

ONLINE SUPPLEMENT

**Sleep Duration and Risk of Fatal and Non-fatal Stroke: a Prospective Study
and Meta-analysis**

Appendix e-1

Search strategy for the systematic review, adapted from previous systematic review ¹

We searched Ovid Medline, EMBASE (from 1980 to May 2014) and the Cochrane Library using a combination of the following key words

1. Sleep/ or sleep.mp.
2. sleep duration.mp.
3. ischemic.mp.
4. ischaemic.mp.
5. hemorrhagic.mp.
6. haemorrhagic.mp.
7. stroke.mp. or Stroke/
8. 3 or 4 or 5 or 6
9. 7 and 8
10. cerebrovascular accident.mp.
11. cerebrovascular disorders.mp. or Cerebrovascular Disorders/
12. cerebral infarction.mp. or Cerebral Infarction/
13. cerebral hemorrhage.mp. or Cerebral Hemorrhage/
14. cerebral haemorrhage.mp.
15. cardiovascular disease.mp. or Cardiovascular Diseases/
16. 10 or 11 or 12 or 13 or 14 or 15
17. 1 or 2
18. 7 or 9 or 16
19. 17 and 18

Flow chart of literature selection

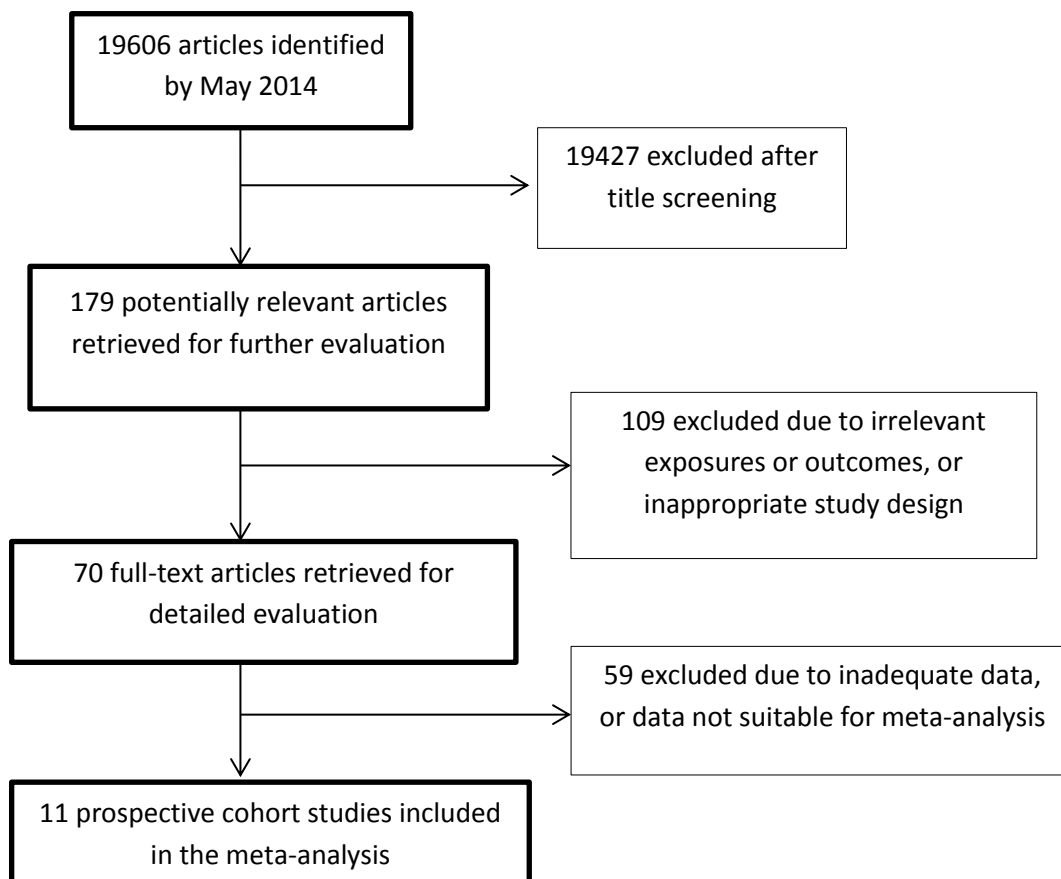


Table e-1 Hazard ratios (95% CI) of sleep duration for the risk of fatal and non-fatal stroke

		Number of events	<6h		6-8h	>8h	
			HR	95%CI	Referent	HR	95%CI
Non-fatal							
All		300					
	† Model 1		1.11	[0.84,1.47]	1.00	1.39	[1.00,1.93]
	‡ Model 2		1.10	[0.83,1.46]	1.00	1.38	[1.00,1.92]
	§ Model 3		1.11	[0.84,1.47]	1.00	1.39	[1.00,1.93]
Men		180					
	† Model 1		1.13	[0.77,1.64]	1.00	1.27	[0.83,1.94]
	‡ Model 2		1.05	[0.72,1.55]	1.00	1.27	[0.83,1.94]
	§ Model 3		1.06	[0.73,1.57]	1.00	1.24	[0.81,1.90]
Women		120					
	† Model 1		1.10	[0.73,1.68]	1.00	1.60	[0.95,2.69]
	‡ Model 2		1.16	[0.76,1.77]	1.00	1.57	[0.93,2.64]
	§ Model 3		1.14	[0.75,1.75]	1.00	1.58	[0.93,2.67]
Fatal							
All		67					
	† Model 1		1.28	[0.72,2.26]	1.00	1.81	[0.95,3.48]
	‡ Model 2		1.27	[0.71,2.26]	1.00	1.88	[0.98,3.63]
	§ Model 3		1.30	[0.73,2.32]	1.00	1.88	[0.97,3.64]
Men		32					
	† Model 1		1.01	[0.41,2.50]	1.00	0.99	[0.34,2.89]
	‡ Model 2		0.98	[0.39,2.46]	1.00	1.06	[0.36,3.13]
	§ Model 3		0.97	[0.38,2.48]	1.00	1.02	[0.34,3.05]
Women		35					
	† Model 1		1.57	[0.73,3.36]	1.00	3.07*	[1.30,7.26]
	‡ Model 2		1.48	[0.67,3.25]	1.00	3.14*	[1.31,7.49]
	§ Model 3		1.58	[0.71,3.51]	1.00	2.64*	[1.07,6.51]

*<0.05

† adjusted for age, sex.

‡ adjusted for † plus social class, education, marital status, smoking, alcohol intake, hypnotic drug use, family history of stroke.

§ adjusted for ‡ plus BMI, physical activity, depression, systolic blood pressure, diastolic blood pressure, pre-existing diabetes and myocardial infarction, cholesterol level, hypertension drug use

Table e-2 Hazard ratios (95% CI)* of sleep duration for the risk of stroke, by subgroups

Subgroups	Number	No. of events	<6h		6-8h	>8h		p for interaction
Follow up length								0.42
Follow up<31/12/2004	515	112	1	[0.62,1.62]	1	1.12	[0.65,1.95]	
Follow up>1/1/2005	9177	234	1.11	[0.81,1.53]	1	1.30	[0.89,1.91]	
Age								0.98
<63	5203	43	1.87	[0.97,3.60]	1	0.92	[0.28,3.07]	
≥63	4489	303	1.09	[0.82,1.44]	1	1.50	[1.09,2.05]	
BMI								0.77
14.4-26.1	4846	163	1.28	[0.88,1.88]	1	1.51	[0.97,2.37]	
26.1-51.6	4846	183	1.07	[0.75,1.54]	1	1.41	[0.93,2.13]	
Physical activity								0.11
Inactive	5295	230	1.18	[0.86,1.63]	1	1.64	[1.14,2.36]	
Active	4397	116	1.11	[0.70,1.74]	1	1.17	[0.67,2.04]	
Alcohol intake								0.44
0.5-5	5037	171	1.14	[0.80,1.63]	1	1.28	[0.80,2.06]	
5.5-120	4655	175	1.21	[0.83,1.77]	1	1.63	[1.08,2.44]	
Smoking status								0.75
Current	742	35	1.69	[0.72,3.96]	1	1.65	[0.63,4.30]	
Former	4241	188	1.2	[0.85,1.71]	1	1.42	[0.93,2.17]	
Never smoked	4709	123	1.04	[0.66,1.62]	1	1.43	[0.86,2.38]	
MDD								0.13
Yes	441	15	0.71	[0.20,2.60]	1	0.53	[0.06,4.88]	
No	9251	331	1.18	[0.91,1.55]	1	1.52	[1.12,2.07]	
Hypertension drug								0.49
Yes	2039	141	1.42	[0.97,2.09]	1	1.57	[0.96,2.58]	
No	7653	205	0.95	[0.67,1.37]	1	1.43	[0.97,2.12]	
Cholesterol level								0.8
2.2-6	5042	169	1.15	[0.79,1.67]	1	1.58	[1.02,2.45]	
6.1-14.4	4650	177	1.16	[0.81,1.68]	1	1.39	[0.91,2.13]	
CRP								0.2
<1	2851	73	1.24	[0.70,2.20]	1	1.59	[0.83,3.06]	
1~3	2748	109	1.70	[1.10,2.64]	1	1.62	[0.92,2.85]	
>3	1677	75	0.72	[0.40,1.31]	1	0.94	[0.44,1.99]	
Preexisting diabetes								0.2
Yes	254	12	4.96	[0.99,24.76]	1	3.20	[0.41,24.91]	
No	9438	334	1.11	[0.85,1.45]	1	1.42	[1.04,1.94]	
Preexisting MI								0.65
Yes	293	29	0.97	[0.36,2.63]	1	1.08	[0.35,3.31]	
No	9399	317	1.16	[0.88,1.52]	1	1.48	[1.08,2.03]	
Sleep well								0.01
Yes	7574	264	1.58	[1.11,2.25]	1	1.64	[1.20,2.24]	
No	1783	66	0.67	[0.40,1.14]	1	0.80	[0.11,6.04]	
Subtypes of stroke								
Ischaemic	9692	136	1.45	[0.97,2.15]	1	1.27	[0.76,2.12]	
Haemorrhagic	9692	75	0.90	[0.49,1.64]	1	1.70	[0.92,3.15]	
Unspecified	9692	230	1.08	[0.78,1.49]	1	1.45	[1.00,2.11]	

* Adjusted for age, sex, social class, education, marital status, smoking, alcohol intake, hypnotic drug use, family history of stroke. BMI: Body Mass Index; MI: Myocardial Infarction.

Table e-3 Summary of studies included in the meta-analysis

Author (Year)	Sex	Country	age at baseline	Events/ Participants	Follow up(years)	Sleep category	Outcome	Adjusted variables
Amagai (2004) ²	Both	Japan	40-69	63/11,325	8.2	<6h/≥9h	fatal	Age, BMI, education, marital status, smoking, alcohol consumption, SBP, total cholesterol
Chen (2008) ³	Women	USA	50-79	1166/93,175	7.5	≤5h/≥10h	fatal+non-fatal	Age, race, socio-economic status, depression, smoking, exercise, hormone replacement, previous CVD, diabetes, hypertension, BMI, high cholesterol
Hamazaki (2011) ⁴	Men	Japan	35-54	30/2282	14.0	<6h/≥8h	fatal+non-fatal	Age, type of job, working hours, mental workload, body mass index, SBP, HbA1c, total cholesterol, current smoking habit, drinking habit, leisure– time physical activity , medication for hypertension and diabetes, hypercholesterolemia
Ikehara (2009) ⁵	Both	Japan	40-79	1964/98,634	14.3	≤4h/>10h	fatal	Age,BMI, history of hypertension, diabetes, alcohol consumption, smoking, education, hours of exercise and walking, employment, perceived mental stress, depression, frequency of fresh fish intake
Kakizaki (2013) ⁶	Both	Japan	40-79	1165/49,256	10.8	≤6h/≥10h	fatal	Age, sex, total caloric intake, BMI, marital status, education, job status, history of myocardial infarction, cancer, stroke, hypertension and diabetes mellitus, smoking status, alcohol drinking, time spent walking, perceived mental stress, self-rated health, physical function
Kim (2013) ⁷	Both	USA	45-75	1259/135,685	12.9	≤5h/≥9h	fatal	Age, ethnicity, education, marital status, history of hypertension or diabetes at enrollment, alcohol consumption, energy intake, BMI, physical activity, hours spent daily watching television, smoking history

Kronholm (2011) ⁸	Both	Finland	25-59	2182/22484	35.0	≤5h/≥10h	fatal+non-fatal	Age, smoking, BMI, SBP, total cholesterol
Leng (2014)	Both	UK	mean: 61.6	346/9692	9.5	<6h/>8h	fatal+non-fatal	Age, sex, social class, education, marital status, smoking, alcohol intake, family history of stroke, BMI, physical activity, depression, hypnotic drug use, systolic blood pressure, pre-existing diabetes, MI, cholesterol level, hypertension drug use
Pan (2014) ⁹	Both	Singapore	45-74	1381/63257	14.7	≤5h/≥9h	fatal	Age, year of recruitment, sex, dialect group, education, BMI, alcohol intake, smoking status, physical activity, daily intake of total energy, vegetables, fruits, dietary fiber, and polyunsaturated fatty acids, history of hypertension, diabetes, CHD, stroke, and cancer
Qureshi (1997) ¹⁰	Both	USA	31+	322/7,844	10.0	<6h/>8h	fatal+non-fatal	Age, sex, race, BMI, education, smoking, SBP, cholesterol, diabetes
Von Ruesten (2012) ¹¹	Both	Germany	35-65	169/23,620	7.8	<6h/≥9h	fatal+non-fatal	Age, sex, sleeping disorders, alcohol intake, smoking status, walking, cycling, sports, employment status, education, BMI, waist-to-hip ratio, prevalent hypertension, history of high blood lipid levels, consumption of caffeinated beverages, satisfaction with life, satisfaction with health, antidepressants use
Westerlund (2013) ¹²	Both	Sweden	median: 52.8	1685/41,192	13.2	≤5h/≥8h	fatal+non-fatal	Age, sex, education, employment status, smoking, alcohol, snoring, work schedule, depressive symptoms, self-rated health, physical activity, BMI, diabetes, lipid disturbance, hypertension

BMI: Body Mass Index; CHD: Coronary Heart Disease; CVD: Cardiovascular Disease; SBP: Systolic Blood Pressure

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