The association between sleep duration and mortality: a review article

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Abstract

Objective:

The aim of this review is to explore the association between sleep duration and all-cause mortality, and to investigate the associated risk with both short and long duration of sleep.

Research design and method:

A systemic review of publications performed using PUBMED, Google scholar, and manual search without language restrictions using keywords such as "sleep", "sleep duration", "mortality", "insomnia", and others.

Results:

Weselected15 cohort studies and two meta-analysis study that studied the association between sleep duration and all-cause and specific cause mortality. Findings from these studies showed an association between long and short sleeping hours in both men and women and mortality compared with who sleep between 7-8 hours daily. The consistent findings led us to draw U-shape relationship between sleep duration and all-cause mortality with the lowest point at 7-8 hours.

Conclusion:

Short and long sleep duration are both independent and significant factors of mortality.

Keywords: Sleep, mortality, Sleep disorders, Review.

I. Introduction:

Sleep is a primitive behavior that all people share. The mechanism of sleep and its effects are still ambiguous. Quality and quantity of sleep are affected by several factors including psychological, behavioral, cultural, social, physiological, and environmental determinants¹. Sleep duration is considered a lifestyle factor as

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physical activity or smoking. Meanwhile, people sleep 1 $\frac{1}{2}$ hour less than people in the last century. Secular trends are associated with changes that occurred with modern society that require more hours of work, shift-work, and availability of commodities(Broman et al., 1996)².

The amount of sleep hours necessary for a human welfare is still unclear. Persons who sleep 6 to 7 hours may complain from short sleeping time, which is actually the current average of population. National Sleep Foundation and most sleep professionals recommend that an adult should obtain 8 hours of sleep per night^{3,4}. It has been estimated that one in five adults has sleep problems and inadequate sleep patterns that in some modern societies is not recognized as a problem⁵. Many studies have shown that sleep duration is a health determinant. Short sleepers who sleep less than 7 hours per night have higher risk of developing health problems, including diabetes and coronary heart disease, than others who sleep 7 to 8 hours per night are at higher risk for a number of adverse health conditions, including endocrine and immune functions impairment, coronary heart disease, and diabetes, compared with individuals reporting 7 or 8 h of sleep per night⁵⁻⁷. Moreover, other prospective studies have shown the relationship between short sleep and mortality⁽⁸⁻¹¹⁾. On the other hand, long sleepers who sleep more than 9 hours per night are at risk of morbidities and mortalities compared with average sleepers^{12,13}. The purpose of this study is to assess the association between sleep duration and all-cause mortality, and to investigate the associated risk with both short and long duration of sleep.

II. Materials and methods

Literature search:

We developed a strategy to select studies that made longitudinal association between sleep duration and mortality. A systemic review of publications was performed using PUBMED, Google scholar, and manual search without language restrictions. We used keywords such as "sleep", "sleep duration", "mortality", "insomnia", and "death". Furthermore, We searched for more articles using the reference lists of original and reviewed articles. No language restrictions were applied in the search process.

Inclusion criteria:

About 360 articles were found that dealt with the relationship between sleep duration and all or specific cause mortality. Only 17 studies fulfilled the criteria of this literature review study, which are cohort study, or metaanalysis of cohort studies that have enough sample size and used relative risk (RR) or hazard ratio (HR) for outcome measurements. We included the most detailed study if multiple reports were published from the same study.

III. Results:

In this literature review, we identified 15 cohort studies and two meta-analysis study that studied the association between sleep duration and all-cause and specific cause mortality. Finding from these studies was an association between long or short sleeping hours in both men and women and mortality compared with who sleep

between 7-8 hours daily. The consistent findings led us to draw U-shape relationship between sleep duration and allcause mortality. The evidence to draw a conclusion regarding the specific mechanism or association with a specific risk factor was unclear. However, the risk of mortality from cardiovascular disease in short sleeper men compared with average sleepers was high, and the risk of death from cardiovascular and cancer mortality in both men and women was also high. Summary of the included articles is presented in the table below.

Article	Sample Size & Gender	Number of Deaths	Main finding(s)
(Ferrie et al.,2007) ¹¹	Men & Women 9781	566	U-shaped associations were found between sleep durations and all-cause mortality. A decrease in sleep duration was associated with cardiovascular mortality; hazard ratio was 2.4 (1.4–4.1 95% Confidence Interval). On the other hand, all cause mortality was associated with increasing sleep duration; hazard ratio was 2.1 (1.4–3.1 95% confidence interval). Adjustment was done for the Socio-economic factors, morbidity, and behaviors.
(Lan et al., 2007) ⁹	Men: 1,748 Women: 1,331	Men: 816 Women: 522	Higher mortality was observed in men who sleep 10 hours or more; hazard ratio was 1.68 (1.12–2.53 95% Confidence Interval). In women who sleep between 9-10 hours per night, the hazard ratio = 1.76 (1.08–2.88 95% Confidence Interval), and who sleep more than 10 hours, hazard ratio = 1.84 and (1.11–3.05 95% Confidence Interval).
(Hublin et al., 2007) ¹⁰	Men: 9,529 Women: 10,265	Men: 1850 Women: 1850	Higher risk of mortality was observed for short sleep duration. In men, hazard ratio= 1.26 ($1.12-1.42$ 95% Confidence Interval), and in women, hazard ratio = 1.21 ($1.05-1.39$ 95% Confidence Interval). For long sleep in men, hazard ratio= 1.25(1.09-1.43 95% Confidence Interval). In women hazard ratio= 1.17 ($1.02-1.35$ 95% Confidence Interval). After adjusting for snoring, results didn't change. The strongest effect of sleep duration on mortality was viewed in young age group who are short sleepers with hazard ratio= 1.62
(Kojima et al., 2000) ¹⁴	Men:	Men:	Longer and shorter sleepers compared with average time of sleep 7-8 hours had increased risk of all-cause mortality. In

	2,437 Women: 2,884	147 Women: 109	males, relative risk for who sleep more than 10 hours=1.94 ($1.01-3.76$ 95% Confidence Interval), and for who sleep less than 7 hours RR=1.90 ($1.10-3.29$ 95% Confidence Interval). In females, for who sleep less than 7 hours RR= 0.92 ($0.53-1.62$ 95% Confidence Interval), and for women who sleep more than 10 hours RR= 0.42 ($0.06-3.02$ 95% Confidence Interval). Males who sleep easily showed lower mortality risk compared to who has difficulty sleeping RR= 0.70 . Female who are on sleeping pills had an elevated risk RR= 1.89 . After adjustments for confounders the results did not change.
(Patel et al., 2004) ¹³	Women 82,969	5,409	The risk of mortality was lowest among nurses who sleep 7 hours per night. After adjusting for age, alcohol, smoking, exercise, obesity, snoring, depression, history of cancer and cardiovascular disease, increased risk of death was associated with sleeping less than 6 hours per night. Sleeping less than 5 hours had RR= $1.15 (1.02-1.29 95\%$ Confidence Interval), and for 6 hours RR= $1.01 (0.94-1.08 95\%$ CI), for 7 hours RR= 1.00 , for 8 hours RR= $1.12 (1.05-1.20 95\%$ CI), and RR for 9 or more hours = $1.42 (1.27-1.58 95\%$ CI).
(Amagai et al., 2004) ¹⁵	Men: 4,419 Women: 6,906	Men: 289 Women: 206	After making adjustment for age, blood pressure, body mass index (BMI), alcohol, smoking, serum cholesterol, and education, the hazard ratio of all-cause mortality for males who sleep less than 6 hours was 2.4 (1.3- 4.2 95% CI), and for who sleep 9 hours or longer was 1.1 (0.8-1.6 95% CI). In females who sleep less than 6 hours hazard ratio= 0.7 (0.2-2.3 95% CI), and for who sleep more than 9 hours 1.5 (1.0-2.4 95% CI). All results are relative to who sleep 7-7.9 hours.
(Gale et al., 1998) ¹⁶	Men & Women 1299	1158	In whole study samples, increased risk of mortality was associated with longer time of sleeping. After adjusting for age, sex, morbidities, and other risk factors, people who sleep 12 hours or more had RR= 1.7 (1.2 - 2.5 95% CI) compared with those who sleep for 9 hours. The lowest risk of mortality was in people who sleep 8 hours per night RR= 0.8 (0.7 to 1.0 95% CI).

(Ikehara et al., 2009) ¹⁷	Men: 41,489 Women: 57,145	Men: 8,548 Women: 5,992	Sleeping 4 hours per night was associated with increase risk of mortality compared with 7 hours sleeping. Common causes were coronary heart disease for women and non-cardiovascular, non-cancer causes and all causes in both sexes. The hazard ratio in both men and women who sleep 4 hours per night was 1.28 (1.01-1.62 95% CI in men) and (1.04-1.59 in women) compared with 7 hours sleeping. In men who sleep 10 hours or more per night the hazard ratio was 1.40 (1.27-1.55 95% CI), and 1.55(1.38-1.75 95% CI) for women.
(Stone et al., 2009) ¹⁸	Women 8,101	1,922	Women who nap daily were 44% more likely to die from any cause (1.23-1.67 95% CI), The risk of death from cardiovascular disease was 58% (1.25-2.00 95%CI), and 59% risk of mortality from non cardiovascular causes (1.24-2.03 95% CI) than who did not nap daily. This relationship remained significant in women with no morbidities. Women who sleep 9 to 10 hours daily were at greater risk of mortality
(Cappuccio et al., 2010) ¹⁹	Men & Women 1,382,999	112,556	Short sleep duration was associated with greater risk of mortality RR= 1.12 (1.06- 1.18 95% CI). Long sleep duration was also associated with greater risk of mortality RR= 1.30 (1.22- 1.38 95% CI).
(Gangwisch et al., 2006) ²⁰	Men: 5,806 Women: 3,983	Men: 273 Women: 1,604	In the age groups (32-59), and (59-86) who reported sleeping 5 hours or less RR=1.27 (1.07-1.52 95% CI), and RR= 1.28 (1.01-1.62 95% CI) respectively compared with sleeping 7 hours daily. In those who reported sleeping more than 9 hours the risk of death= 1.04 (0.66-1.63 95% CI) in age group (32-59), and in age group (59-86), RR= 1.36 (1.17-1.59 95% CI)
(Burazeri et al., 2003) ²¹	Men: 716 Women:	Men: 198 Women:	Men who sleep (>8h) had an elevated risk of all-cause mortality (adjusted hazard ratio, 2.1(95% CI 1.2-3.7), and a stronger association with cardiovascular mortality (hazard ratio, 2.9; 95% CI, 1.2-7.1). No association in women,

	915	205	although those who slept 6-8 h seemed to have the lowest risk.
(Heslop et al., 2002) ²²	Men: 6,022 Women: 1,006	Men: 2,303 Women: 262	The risk of death in men who sleep less than 7 hours was 1.00 (0.89-1.12 95% CI), and 0.98 (0.7-1.38 95% CI) in women compared with who sleep 7 to 8 hours daily. The risk of death in men who sleep more than 8 hours was 0.81 (0.68-0.97 95% CI), and 1.20 (0.71-2.31 95% CI) in women.
(Yoo et al., 2002) ²³	Men & Women 35,692	Not reported	The hazard ratios for sleep durations and mortality show U- shape relation with lowest point at 7-8 hours sleeping. HR for people who sleep less than 5 hours was $1.21 (1.03-1.41 95\%$ CI), and for those who sleep 10 hours or more HR= $1.36 (1.07-$ 1.72 95 % CI). Risk of mortality because of cardiovascular disease for people who sleep 5 hours or less HR= $1.40 (1.02-$ 1.93 95% CI). The risk of death from respiratory diseases was shown in both long and short sleepers.
(Wang et al, 2020) ²⁴	Men: 40,087 Women: 12512	1778	Compared to normal sleeping hours, increased risk of all cause mortality with decreasing pattern in sleeping hours, (HR, 1.34; 95% CI, 1.15-1.57). Low sleeping pattern was associated with trisk of CVEs (HR, 1.47; 95% CI, 1.05-2.05) and death (HR, 1.50; 95% CI, 1.07-2.10). They found sleep duration with lower or unstable patterns had a significant association with increased risk of subsequent first CVEs and all-cause mortality
(Pan et al, 2014) ²⁵	Men & Women 63257	1381	Multivariate Cox regression analysis showed increased risk with both long and short sleepers. For <= 5 hours, HR= 1.25 (1.05-1.50), for >=9 hours HR= (1.54; 1.16-2.03). History of hypertension increased the HR for long and short sleepers. With short (1.54; 1.16-2.03) and long durations of sleep (1.95; 1.48-2.57)
(Li et al.,	Men &	43,021	Meta-analysis of 14 studies concerned with cancer mortality and sleeping hours. Relative risk of cancer mortality in short

$2019)^{26}$	Women	sleepers < 7 hours was (RR= 1.02; 0.99-1.05), 4-5 hours of
	866,877	sleep (RR=1.08; 1.02-1.13, and for > 8 hours was (RR= 1.05; 1.02-1.08)

Table 1: Included studies with sample size, number of deaths, and main findings

In table 2, RR and HR of s	hort sleep are listed for the	studies above and for long	sleep are listed in table 3.
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Study (Ferrie et al.,	Sleep Duration in Hours	Relative Risk (RR) or Hazard Ratio (HR); (95%, CI) HR= 2.4 (1.4–	Study (Ikehara et al.,	Sleep Duration in Hours ≤ 4	Relative Risk (RR) or Hazard Ratio (HR) and (95%, CI) Men HR=1.28
2007) ¹¹		4.1)	(include of all., 2009) ¹⁷		(1.01-1.62) Women HR=1.28 (1.04-1.59)
(Hublin et al., 2007) ¹⁰	< 7	Men HR= 1.26 (1.12–1.42) Women HR=1.21 (1.05–1.39)	(Cappuccio et al., 2010) ¹⁹	≤5	RR= 1.12 (1.06- 1.18)
(Kojima et al., 2000) ¹⁴	< 7	Men RR=1.90 (1.10–3.29) Women RR=0.92 (0.53–1.62)	(Gangwisch et al., 2006) ²⁰	≤5	RR=1.28 (1.01- 1.62)
(Patel et al., 2004) ¹³	≤ 6 ≤ 5	RR= 1.15 ((1.02– 1.29) RR=1.01 (0.94-1.08)	(Heslop et al., 2002) ²²	≤5	Men HR=1.00 (0.89-1.12) Women HR= 0.98 (0.7- 1.38)
(Amagai et al., 2004) ¹⁵	≤ 6	Men HR=2.4 (1.3- 4.2) Women HR=0.7 (0.2- 2.3)	(Yoo et al., 2002) ²³	≤5	HR=1.21 (1.03- 1.41)

(Wang et al,	<7	HR=1.50 (1.07-	(Pan et al., 2014) ²⁵	≤ 5	HR= 1.25 (1.05-
2020) ²⁴		2.10)			1.50)

 Table 2 Short sleep outcomes represented with Relative Risk (RR) or Hazard Ratio (HR) and 95% confidence

 interval

Study	Sleep Duration in Hours	Relative Risk or Hazard Ratio (HR) (95%, CI)	Study	Sleep Duration in Hours	Relative Risk or Hazard Ratio (HR) (95%, CI)
(Ferrie et al., 2007) ¹¹	> 9	HR= 2.1 (1.4– 3.1)	(Ikehara et al., 2009) ¹⁷	> 10	Men HR=1.40 (1.27- 1.55) Women HR=1.55 (1.38- 1.75)
(Lan et al., 2007) ⁹	9 -10 >10	HR= 1.76 (1.08–2.88) HR= 1.84 (1.12–2.53)	(Cappuccio et al., 2010) ¹⁹	>9	RR= 1.30 (1.22-1.38)
(Kojima et al., 2000) ¹⁴	>10	Men RR=1.94 (1.01–3.76) Women RR=0.42 (0.06–3.02)	(Gangwisch et al., 2006) ²⁰	> 9	RR=1.04 (0.66-1.63)
(Patel et al., 2004) ¹³	>9	RR=1.42 1.27-1.58	(Stone et al., 2009) ¹⁸	>9	Women RR=1.59 (1.24-2.03)
(Amagai et al., 2004) ¹⁵	> 9	Men HR= 1.1 (0.8-1.6) Women	(Heslop et al., 2002) ²²	> 8	Men HR=0.81 (0.68- 0.97) Women HR=1.20 (0.71-

		HR=1.5			2.31)
		(1.0-2.4)			
(Gale et al.,	>12	RR= 1.7	(Yoo et al,	> 10	HR=1.36 (1.07-
1998)			2002) ²³		1.72)
(Li et al.,	>8	RR= 1.05	(Pan et al.,	>9	HR= 1.54
2019)		(1.02-1.08)	2014) ²⁵		(1.16-2.03)

 Table 3: Long sleep outcomes represented with Relative Risk (RR) or Hazard Ratio (HR) and 95%

 confidence interval

IV. Discussion:

People who report short sleeping hours (≤ 4 hours, ≤ 5 hours, ≤ 6 hours, or ≤ 7 hours) were at high risk ok of mortality. Fourteen studies reported RR and HR with 95% CI demonstrated the association between all-cause mortality and short sleep. Thirteen of them indicated the increased risk of mortality. This suggestion of high risk of mortality in short sleeper is independent from other risk factors for disease and stress. Data from some studies indicated that the relationship between mortality and sleep duration is because individual differences among participants. For example, individuals who report short sleeping were having lower overall health, or have been diagnosed with some medical conditions including depression than average sleepers ^(9,10,11,13,27,28).

Sleep difficulties have direct effect on mortality. They can be caused by some sleep disorders, increasing age, or working more hours than average people.People who sleep less than average people were found at risk of increasing weight and Type 2 diabetes mellitus because of adverse effect on metabolism of glucose and regulation of appetite that is driven by increasing level of leptin and ghrelin ^{29,30}. The increase in cortisol level and abnormal secretion of growth hormone were found in short sleepers that might explain occurrence of hypertension and cardiovascular disease in short sleepers^(20,30,31).

Fourteen studies reported RR and HR with 95% CI demonstrate the association between all-cause mortality and long sleep duration. Ten of them indicated the increased risk of mortality.Grandner et al. ³² hypothesized number of mechanisms that might be associated with increasing mortality in long sleepers: (I) negative heath outcome because of increased amount of sleep fragmentation¹⁵. (II) Disturbance of cytokine level which showed mortality effect. (III) Because of long sleep, shortness of physiological challenge may occur such as exposure to mild stressor or lack of physical activity³⁴. (IV) Disturbance in ratio between daylight and night or photoperiod has shown an adverse effect on other species such as chickens and has been associated with increasing mortality. All of these hypotheses go together with the physiological changes in normal aging and lead to premature death in both men and women ^(1,9,26).

The results are inherited of the studies we derived data from and multiple limitations were obtained in these studies including using of a single survey to assess sleep duration, and methods of controlling confounding such as morbidities. Further research is needed to study the association between sleep duration and specific-cause and all-cause mortality. Additional researches are needed to assess the mechanisms underlying the associations.

V. Conclusion:

Sleep duration is still an unrecognized public health problem in developed communities. We can conclude that long and short sleep durations independent risk factors of mortality. The minimum risk is shown in people who sleep 7 to 8 hours per night.

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