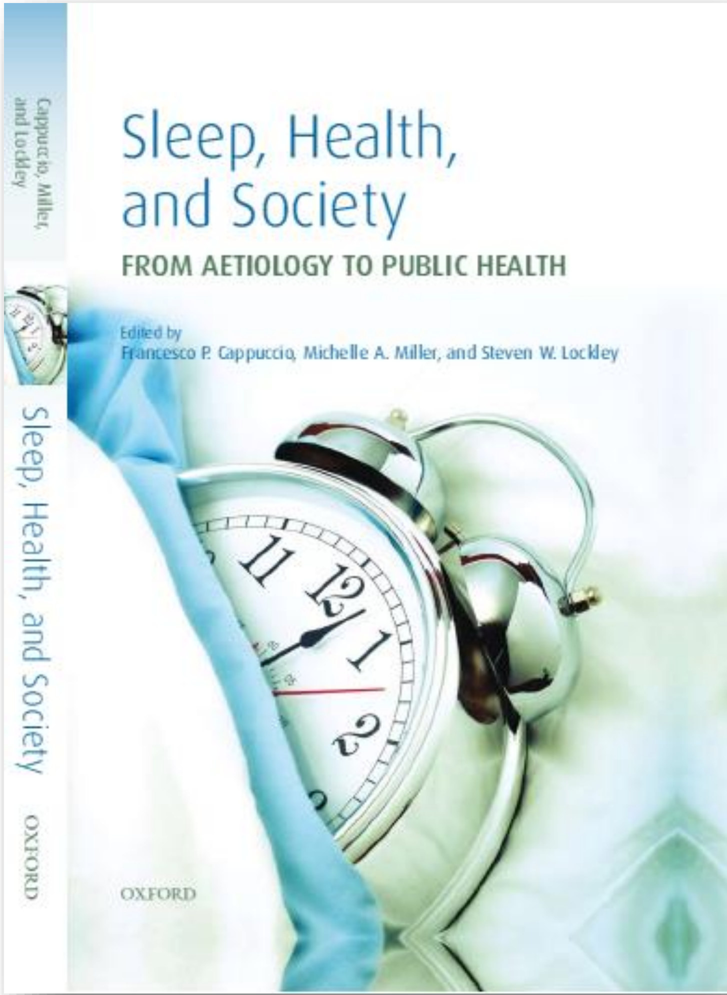
Sleep and Health



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26th October 2015

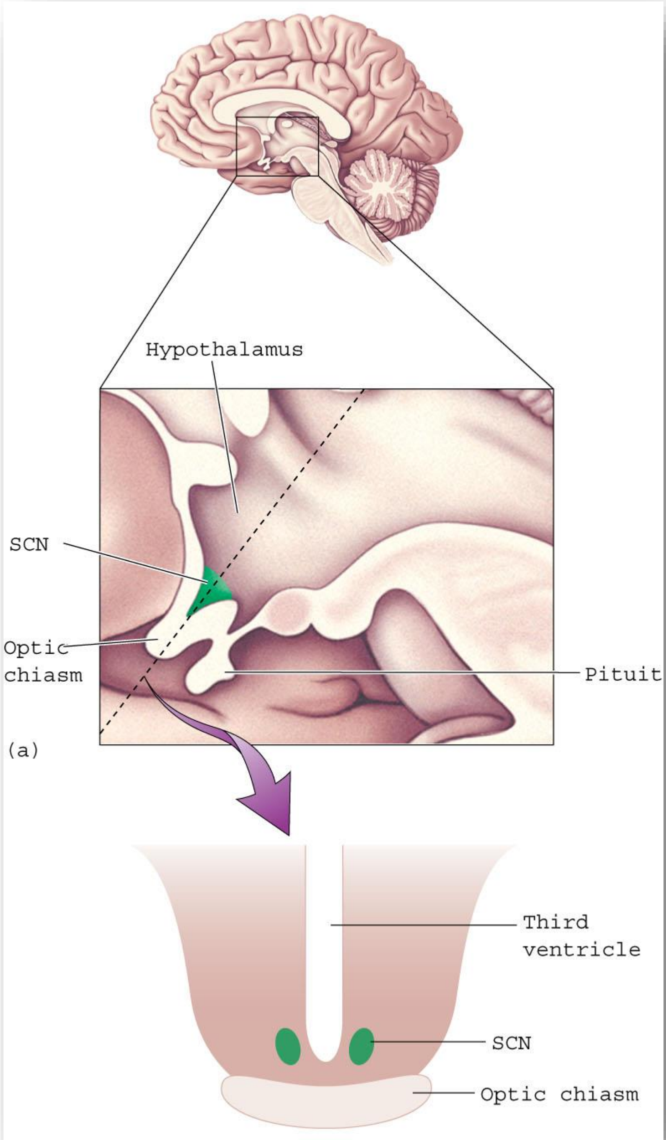
What is 'sleep'?

Thánatos (Death) and Hypnos (Sleep)
as twin brothers, the sons of Nyx (Night)
and Erebos (Darkness).
Hesiod, Theogony (c.800 BC)

Sleep represents the idea of death, making the struggle to remain conscious and the struggle to remain alive the same.
Homer, Odyssey (c.700BC)

Sleep (Somnus) as a kinsman to death
Aeneid, Virgil (70-19BC)

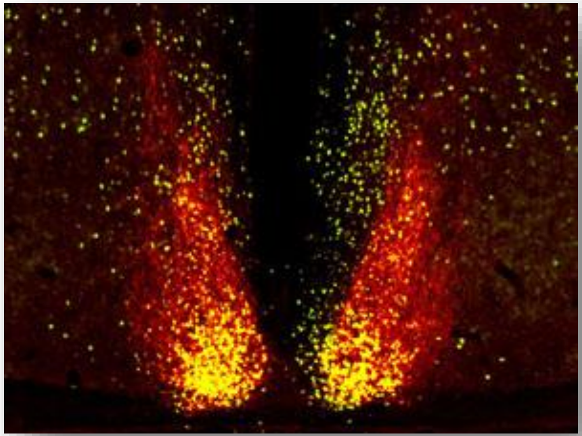
Sleep that knits up the ravel's sleeve of care,
The death of each day's life, sore labour's bath,
Balm of hurt minds, great nature's second course,
Chief nourisher in life's feast.
W Shakespeare, Macbeth, Act 2 Scene 2



How do we know when to sleep?

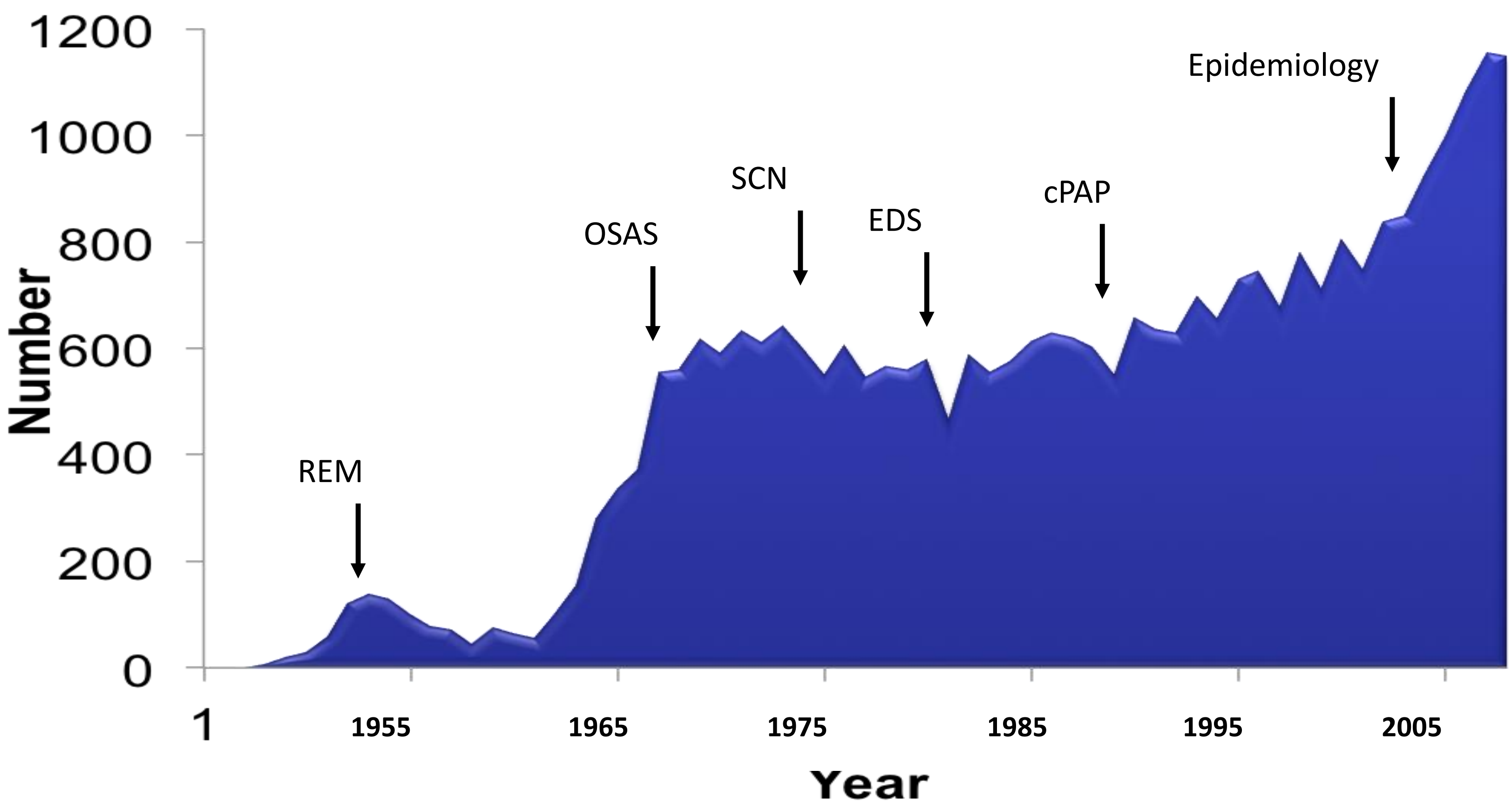
The ‘body clock’ or circadian pacemaker is situated in suprachiasmatic nucleus (SCN) of hypothalamus

It controls the timing of most 24-h behavioral and physiological rhythms including the sleep-wake cycle, alertness and performance rhythms, hormone production, temperature regulation, and metabolism.



‘circadian’ means ‘about a day’ from the Latin circa = about and dies = day

Publication trends in the field of sleep research (Medline search 1945-2008 for *sleep*)



Cappuccio FP, Miller MA, Lockley SW. Sleep, Health and Society, Oxford University Press, 2010

Sleep, Health & Society Programme©

Sleep, Health & Society

Social & Cultural determinants
e.g. age, gender, ethnicity, SES, medicalization, politics, media, industry

Sleep and Health in History
e.g. norms by time, culture, geography, religion, beliefs etc

Public Health & Policy
Occupational: e.g. shift work, EWTD Junior doctors

Environment: physical & social

Economics: e.g. cost-effectiveness, productivity

Life Sciences
e.g. biomarkers, trajectories

Pregnancy
e.g. Maternal and Foetal Outcomes

Mental Health
e.g. Depression, Schizophrenia, Pain, Cognition,

Research-Led Teaching
e.g. SSM Sleep Medicine, PGRs

Chronic Disease
e.g. CVD, CHD, Stroke, Diabetes, Obesity, Hypertension, High lipids

Behavioural Interventions
e.g. RCTs, CBT, Community RCTs

How much sleep do we need?

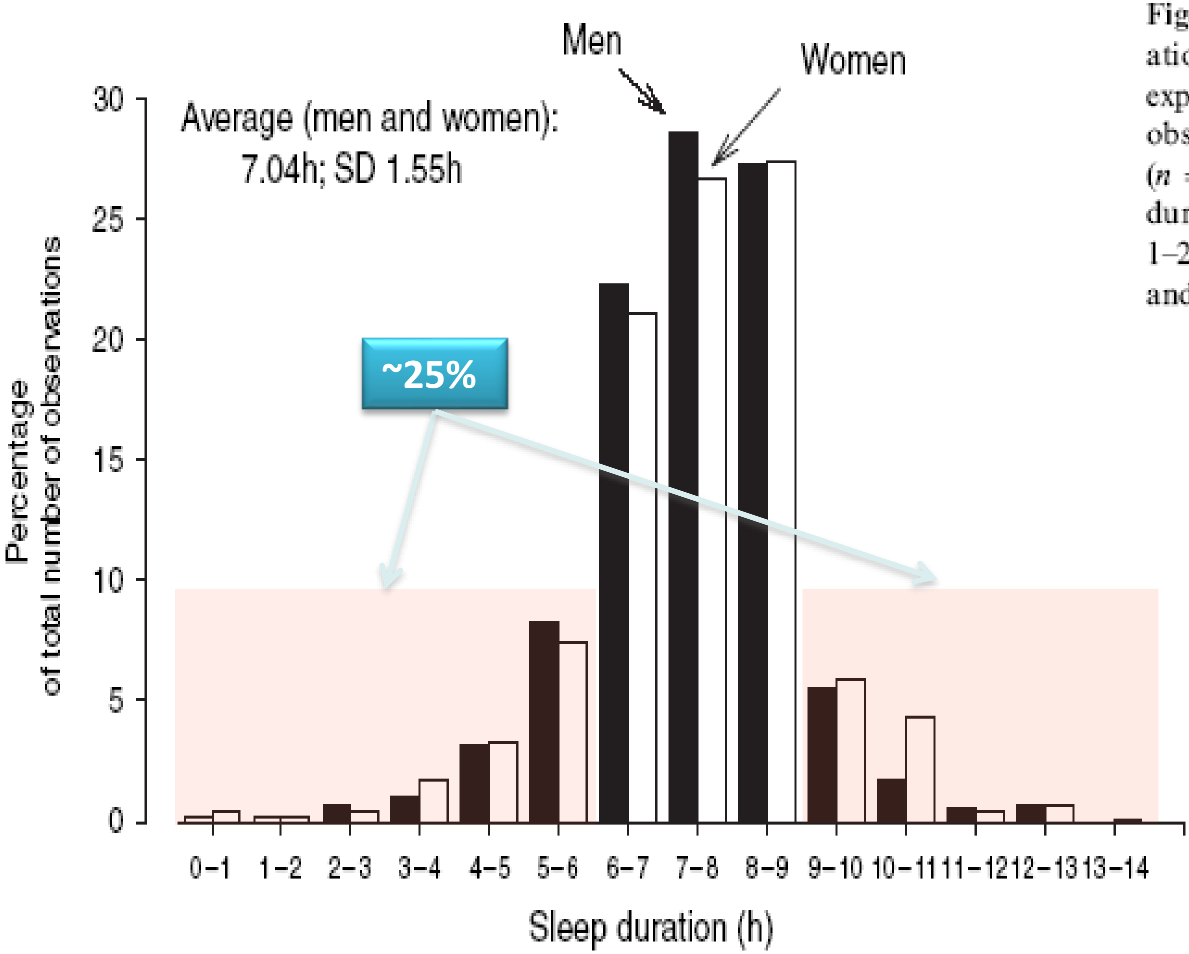
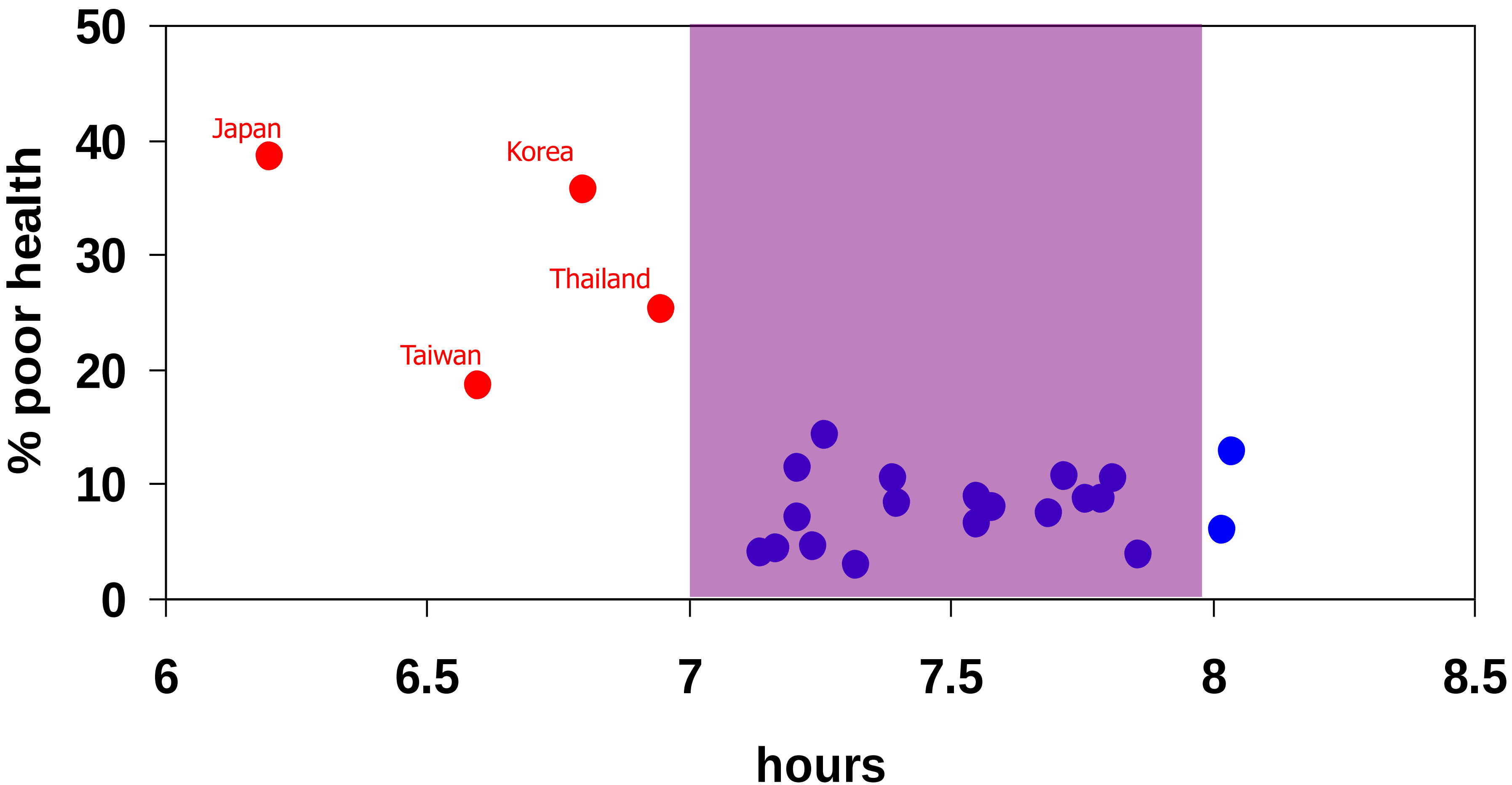


Figure 1. Distribution of reported sleep duration in British men and women. Data are expressed as percentage of total number of observation for men (n = 941) and women (n = 1056) separately. 0–1 refers to sleep durations lasting up to and including 59 min, 1–2 refers to durations lasting between 1 h and 1 h 59 min, etc.

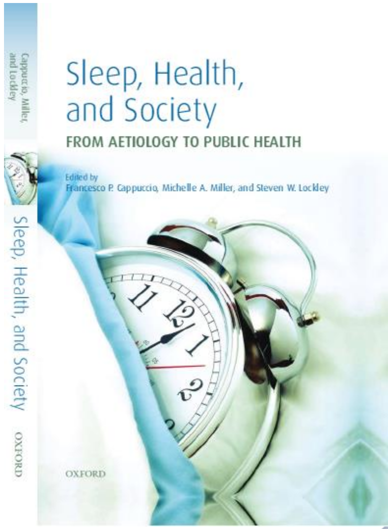
JA Groeger et al. J Sleep Res 2004;13:359-71

Sleep duration and self-rated health problems



Steptoe A et al. Arch Int Med 2006;166:1689-92

Focusing on sleep deprivation (short sleep)



Short sleep

Mechanisms

- Inflammation
- Appetite
- Neuro
- Endocrine
- Molecular
- Genetic

Risk factors

- Hypertension
- Diabetes
- Obesity
- High cholesterol
- High trigs
- Low HDL-chol
- Metabolic synd.

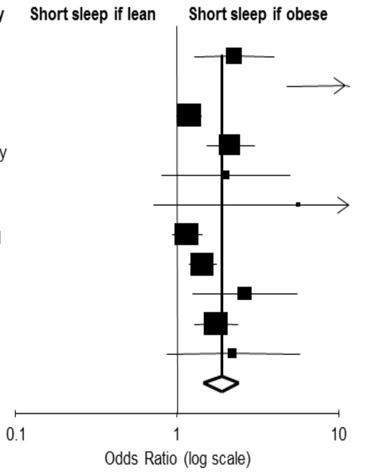
Outcomes

- Death
- CHD
- Stroke
- Heart failure

Short duration of sleep and prevalence of obesity

Children and Adolescents (age 2-20 years)

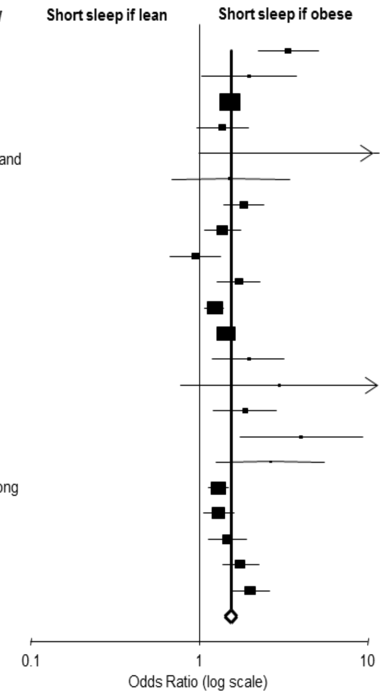
First author	Year	Country	Odds Ratio (95% CI)
Locard	1992	France	2.25 (1.27 to 3.97)
BenSlama	2002	Tunisia	11.02 (4.75 to 25.60)
Sekine	2002	Japan	1.19 (0.99 to 1.41)
Von Kries	2002	Germany	2.16 (1.55 to 3.01)
Agras	2004	USA	1.99 (0.79 to 5.01)
Giugliano	2004	Brazil	5.64 (0.72 to 44.17)
Padez	2005	Portugal	1.15 (0.93 to 1.43)
Reilly	2005	UK	1.45 (1.19 to 1.76)
Chaput	2006	Canada	2.64 (1.25 to 5.56)
Chen	2006	Taiwan	1.75 (1.28 to 2.40)
Seicean	2007	USA	2.23 (0.87 to 5.70)
Combined effect: p<0.0001			**1.89 (1.46 to 2.43)**



Heterogeneity: Q=46.6; p<0.001
Begg's test: p=0.12

Adults (age 15-102 years)

First author	Year	Country	Odds Ratio (95% CI)
Vioque	2000	Spain	3.35 (2.22 to 5.06)
Shigeta	2001	Japan	1.97 (1.03 to 3.77)
Kripke	2002	USA	1.52 (1.46 to 1.58)
Cournot	2004	France	1.38 (0.97 to 1.96)
Hasler	2004	Switzerland	10.8 (0.99 to 118.1)
Bjorkelund	2005	Sweden	1.52 (0.68 to 3.40)
Gangwisch 1	2005	USA	1.84 (1.40 to 2.42)
Gangwisch 2	2005	USA	1.38 (1.07 to 1.78)
Gangwisch 3	2005	USA	0.95 (0.67 to 1.35)
Singh	2005	USA	1.70 (1.27 to 2.28)
Moreno	2006	Brazil	1.22 (1.06 to 1.40)
Vahtera	2006	Finland	1.43 (1.35 to 1.52)
Watari (men)	2006	Japan	1.95 (1.20 to 3.19)
Watari (women)	2006	Japan	2.97 (0.77 to 11.50)
Bjortvan	2007	Norway	1.88 (1.22 to 2.89)
Chaput (men)	2007	Canada	4.01 (1.73 to 9.33)
Chaput (women)	2007	Canada	2.64 (1.25 to 5.56)
Ko	2007	Hong Kong	1.30 (1.13 to 1.49)
Tuomilehto	2007	Finland	1.30 (1.05 to 1.61)
Fogelholm (men)	2007	Finland	1.46 (1.13 to 1.89)
Fogelholm (women)	2007	Finland	1.75 (1.36 to 2.26)
Stranges	2008	UK	2.01 (1.56 to 2.60)
Combined effect: p<0.0001			**1.55 (1.43 to 1.68)**

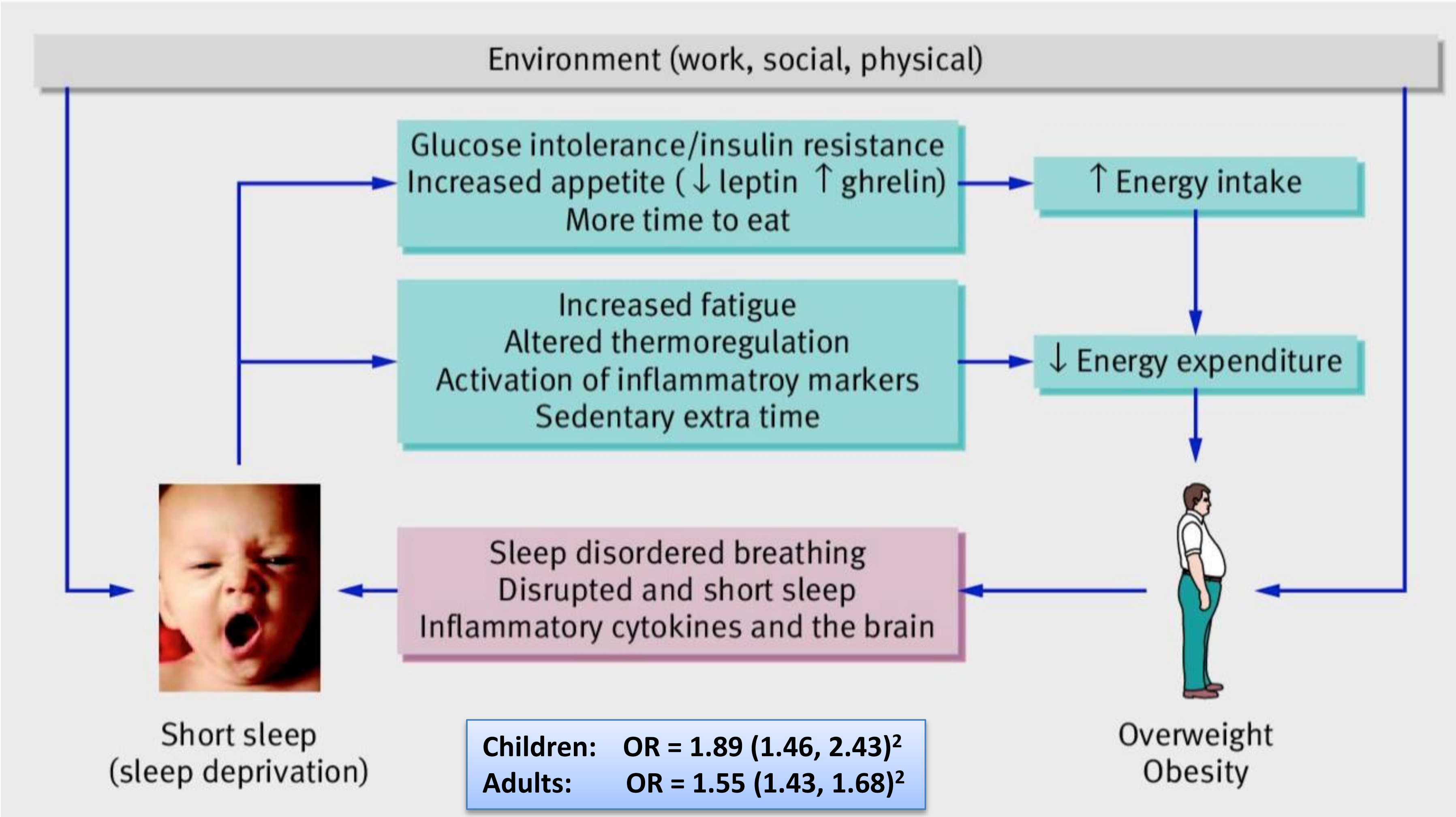


Heterogeneity: Q=64.0, p<0.001
Begg's test: p=0.09

Cappuccio FP et al. Sleep 2008; 31: 619-26

Is prolonged lack of sleep associated with obesity?

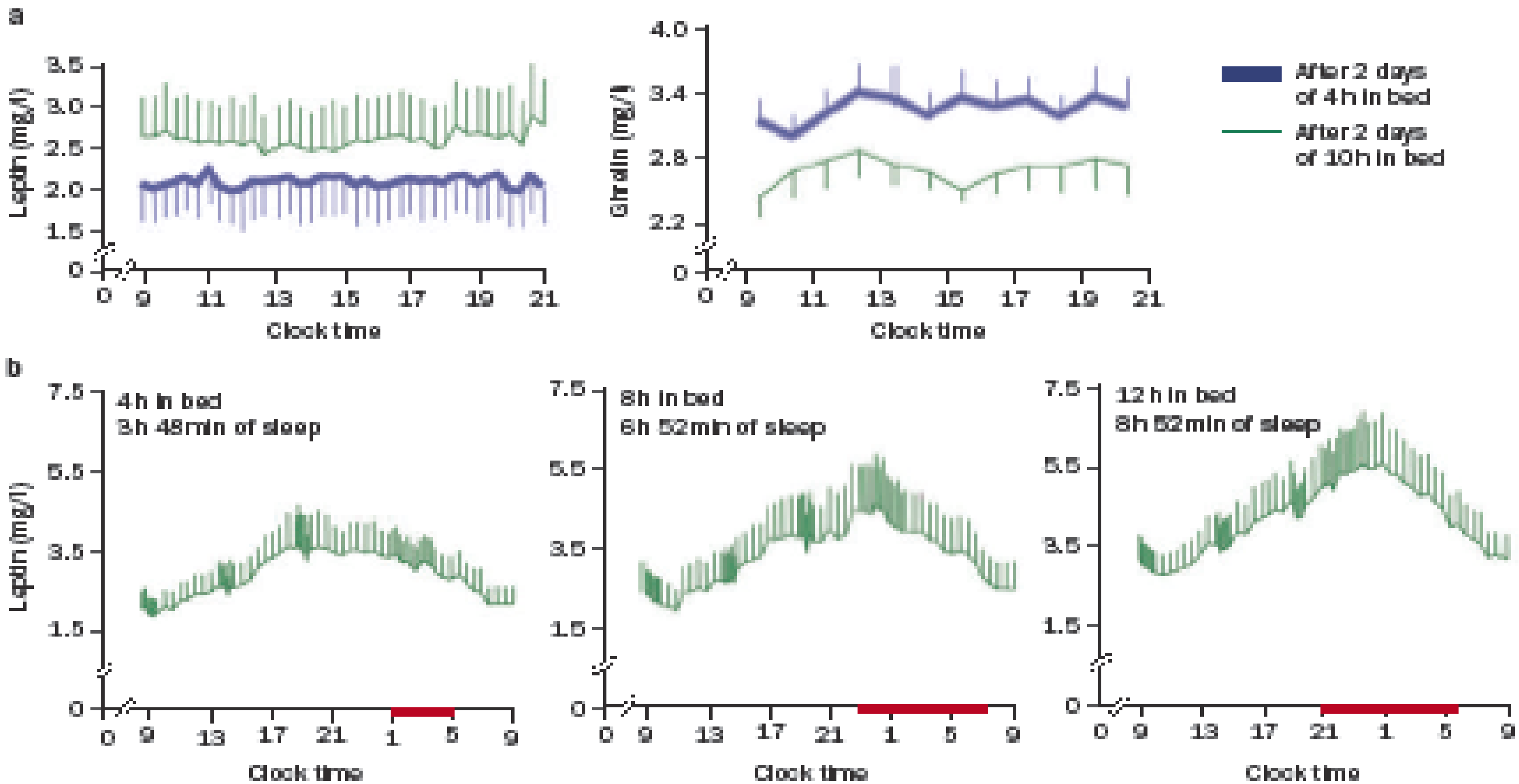
Bi-directional model of the sleep deprivation-obesity association[1]



[1] *Cappuccio FP & Miller MA. Br Med J 2011; 342: d3306*

[2] *Cappuccio FP et al. Sleep 2008; 31: 619-26*

Effect of sleep duration on leptin and ghrelin levels

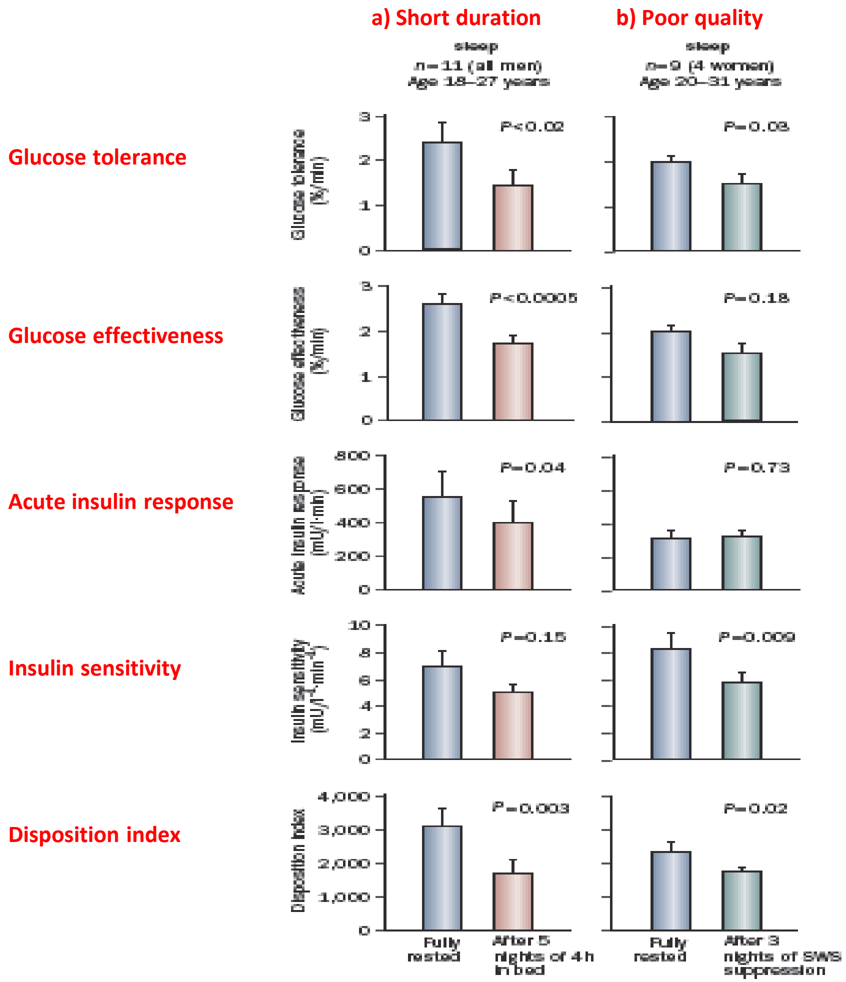


a) Mean (seM) leptin and serum plasma ghrelin levels in healthy individuals after 2 days with 4 h or 10 h sleep periods

b) Mean (seM) 24 h serum leptin profiles after 6 days of 4 h, 8 h and 12 h in bed in nine healthy, lean men, studied at bed rest who ate three identical carbohydrate-rich meals. At the end of these study periods, the participants slept an average of 3 h 48 min in the 4 h in bed group, 6 h 52 min in the 8 h in bed group, and 8 h 52 min in the 12 h in bed group.
All characteristics of the 24 h leptin profile increased from the 4 h to the 12 h bedtime condition. The bars represent sleep periods

Spiegel K et al. Nat Rev Endocrinol 2009;5:253-61

IV GTT in healthy individuals when fully rested and after sleep manipulations

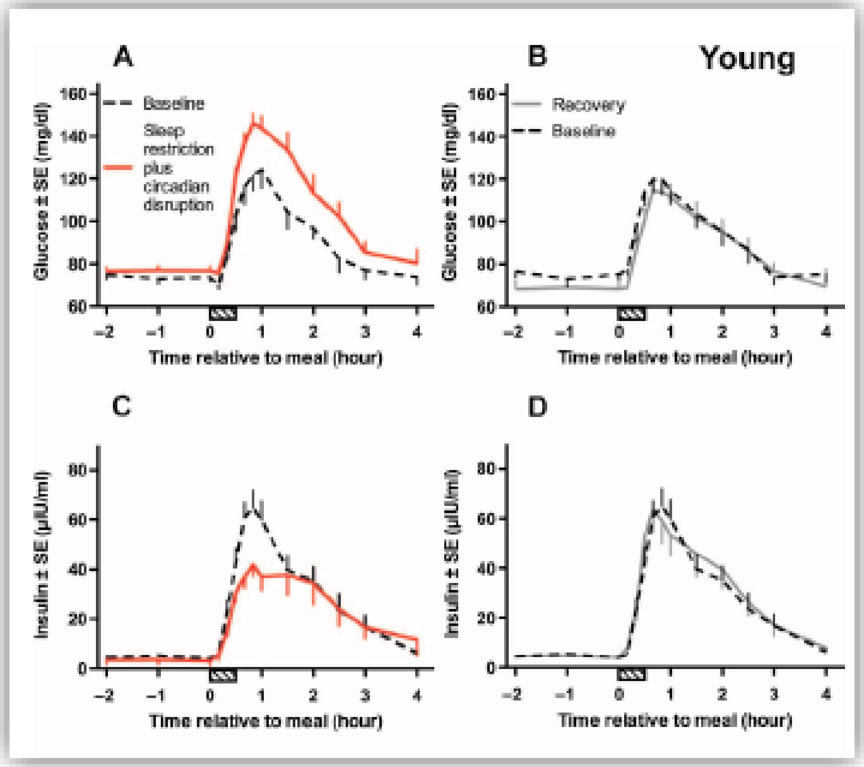


a) results when fully rested and after 5 nights of 4 h in bed
b) results during baseline sleep and after 3 nights of suppression of slow-wave sleep

Spiegel K et al. Nat Rev Endocrinol 2009;5:253-61

Prolonged sleep restriction with circadian disruption impairs glucose metabolism

- >5wks optimal sleep
- 3 weeks of sleep restriction (5.6h per 24h) +
- Circadian disruption (recurrent ‘28h’ days)
- 9 days recovery
- Prolonged sleep restriction with concurrent circadian disruption decreased resting metabolic rate and increased post-prandial plasma glucose (from inadequate insulin secretion)

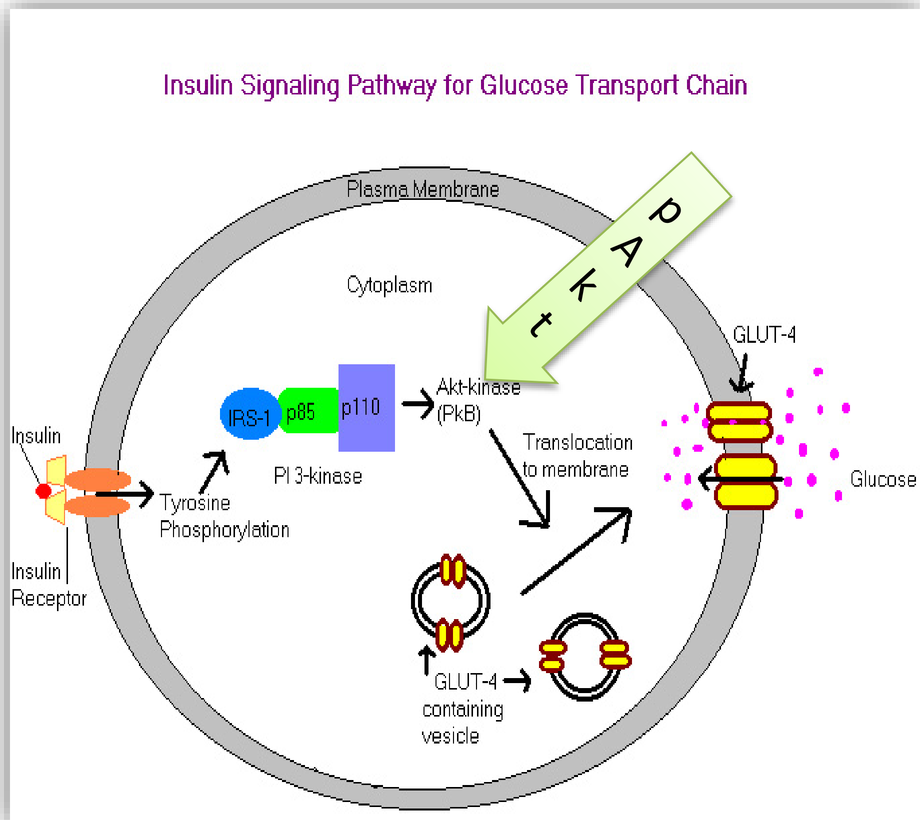


Buxton OM et al. Sci Translat Med 2012; 4(129): 129ra43

Annals of Internal Medicine | EDITORIAL

A New Challenge to Widely Held Views on the Role of Sleep

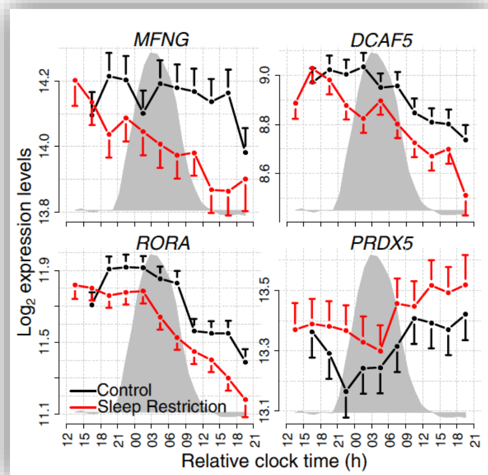
- RCT cross-over in 7 young adults
- 4 days of 4.5h or 8.5h in bed
- Adipocytes from subcutaneous fat on both periods
- In-vitro ability of insulin to increased levels of pAkt assessed (measure of cellular insulin sensitivity)
- Total body insulin sensitivity assessed by IVGTT
- During sleep restriction, both cellular and total body insulin sensitivity decreased by ~30%

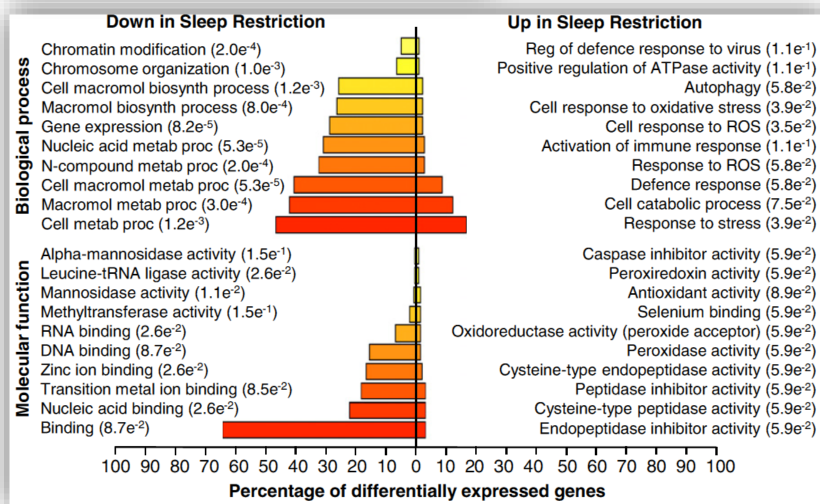


Broussanrd JL et al. Ann Intern Med 2012; 157: 549-57
Cappuccio FP & Miller MA. Ann Intern Med 2012; 157: 593-4

Sleep restriction and gene expression

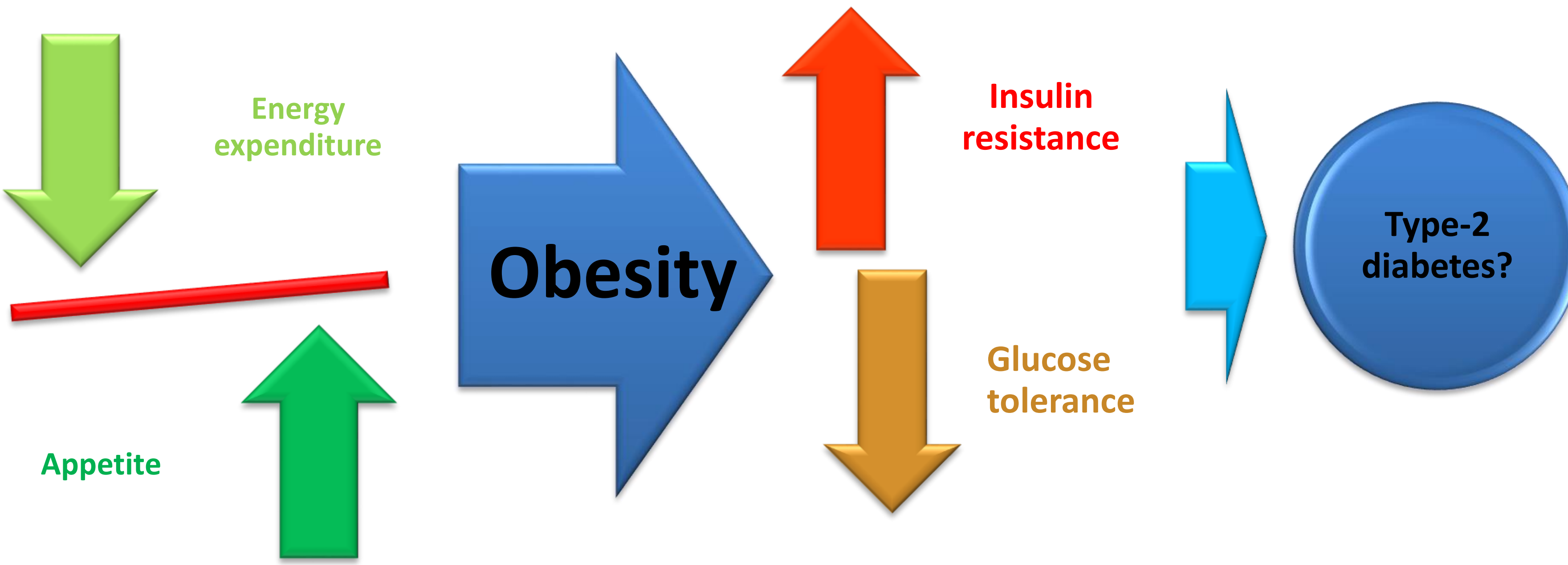
- 26 participants
- 1 wk sleep restriction (5.7h per 24h)
- 1 wk control (8.5h per 24h)
- Whole-blood RNA at the end of each period
- Control for light, activity, food
- Transcriptome analysis revealed that 711 genes were up- or down-regulated during sleep restriction
- Genes affected associated with circadian rhythms, sleep haemostasis, oxidative stress and metabolism.





Möller-Levet CS et al. PNAS 2013; 110(12): E1132-41.

Short sleep and metabolic consequences?



Rationale

- In *short-term*, *acute*, laboratory and cross-sectional observational studies disturbed or reduced sleep is associated with glucose intolerance, insulin resistance, reduced acute insulin response to glucose and a reduction in the disposition index, thus predisposing to type 2 diabetes.

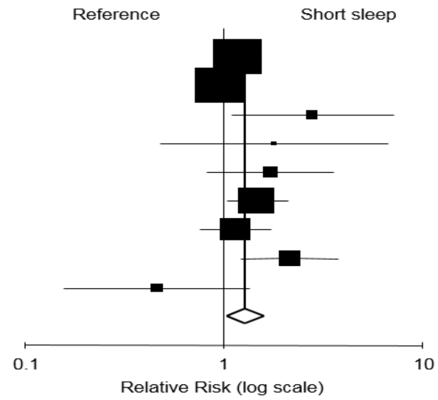
- The causality of the association, the generalizability of the results and their extrapolation to *longer-term* effects of *sustained* sleep disturbances are studied in prospective population studies to establish a temporal sequence between exposure and outcome

Short duration of sleep and incidence of type-2 diabetes

Exposure:

Short sleep duration

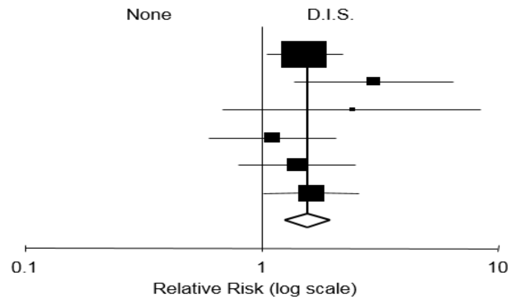
Author	Year	Country	Relative Risk (95% CI)
Ayas	2003	USA	1.19 (0.97 to 1.44)
Biorkelund	2005	Sweden	0.97 (0.83 to 1.14)
Mallon (men)	2005	Sweden	2.80 (1.09 to 7.18)
Mallon (women)	2005	Sweden	1.80 (0.49 to 6.71)
Yaggi	2006	USA	1.72 (0.81 to 3.61)
Gangwisch	2007	USA	1.48 (1.04 to 2.11)
Hayashino	2007	Japan	1.15 (0.76 to 1.74)
Beihl (white)	2009	USA	2.16 (1.22 to 3.81)
Beihl (black)	2009	USA	0.47 (0.16 to 1.37)
Combined effect: p=0.024			**1.28 (1.03 to 1.60)**



Heterogeneity: I^2=58%, p=0.015
Publication bias: Egger's test p=0.14

Difficulty in initiating sleep

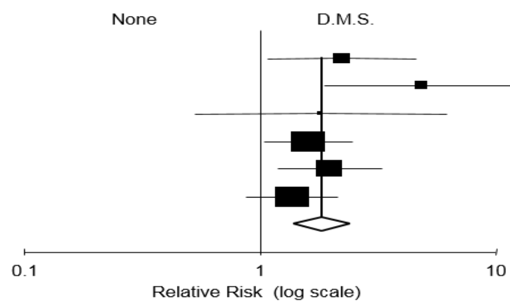
Author	Year	Country	Relative Risk (95% CI)
Nilsson	2004	Sweden	1.52 (1.05 to 2.21)
Kawakami	2004	Japan	2.97 (1.36 to 6.51)
Mallon (men)	2005	Sweden	2.41 (0.69 to 8.45)
Meisinger (men)	2005	Germany	1.11 (0.59 to 2.07)
Meisinger (women)	2005	Germany	1.42 (0.80 to 2.51)
Hayashino	2007	Japan	1.62 (1.01 to 2.59)
Combined effect: p<0.0001			**1.57 (1.25 to 1.97)**



Heterogeneity: I^2=0%, p=0.50
Publication bias: Egger's test p=0.37

Difficulty in maintaining sleep

Author	Year	Country	Relative Risk (95% CI)
Kawakami	2004	Japan	2.23 (1.08 to 4.60)
Mallon (men)	2005	Sweden	4.81 (1.88 to 12.3)
Mallon (women)	2005	Sweden	1.80 (0.52 to 6.20)
Meisinger (men)	2005	Germany	1.60 (1.04 to 2.46)
Meisinger (women)	2005	Germany	1.97 (1.19 to 3.29)
Hayashino	2007	Japan	1.36 (0.87 to 2.14)
Combined effect: p<0.0001			**1.84 (1.39 to 2.43)**



Heterogeneity: I^2=22%, p=0.27
Publication bias: Egger's test p=0.15

Cappuccio FP et al. Diabetes Care; 2010; 33: 414-20

Sleep duration and Hypertension

Sleep (h/d)	Men	Women
	The Western New York Health Study[1] (cross-sectional)	
	n=1,317	n=1,710
<6	0.93 (0.62 – 1.41)	1.66 (1.09 - 2.53)
6-8	1.0	1.0
>8	1.39	0.69
	Whitehall II Study[2] (prospective; f-up 5 yrs)	
	n=2,686	n=1,005
≤5	0.96 (0.62 – 1.48)	1.94 (1.08 – 3.50)
6	1.07 (0.86 – 1.34)	1.56 (1.07 – 2.27)
7	1.0	1.0
8	1.07 (0.80 – 1.42)	1.17 (0.74 – 1.86)
9+	0.36 (0.11 – 1.19)	0.92 (0.26 – 3.27)

[1] *Stranges S et al. J Hypertens 2010;28:896-902*

[2] *Cappuccio FP et al. Hypertension 2007:50:694-701*

Prospective association between sleep-disordered breathing and hypertension

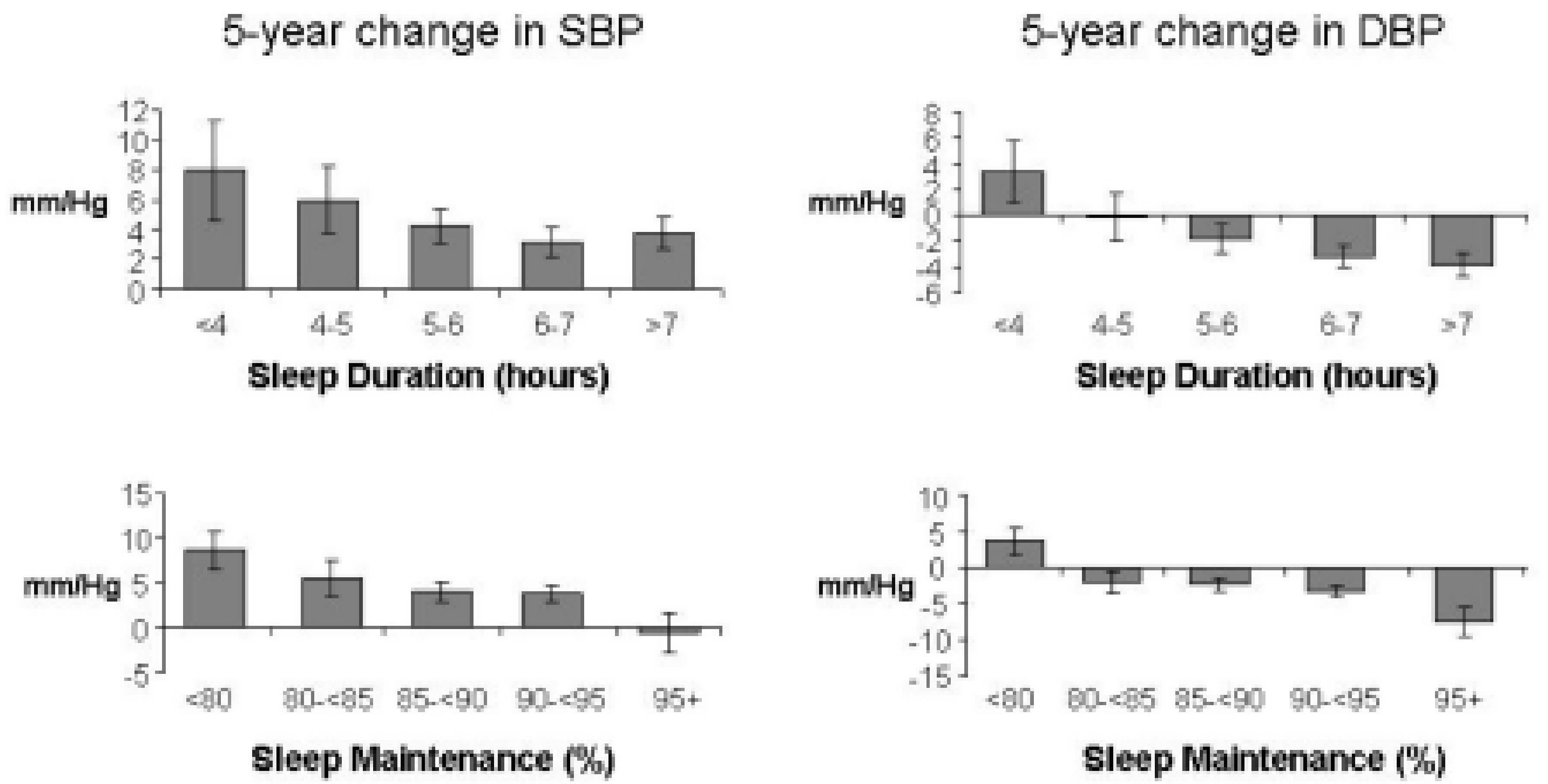
(The Sleep Heart Health Study)

TABLE 2. ADJUSTED ODDS RATIOS* OF INCIDENT HYPERTENSION AT FOLLOW-UP IN RELATION TO BASELINE APNEA-HYPOPNEA INDEX AMONG 2,470 SLEEP HEART HEALTH STUDY SUBJECTS WITHOUT HYPERTENSION AT BASELINE

Baseline AHI	n	Model 1†	Model 2‡	Model 3§
0–4.9	1,511	—	—	—
5–14.9	629	1.13 (0.90–1.43)	0.92 (0.72–1.17)	0.94 (0.73–1.22)
15–29.9	234	1.54 (1.12–2.11)	1.12 (0.80–1.56)	1.09 (0.77–1.54)
≥30	97	2.19 (1.39–3.44)	1.51 (0.93–2.47)	1.50 (0.91–2.46)

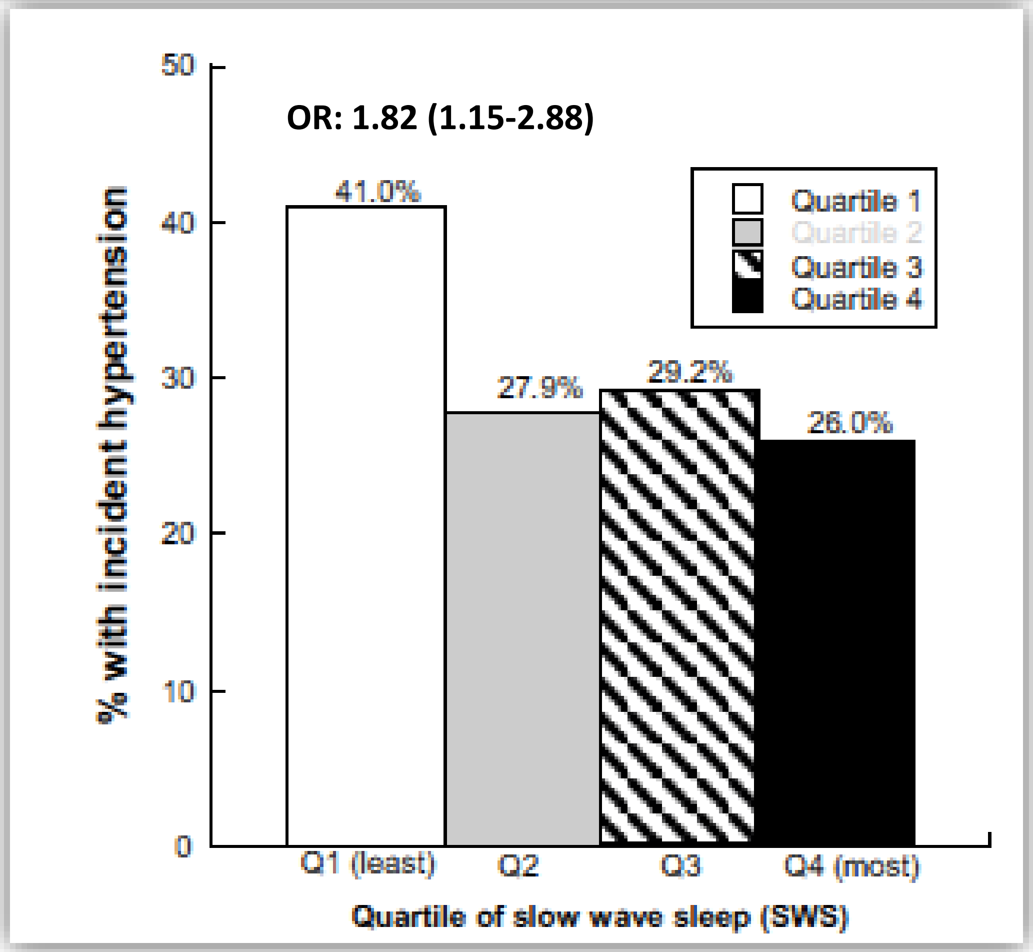
O’Connor GT et al. AJRCCM 2009; 179: 1159-64

Association between sleep and change in blood pressure in mid life: The CARDIA Sleep Study



Knutson KL et al. Arch Intern Med 2009; 169: 1055-61

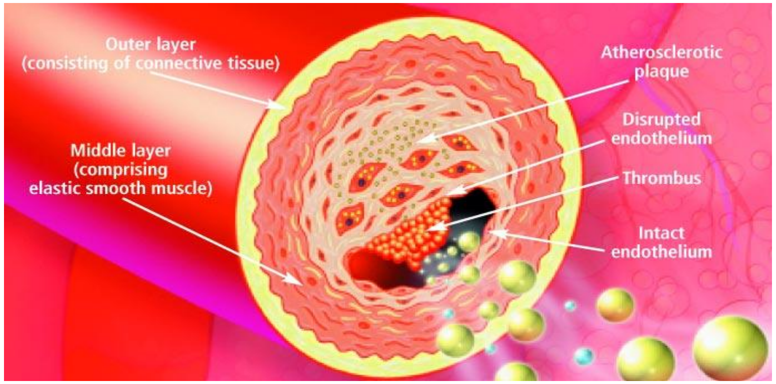
Decreased Slow Wave Sleep increases the risk of hypertension in elderly men



Fung MM et al. Hypertension 2012; 169: 1055-61

Inflammation and Sleep

- Inflammatory markers are elevated in individuals undergoing short term sleep deprivation studies.
- Short sleep may lead to increased secretion of inflammatory cytokines, which in turn may lead to an increase in cardiovascular risk



Miller MA et al. Curr Vasc Pharmacol 2007; 5(2): 93-102

Cross sectional relationship between hs-CRP and duration of sleep (hours) in women

	Coef. (95% CI)	*Coef. (95% CI)*	*reference*	*Coef. (95% CI)*	*Coef. (95% CI)*	*p-value*†
	<=5 (n=56)	**6 (n=269)**	**7 (n=578)**	**8 (n=303)**	**9+ (n=43)**	
Model 1	**1.55*** (1.09, 2.21)	1.03 (0.87, 1.23)	1	1.01 (0.85, 1.19)	1.45* (1.01, 2.07)	0.004
Model 2	**1.49*** (1.07, 2.09)	0.95 (0.81, 1.12)	1	0.93 (0.79, 1.09)	1.27 (0.91, 1.77)	**0.03**
Model 3	1.38 (1.00, 1.92)	0.94 (0.80, 1.10)	1	1.00 (0.86, 1.17)	1.43* (1.03, 1.97)	**0.02**
Model 4	**1.42*** (1.02, 1.96)	0.95 (0.82, 1.11)	1	1.00 (0.86, 1.16)	1.35 (0.99, 1.85)	**0.04**

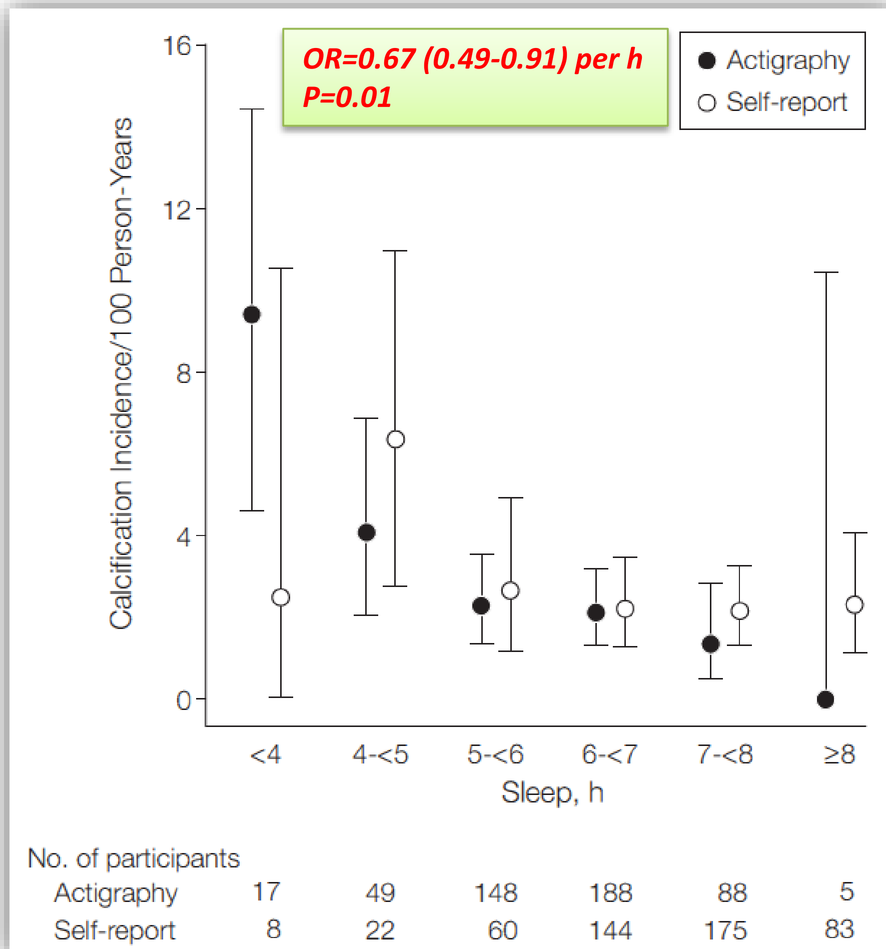
Geometric mean ratio by category of sleep duration (<=5, 6, 7, 8, 9+) with 7hrs sleep as the reference. * P-values at 0.05 significance level for contrast between sleep categories and the reference (7 hours).†P-values for test of nonlinear trends

Model 1: adjusted for age and marital status; Model 2: Model 1 + BMI; Model 3: Model 2 + smoking; Model 4: Model 3 + Systolic blood pressure and Trigs

Miller MA et al. Sleep 2009; 32: 857-64

Incidence of Coronary Calcifications by sleep duration

(The Chicago CARDIA Cohort Study)

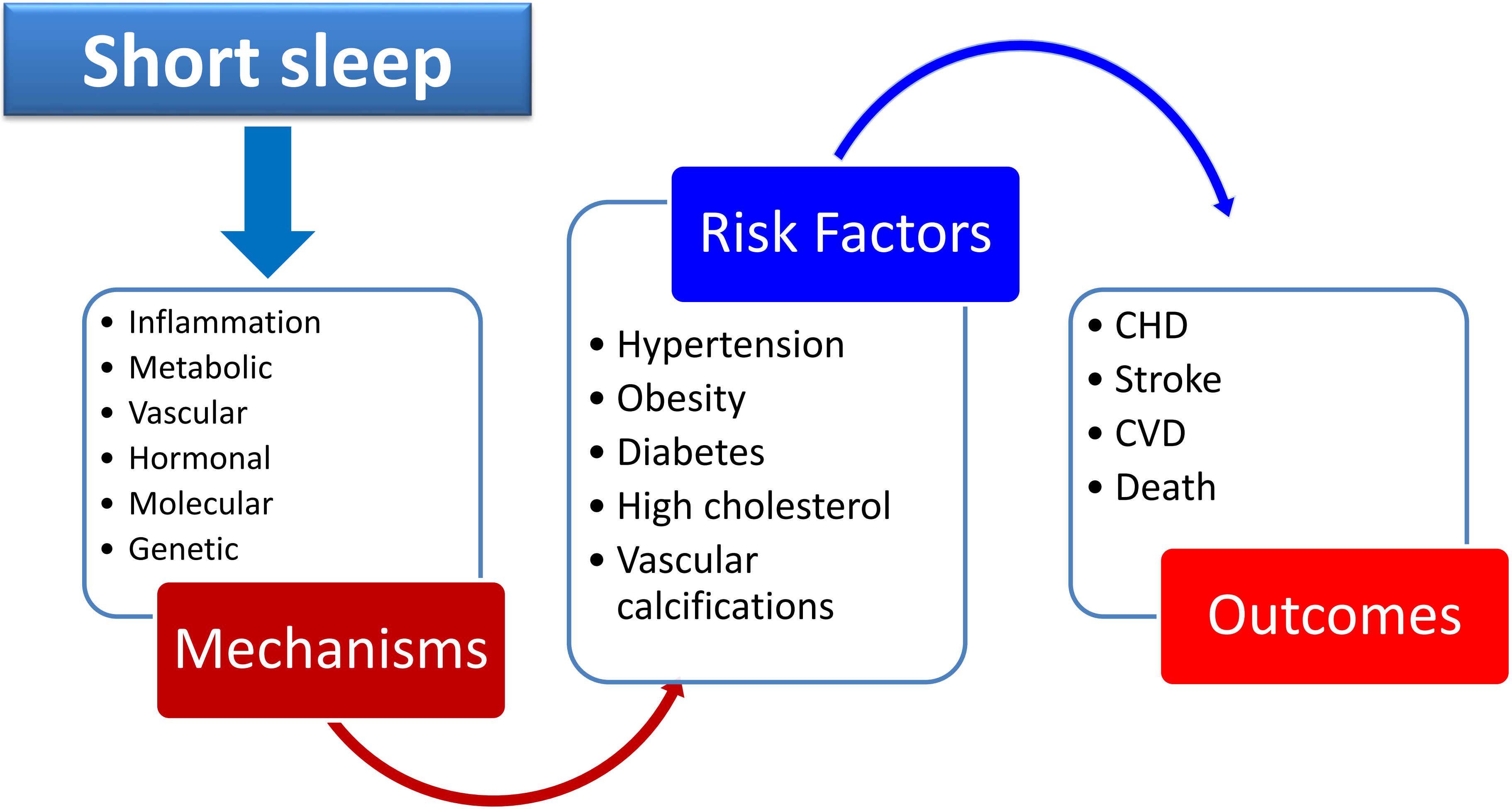


Effect stronger in women

Women (n=291)
0.48 (0.27- 0.85)

Men (n=203)
0.76 (0.52 -1.10)

King CR et al. JAMA 2008; 300(24): 2859-66

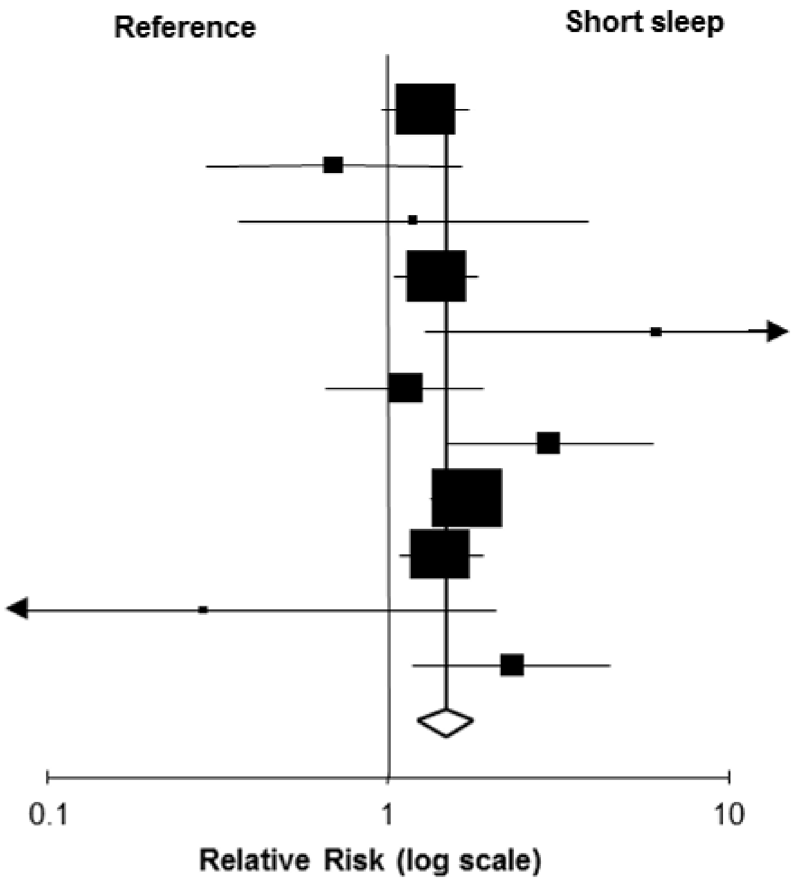


Modified from: Cappuccio FP & Miller MA. Sleep 2011; 34(11): 1457-8

Short sleep and incidence of C.H.D.

First author	Year	Country	Relative Risk (95% CI)
Qureshi	1997	USA	1.30 (0.97 to 1.74)
Mallon (men)	2002	Sweden	0.70 (0.29 to 1.65)
Mallon (women)	2002	Sweden	1.20 (0.37 to 3.88)
Ayas	2003	USA	1.39 (1.06 to 1.83)
Amagai (men)	2004	Japan	6.17 (1.29 to 29.6)
Meisinger (men)	2007	Germany	1.13 (0.66 to 1.91)
Meisinger (women)	2007	Germany	2.97 (1.47 to 6.02)
Shankar (men)	2009	Singapore	1.70 (1.34 to 2.15)
Shankar (women)	2009	Singapore	1.43 (1.09 to 1.89)
Ikehara (men)	2009	Japan	0.29 (0.04 to 2.05)
Ikehara (women)	2009	Japan	2.32 (1.19 to 4.51)
Combined effect: p<0.0001			**1.48 (1.22 to 1.80)**

Heterogeneity: I^2=44%; p=0.059
Egger's test: p=0.95

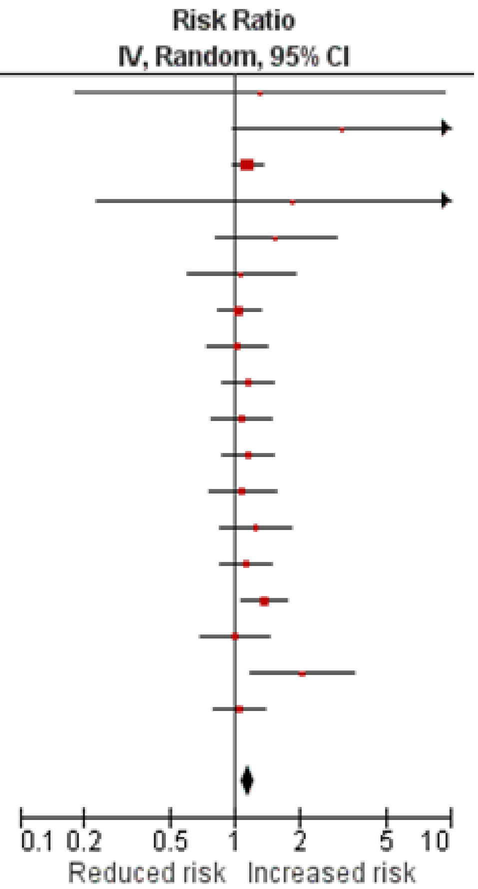


Cappuccio FP et al. Eur Heart J 2011; 32: 1484-92

Short sleep and incidence of stroke

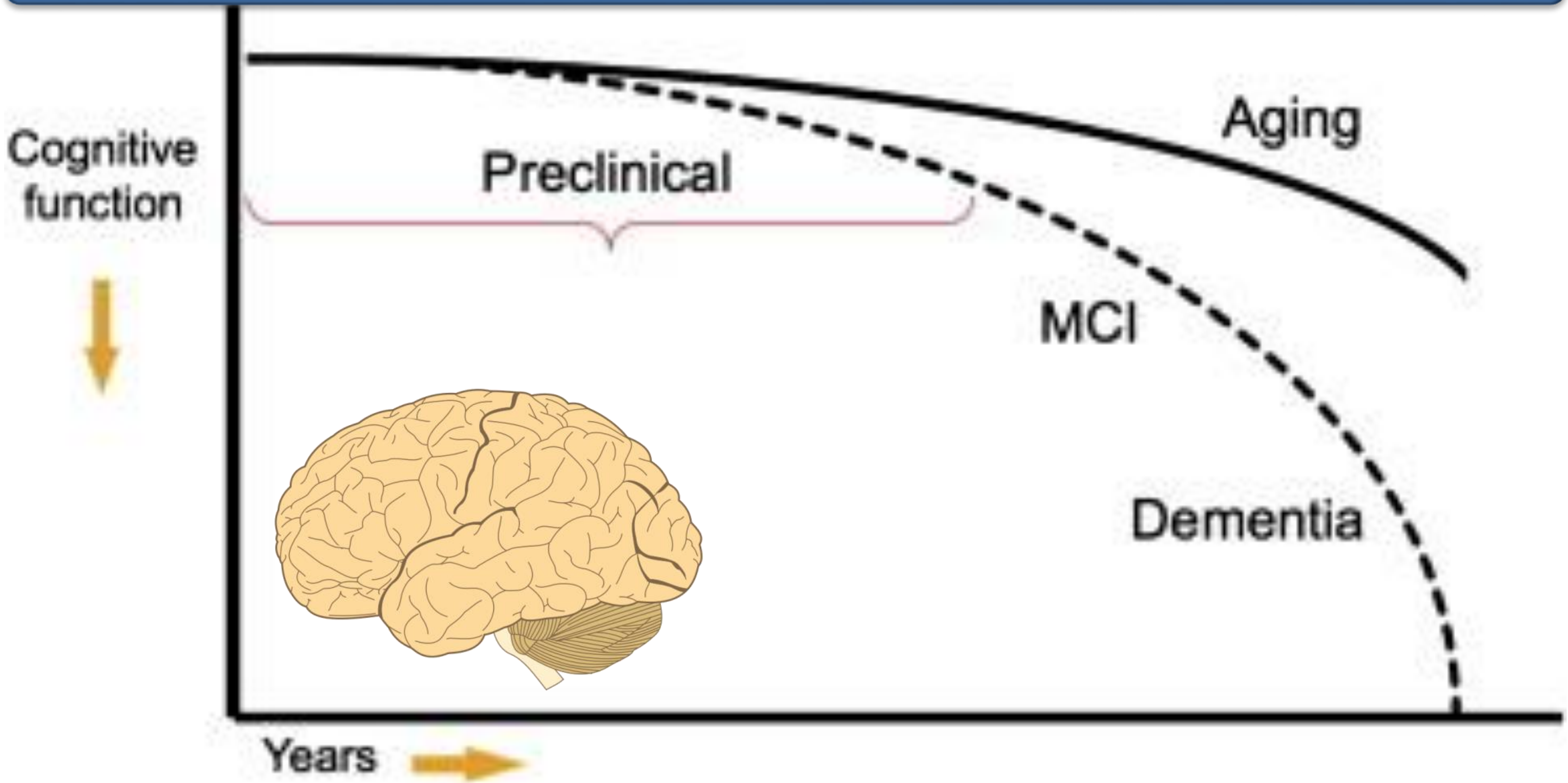
Study or Subgroup	log[Risk Ratio]	SE	Events Total	Participants Total	Weight	Risk Ratio IV, Random, 95% CI
Amagai 2004 (men)	0.2624	1.0088	34	4419	0.1%	1.30 [0.18, 9.39]
Amagai 2004 (women)	1.16	0.6022	29	6906	0.4%	3.19 [0.98, 10.38]
Chen 2008	0.131	0.0824	1166	93175	21.4%	1.14 [0.97, 1.34]
Hamazaki 2011 (men)	0.6098	1.061	30	2282	0.1%	1.84 [0.23, 14.72]
Ikehara 2009 (men)	0.4383	0.3311	1038	41489	1.3%	1.55 [0.81, 2.97]
Ikehara 2009 (women)	0.0677	0.2952	926	57145	1.7%	1.07 [0.60, 1.91]
Kakizaki 2013	0.0488	0.1139	1165	49256	11.2%	1.05 [0.84, 1.31]
Kim 2013 (men)	0.0198	0.1637	627	61936	5.4%	1.02 [0.74, 1.41]
Kim 2013 (women)	0.1484	0.1409	632	73749	7.3%	1.16 [0.88, 1.53]
Kronholm 2011 (men)	0.0677	0.1679	1057	11373	5.2%	1.07 [0.77, 1.49]
Kronholm 2011 (women)	0.1398	0.1424	1125	11917	7.2%	1.15 [0.87, 1.52]
Leng 2014 (men)	0.077	0.186	198	4444	4.2%	1.08 [0.75, 1.56]
Leng 2014 (women)	0.2231	0.1968	148	5248	3.8%	1.25 [0.85, 1.84]
Pan 2014 (men)	0.1222	0.1393	693	27954	7.5%	1.13 [0.86, 1.48]
Pan 2014 (women)	0.3148	0.1214	688	35303	9.9%	1.37 [1.08, 1.74]
Qureshi 1997	0	0.1893	285	7844	4.1%	1.00 [0.69, 1.45]
von Ruesten 2012	0.7227	0.2843	169	23620	1.8%	2.06 [1.18, 3.60]
Westerlund 2013	0.0488	0.1387	1685	41192	7.6%	1.05 [0.80, 1.38]
Total (95% CI)			**11695**	**559252**	**100.0%**	**1.15 [1.07, 1.24]**

Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 12.90$, $df = 17$ ($P = 0.74$); $I^2 = 0\%$
Test for overall effect: $Z = 3.68$ ($P = 0.0002$)



Cappuccio FP et al. Eur Heart J 2011; 32: 1484-92
updated in: Leng Y et al. Neurology 2015; 84: 1072-9

Cognitive function with age



Policy concerns:
MCI increasing with aging population
Factors delaying MCI and dementia by and large unknown

Is sleep important for cognitive wellbeing?

English Longitudinal Study of Aging (ELSA)

Prospective population study of British men and women, aged 50+ years

Wave 1 (2002/3)
N = 12,099
- Main interview (inc. **cognition**)

Wave 2 (2004/5)
N = 9,432
- Main interview (inc. **cognition**)
- Nurse visit

Wave 3 (2006/7)
N = 9,771
- Main interview (inc. **cognition**)

Wave 4 (2008/9)
N = 11,050
- Main interview (inc. **cognition**)
- Nurse visit
- **Sleep data**

ESRC SDAI Phase 1
Cross-sectional

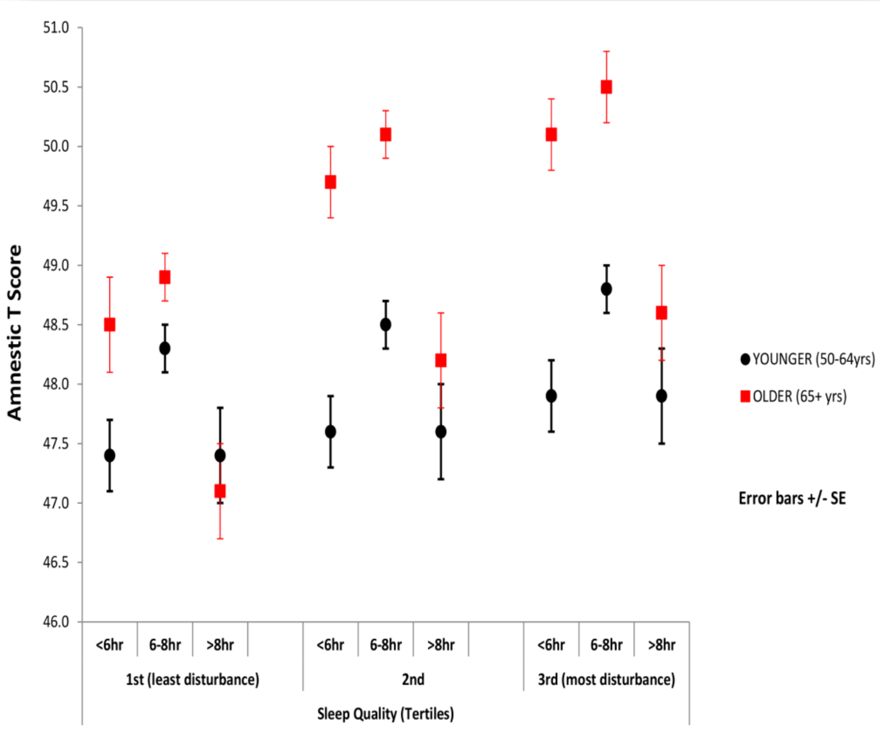
Wave 5 (2010/11)
N = 10,275 (approx)
- Main interview (inc. **cognition**)

ESRC SDAI Phase 2
2-yrs Prospective
(analysis pending)

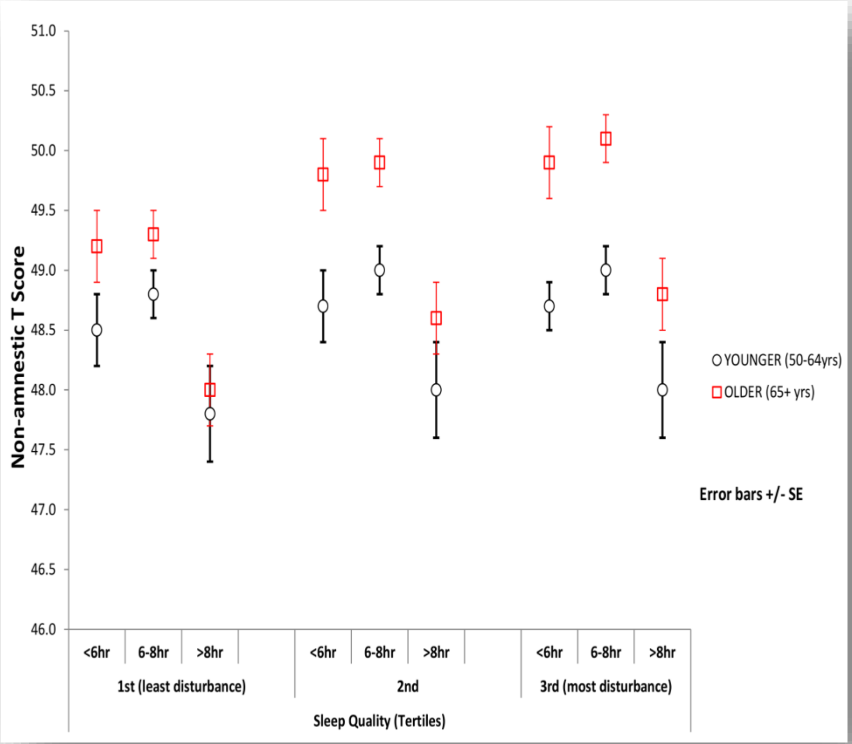
Miller MA et al. PLoS ONE 2014; 9 (6): e100991

Cognitive function by sleep duration adjusted by sleep quality in younger and older people

Amnestic T-scores (memory)



Non-amnestic T-scores (non-memory)



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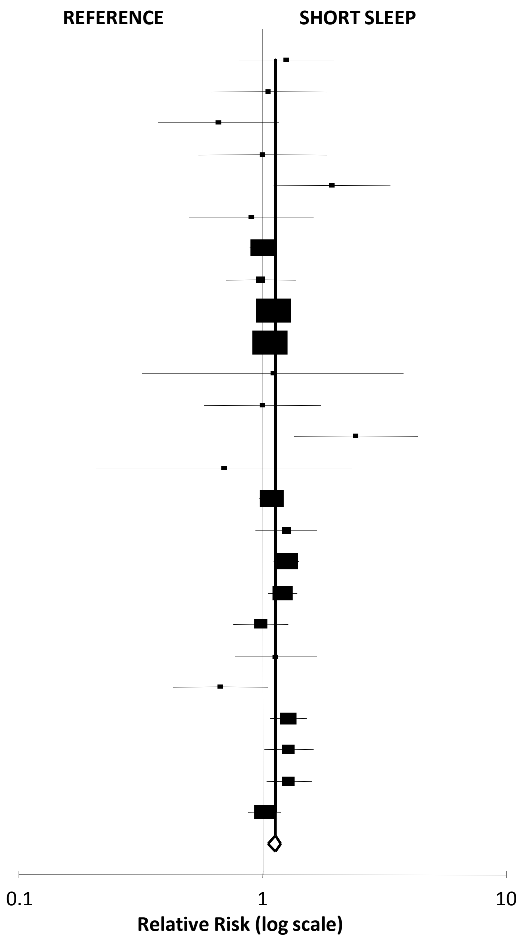
Miller MA et al. PLoS ONE 2014; 9 (6): e100991

Short duration of sleep and all-cause mortality

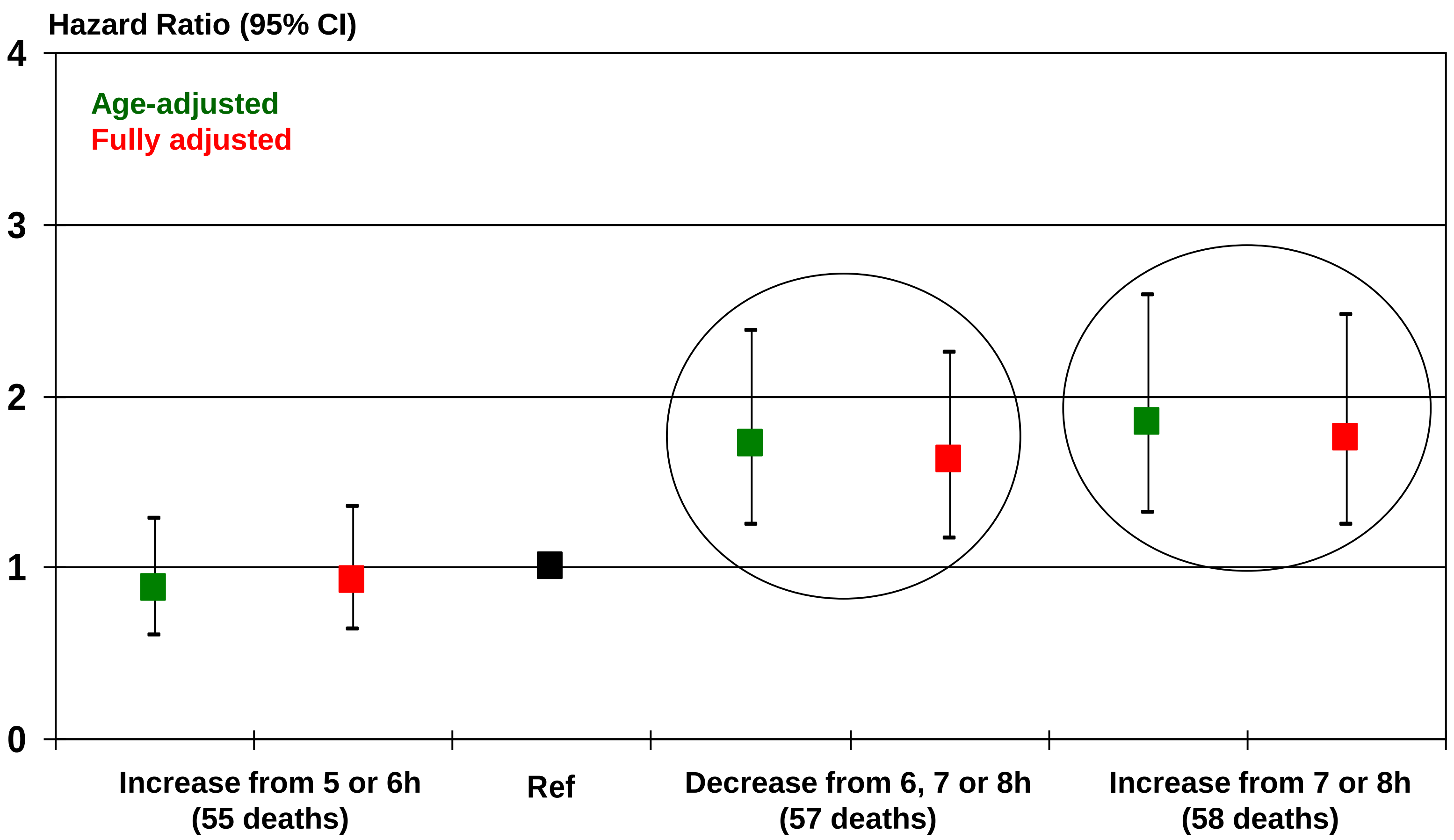
First author	Year	Sample size	Deaths	Short Sleep v Reference	Relative Risk (95% CI)
Tsubono	1993	4,318	207	≤6 v 7-8h	1.26 (0.80 to 1.98)
Ruigomez (men)	1995	395	224	<7 v 7-9h	1.06 (0.61 to 1.84)
Ruigomez (women)	1995	594			0.66 (0.37 to 1.16)
Gale	1998	1,299	1,158	≤7 v 9h	1.00 (0.54 to 1.84)
Kojima (men)	2000	2,438	147	<7 v 7-8.9h	1.93 (1.12 to 3.35)
Kojima (women)	2000	2,884	109		0.90 (0.50 to 1.61)
Heslop (men)	2002	6,022	2,303	<7 v 7-8h	1.00 (0.89 to 1.12)
Heslop (women)	2002	1,006	262		0.98 (0.70 to 1.37)
Kripke (men)	2002	480,841	45,200	5 v 7h	1.11 (1.04 to 1.17)
Kripke (women)	2002	636,095	32,440		1.07 (1.01 to 1.14)
Mallon (men)	2002	906	165	<6 v 7h	1.11 (0.32 to 3.80)
Mallon (women)	2002	964	101		1.00 (0.58 to 1.73)
Amagai (men)	2004	4,419	289	<6 v 7-7.9h	2.41 (1.34 to 4.34)
Amagai (women)	2004	6,906	206		0.70 (0.21 to 2.35)
Patel	2004	82,969	5,409	≤5 v 7h	1.08 (0.96 to 1.22)
Ferrie	2007	9,871	566	≤5 v 7h	1.25 (0.93 to 1.67)
Hublin (men)	2007	9,529	1,850	<7 v 7-8h	1.26 (1.12 to 1.42)
Hublin (women)	2007	10,265	1,850		1.21 (1.05 to 1.39)
Lan (men)	2007	1,748	816	<7 v 7-7.9h	0.98 (0.76 to 1.26)
Lan (women)	2007	1,331	522		1.14 (0.77 to 1.69)
Gangwisch (32-59)	2008	5,806	273	≤5 v 7h	0.67 (0.43 to 1.05)
Gangwisch (60-86)	2008	3,983	1,604		1.27 (1.07 to 1.52)
Ikehara (men)	2009	41,489	8,548	≤4 v 7h	1.28 (1.01 to 1.62)
Ikehara (women)	2009	57,145	5,992		1.28 (1.04 to 1.59)
Stone	2009	8,101	1,922	<6 v 6-8h	1.02 (0.87 to 1.19)
Combined effect: P<0.01		**1,381,324**	**112,163**		**1.12 (1.06 to 1.18)**



Heterogeneity: I^2=39%; Q=39.4, p=0.02
Publication bias: Egger's test: p=0.74

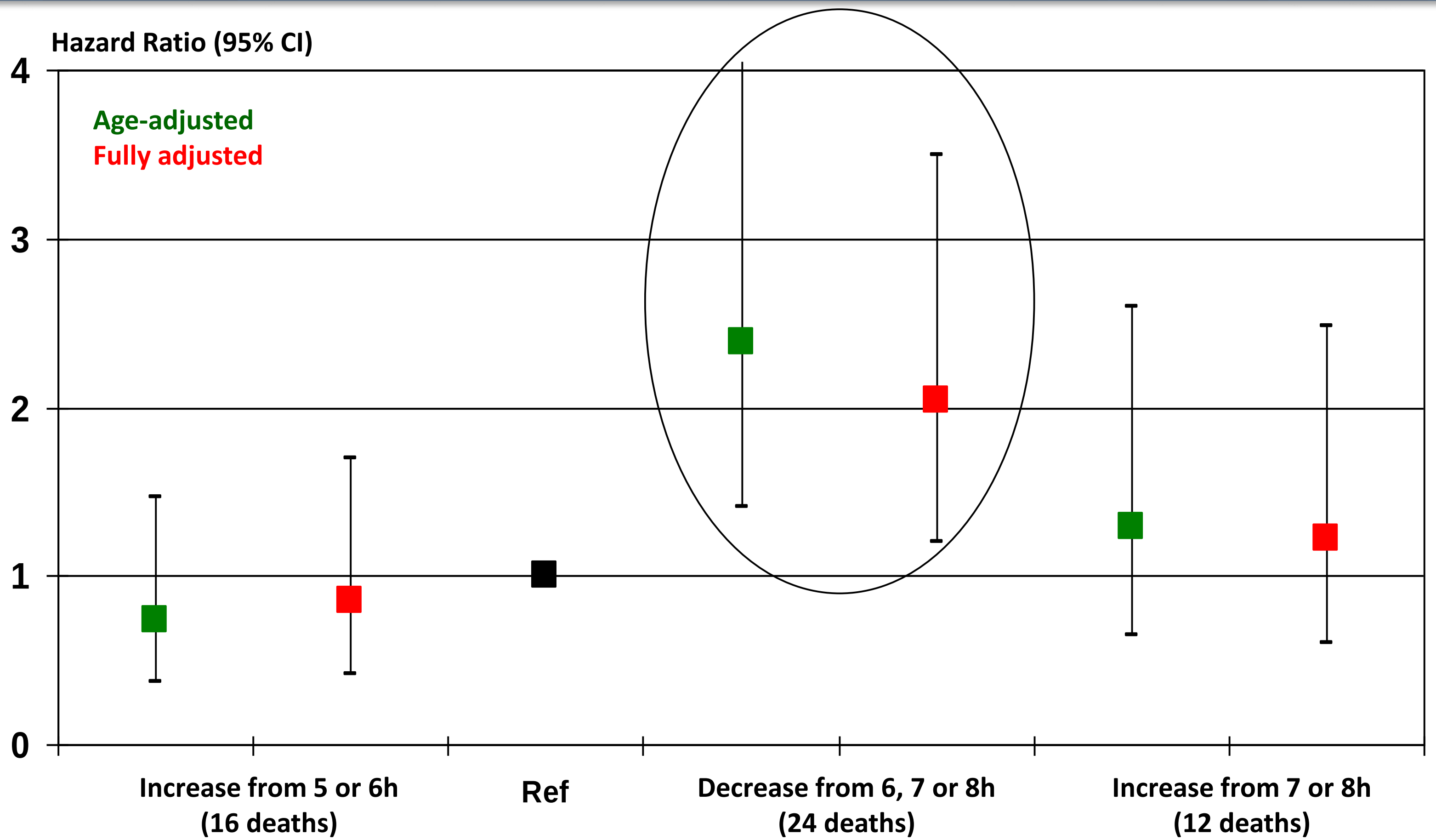
Cappuccio FP et al. Sleep 2010; 33:585-92

All-Cause mortality from Phase 3 by the change in sleep between Phase 1 and Phase 3

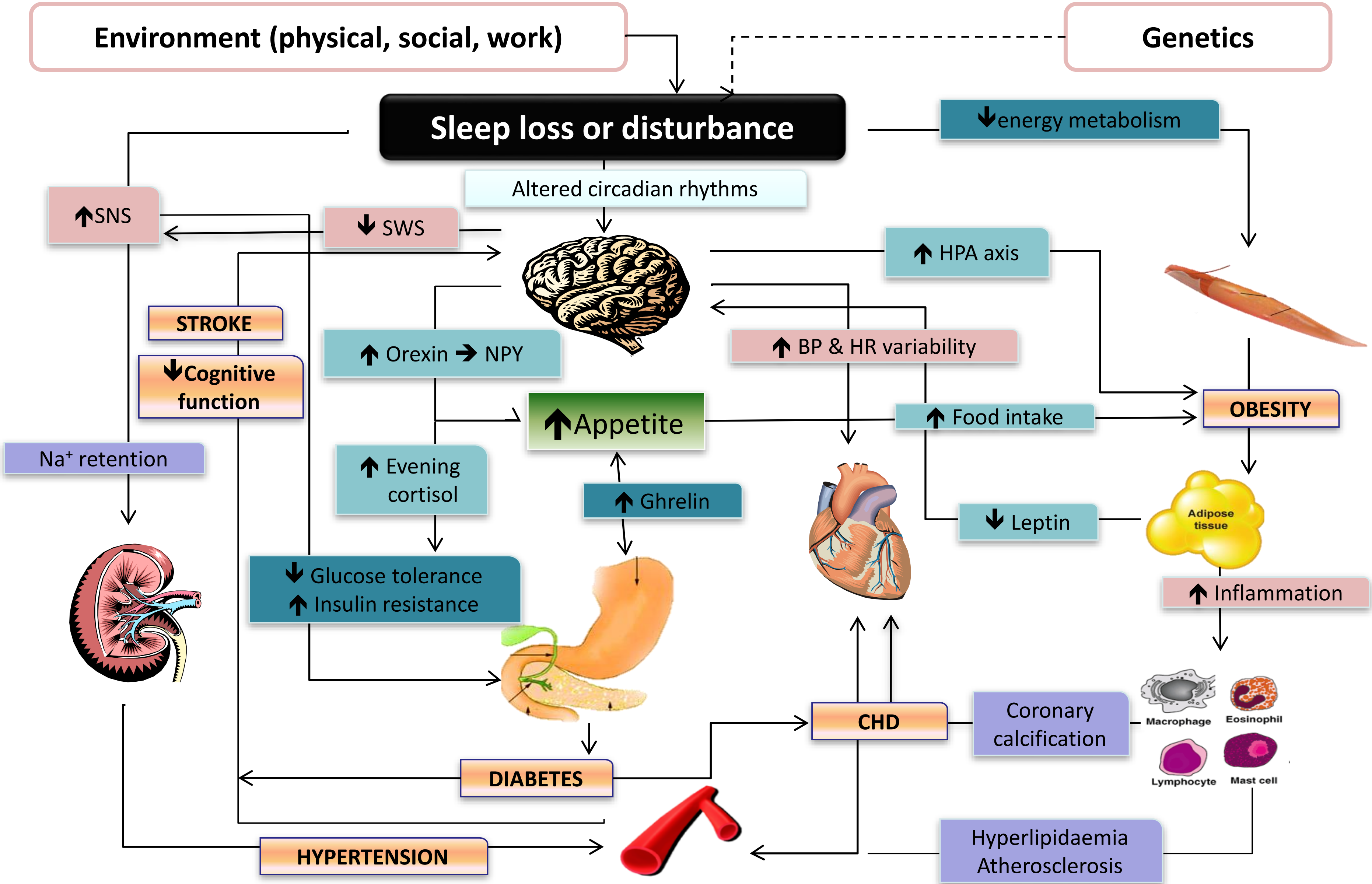


Ferrie JE et al. Sleep 2007; 30: 1659-66

CVD mortality from Phase 3 by the change in sleep between Phase 1 and Phase 3



Ferrie JE et al. Sleep 2007; 30: 1659-66



Miller MA & Cappuccio FP. J Hum Hypert 2013;27:583-8

Summary

The association between short duration of sleep and cardio-metabolic risk factors and outcomes may reflect causality as

- The effect is <u>strong</u>: large relative risk
- It is <u>consistent</u>: confirmed in different populations for several end-points
- It shows a <u>temporal sequence</u>: short sleep preceding end-points
- <u>Dose – response</u>: it consistently shows a threshold effect
- <u>Biological plausibility</u>: there are several potential mechanisms involved

Conclusions

Short sleep duration

- associated with increased risk of obesity both in adults and in children.
- prospective studies confirm a temporal sequence in infants, children and adolescents
- quantity and quality of sleep are significant predictors of type 2 diabetes
- it predicts hypertension, coronary heart disease, stroke and CVD
- affects all-cause mortality via increases in cardiovascular deaths

Plausible mechanisms exist to explain the associations (metabolic, biochemical, cellular, genetic)

Unresolved issues

- Cause, consequence or symptom?
  - Residual confounding? Reverse causality?
  - Evidence from cross-sectional and case-control designs inappropriate
- Short vs long term effects?
- Life-time trajectories?
- Time in bed vs time asleep vs naps?
- Self-report vs direct sleep assessment?
- Sleep vs phase of sleep?
- Age- and Gender-effects?
- Genetic determinants?
- Reversibility of effect?
- More research
  - (i) to understand the mechanisms by which sleep disturbances are linked to chronic conditions of affluent societies
  - (ii) to establish the reversibility of its effects

Acknowledgments

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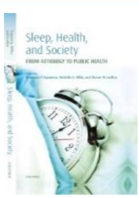

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